



women & children's  
health research institute



**2019** **RESEARCH DAY**  
**ABSTRACT BOOK**

**#wchriRD2019**



## THANK YOU

These amazing research projects wouldn't be possible without the continued partnership of the University of Alberta, Alberta Health Services, the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Through the support of our partners, we are able to gather some of the most brilliant minds in research together to collaborate and share ideas that will make the future of both women and children brighter.



# ALPHABETICAL LIST OF PRESENTERS

Name	#	Time	Room
Afsharipour, Babak	138	9-10	Ballroom
Afzalzada-Ahrari, Malema	99	9-10	Ballroom
Ahmad, Attila	196	1:45-2:45	Ballroom
AL Riyami, Hilal	64	all day	Foyer
Alam, Abrar	23	10:15-11:45	Chancellor Room
Almubarak, Asra	148	9-10	Ballroom
Amjad, Sana	91	all day	Foyer
Amodu, Oluwakemi	113	9-10	Ballroom
Anjum, Bushra	224	1:45-2:45	Ballroom
Antunes Lopes, Nayara	112	9-10	Ballroom
Aslesh, Tejal	219	1:45-2:45	Ballroom
Assi, Ali	73	all day	Foyer
Babolmorad, Ghazal	119	9-10	Ballroom
Babyn, Katherine	175	1:45-2:45	Ballroom
Baddam, Pranidhi	17	10:15-11:45	Consulate Room
Baqays, Abdulsalam	134	9-10	Ballroom
Bedi, Iqwak	108	9-10	Ballroom
Beggs, Megan	24	10:15-11:45	Chancellor Room
Beigh, Mirza	125	9-10	Ballroom
Bennett, Jessica	120	9-10	Ballroom
Bhaloo, Zafira	62	3-4:30	Chairman Room
Biancardi, Vivian	232	1:45-2:45	Ballroom
Bianchi Lemieszek, Marina	103	9-10	Ballroom
Bilyk, Lena	26	10:15-11:45	Chairman Room
Bird, Melissa	164	9-10	Ballroom
Bitar, Eyad	57	3-4:30	Chairman Room
Boparai, Rakhbeer	12	10:15-11:45	Leduc Room
Boyd, Kassi	141	9-10	Ballroom
Bui, An	215	1:45-2:45	Ballroom
Burnett, Mervin	63	all day	Foyer
Buschmann, Rob	69	all day	Foyer
Campbell, Alyson	166	1:45-2:45	Ballroom
Cao, Amanda	122	9-10	Ballroom
Carla, Sosa	156	9-10	Ballroom
Catena, Gina	58	3-4:30	Chairman Room
Chan, Andrew	20	10:15-11:45	Chancellor Room
Chan, Jackie	206	1:45-2:45	Ballroom
Chen, Huachen	45	3-4:30	Consulate Room
Chen, Lu Kun	218	1:45-2:45	Ballroom
Cheung, Daphne	107	9-10	Ballroom
Choi, Won-Shik (Daniel)	179	1:45-2:45	Ballroom
Choudhury, Bipasha	223	1:45-2:45	Ballroom
Chow, Braden	101	9-10	Ballroom
Crosley, Powel	86	all day	Foyer
Cunningham, Chentel	167	1:45-2:45	Ballroom
Desai, Vidhi	117	9-10	Ballroom
Deschenes, Sadie	132	9-10	Ballroom
Dicipulo, Renee	153	9-10	Ballroom

Name	#	Time	Room
Dijk, Stephanie	36	3-4:30	Turner Valley Room
Durber, Chelsea	2	10:15-11:45	Turner Valley Room
Dzierlega, Kasia	150	9-10	Ballroom
Eaton, Andrea	227	1:45-2:45	Ballroom
Elawad, Dalia	163	9-10	Ballroom
Elliot, Victoria	48	3-4:30	Consulate Room
Elyasi, Maryam	168	1:45-2:45	Ballroom
Evanchuk, Jenna	39	3-4:30	Leduc Room
Fakhr, Yuliya	118	9-10	Ballroom
Fan, Lu'an	142	9-10	Ballroom
Fellus, Sapir	187	1:45-2:45	Ballroom
Ferdinands, Alexa	31	3-4:30	Turner Valley Room
Firouzeh, Pegah	210	1:45-2:45	Ballroom
Flynn, Rachel	170	1:45-2:45	Ballroom
Fox, Sabrina	155	9-10	Ballroom
Ganguly, Esha	7	10:15-11:45	Leduc Room
Gates, Allison	78	all day	Foyer
Gates, Michelle	80	all day	Foyer
Ghoman, Simran	202	1:45-2:45	Ballroom
Giffin, Nick	60	3-4:30	Chairman Room
Githaka, John Maringa	46	3-4:30	Consulate Room
Godziuk, Devyn	216	1:45-2:45	Ballroom
Golden-Plotnik, Stevi	81	all day	Foyer
Goodkey, Kara	217	1:45-2:45	Ballroom
Goonasekera, Michelle	85	all day	Foyer
Greenwell, Amanda	194	1:45-2:45	Ballroom
Ha, Christine	102	9-10	Ballroom
Hai, Tasmia	212	1:45-2:45	Ballroom
Han, Angela	123	9-10	Ballroom
Harake, Danielle	197	1:45-2:45	Ballroom
Hartling, Lisa	83	all day	Foyer
Heath, Devon	43	3-4:30	Consulate Room
Henneberry, Molly	111	9-10	Ballroom
Herzog, Jens	149	9-10	Ballroom
Hoffman, Janlyn	8	10:15-11:45	Leduc Room
Holody, Claudia	38	3-4:30	Leduc Room
Holt, Chris	22	10:15-11:45	Chancellor Room
Huang, Yiqing	221	1:45-2:45	Ballroom
Huie, Michelle	59	3-4:30	Chairman Room
Hula, Natalia	10	10:15-11:45	Leduc Room
Hurd, Caitlin	21	10:15-11:45	Chancellor Room
Jamieson, Lockhart	27	10:15-11:45	Chairman Room
Janes, Tara	88	all day	Foyer
Johnson, Peter Anto	16	10:15-11:45	Consulate Room
Johnson, Sarah	211	1:45-2:45	Ballroom
Kang, Jimmy	183	1:45-2:45	Ballroom
Kaur, Amanpreet	195	1:45-2:45	Ballroom
Kebbe, Maryam	228	1:45-2:45	Ballroom

# ALPHABETICAL LIST OF PRESENTERS

Name	#	Time	Room
Kennedy, Josh	140	9-10	Ballroom
Keshavarz, Hedieh	25	10:15-11:45	Chairman Room
Khetarpal, Nitya	105	9-10	Ballroom
Khodaei, Mahdiah	51	3-4:30	Chancellor Room
Kibalnyk, Yana	220	1:45-2:45	Ballroom
Kim, Chan	191	1:45-2:45	Ballroom
Kimber, Miranda	40	3-4:30	Leduc Room
Knisley, Lisa	98	9-10	Ballroom
Krysa, Jacqueline	89	all day	Foyer
Labban, Wasim	214	1:45-2:45	Ballroom
Ladak, Zeenat	54	3-4:30	Chancellor Room
Landry, Takaaki	121	9-10	Ballroom
Latif, Asna	190	1:45-2:45	Ballroom
Lau, Stuart	96	all day	Foyer
Leclair, Guillaume	205	1:45-2:45	Ballroom
Lee, Laura	176	1:45-2:45	Ballroom
Li, Jia Hang	109	9-10	Ballroom
Li, Nicholas	104	9-10	Ballroom
Li, Yutong (Jessica)	222	1:45-2:45	Ballroom
Lim, Kenji Rowel	50	3-4:30	Chancellor Room
Lin, Lily	198	1:45-2:45	Ballroom
Lopresti, Sabrina	143	9-10	Ballroom
Louie-Poon, Samantha	165	9-10	Ballroom
Luong, Deandra	130	9-10	Ballroom
Maadi, Hamid	44	3-4:30	Consulate Room
MacDonald, Tate	53	3-4:30	Chancellor Room
Mackie, Andrew	66	all day	Foyer
Mah, Richard	115	9-10	Ballroom
Maki, Claudia	97	9-10	Ballroom
Mander, Inderdeep	34	3-4:30	Turner Valley Room
Mangat, Avneet	200	1:45-2:45	Ballroom
Manz, Joren	174	1:45-2:45	Ballroom
Marani, Safia	95	all day	Foyer
Mason, Alleson	135	9-10	Ballroom
Matta, Mirna	94	all day	Foyer
Meah, Victoria	29	10:15-11:45	Chairman Room
Meherali, Salima	79	all day	Foyer
Mella, Allison	136	9-10	Ballroom
Mevawala, Amynah	173	1:45-2:45	Ballroom
Misita, Dragana	93	all day	Foyer
Mitchell, Nikki	41	3-4:30	Leduc Room
Mohseni, Mahsa	192	1:45-2:45	Ballroom
Moray, Amol	90	all day	Foyer
Morin, Estelle	225	1:45-2:45	Ballroom
Morin, Sarah	160	9-10	Ballroom
Morris, Heather	3	10:15-11:45	Turner Valley Room
Morrison, Ellen	82	all day	Foyer
Mustofa, Jannatul	201	1:45-2:45	Ballroom

Name	#	Time	Room
Myre, Maxine	47	3-4:30	Consulate Room
Nguyen, Jasmine	182	1:45-2:45	Ballroom
Nguyen, Kim-Cuong	208	1:45-2:45	Ballroom
Ngwezi, Deliwe	92	all day	Foyer
Nie, Chunpeng	203	1:45-2:45	Ballroom
Nielsen, Charlene	49	3-4:30	Chancellor Room
Noble, Ronan	186	1:45-2:45	Ballroom
Novak, Chris	56	3-4:30	Chairman Room
Obiakor, Chinwe Vivien	33	3-4:30	Turner Valley Room
Olugbuyi, Yomi	199	1:45-2:45	Ballroom
O'Neill, Marcus	76	all day	Foyer
O'Reilly, Amanda	172	1:45-2:45	Ballroom
Orsso, Camila	158	9-10	Ballroom
Pagee, Abbey	37	3-4:30	Leduc Room
Pajkic, Andrea	137	9-10	Ballroom
Pajunen, Kiera	65	all day	Foyer
Palichuk, Airlie	4	10:15-11:45	Turner Valley Room
Palmer, Sophie	188	1:45-2:45	Ballroom
Pandya, Vrajesh	30	10:15-11:45	Chairman Room
Panigrahi, Rashmi	178	1:45-2:45	Ballroom
Pasha, Mazhar	110	9-10	Ballroom
Patel, Siddhi	133	9-10	Ballroom
Patricny, Nicol	6	10:15-11:45	Turner Valley Room
Petrova, Alexandra	74	all day	Foyer
Pham, Thanh-Tu	146	9-10	Ballroom
Pherwani, Simran	127	9-10	Ballroom
Plesuk, Tabatha	84	all day	Foyer
Punjani, Neelam	5	10:15-11:45	Turner Valley Room
Qureshi, Mosarrat	72	all day	Foyer
Raza, Sarah	144	9-10	Ballroom
Reklow, Robert	18	10:15-11:45	Consulate Room
Richter, Solina	87	all day	Foyer
Roshmi, Rohini Roy	154	9-10	Ballroom
Roth, Daniela	14	10:15-11:45	Consulate Room
Ruel, Nicholas	193	1:45-2:45	Ballroom
Ruiz, Martha	1	10:15-11:45	Turner Valley Room
Saadat, Saba	116	9-10	Ballroom
Sacrey, Lori	68	all day	Foyer
Sáez, Tamara	42	3-4:30	Leduc Room
Saini, Jashan	230	1:45-2:45	Ballroom
Saini, Jasmeen	231	1:45-2:45	Ballroom
Sample, Dory	75	all day	Foyer
Sanchez Enkerlin, Annette	157	9-10	Ballroom
Sanderson, Matthea	152	9-10	Ballroom
Sanni, Omolara	114	9-10	Ballroom
Saurette, Matthew	52	3-4:30	Chancellor Room
Sayed, Tehzeeb	213	1:45-2:45	Ballroom
Serrano-Lomelin, Jesus	15	10:15-11:45	Consulate Room

# ALPHABETICAL LIST OF PRESENTERS

Name	#	Time	Room
Shah, Prachi	177	1:45-2:45	Ballroom
Shaha, Sumaiyah	189	1:45-2:45	Ballroom
Shigemitsu, Sachie	126	9-10	Ballroom
Shillington, Jessica	70	all day	Foyer
Simin, Irina	139	9-10	Ballroom
Singh, Simran	145	9-10	Ballroom
Skow, Rachel	11	10:15-11:45	Leduc Room
Stretch, Kendyl	184	1:45-2:45	Ballroom
Sung, Hyelin	229	1:45-2:45	Ballroom
Tan, Qiming	159	9-10	Ballroom
Teramachi, Yozo	129	9-10	Ballroom
Tessier, Carmen	32	3-4:30	Turner Valley Room
Tham, Edythe	67	all day	Foyer
Thereza-Bussolaro, Claudine	204	1:45-2:45	Ballroom
Thompson, Alexa	180	1:45-2:45	Ballroom
Thompson, Alison	226	1:45-2:45	Ballroom
Toohey, Alexander	162	9-10	Ballroom
Trakulmungskichkam, Thotsapon	128	9-10	Ballroom
Truong, Linda	209	1:45-2:45	Ballroom

Name	#	Time	Room
Tulli, Mia	71	all day	Ballroom
Tun, Mon	9	10:15-11:45	Leduc Room
Valji, Rafiaa	61	3-4:30	Chairman Room
van der Leek, Aaron	161	9-10	Ballroom
van Eeden, Charmaine	13	10:15-11:45	Consulate Room
Voaklander, Britt	106	9-10	Ballroom
Vu, Ngoc Khanh	35	3-4:30	Turner Valley Room
Watson, Adrienne	147	9-10	Ballroom
Weaver, Olivia	28	10:15-11:45	Chairman Room
Webster, Kirsten	185	1:45-2:45	Ballroom
Wewala, Gayathri	124	9-10	Ballroom
Wine, Osnat	169	1:45-2:45	Ballroom
Wingert, Aireen	77	all day	Ballroom
Wollin, Bethany	100	9-10	Ballroom
Wong, Jason	19	10:15-11:45	Chancellor Room
Wooldridge, Amy	181	1:45-2:45	Ballroom
Yaworski, Amanda	55	3-4:30	Chairman Room
Yoon, Kevin	151	9-10	Ballroom
Young, Kennedi	207	1:45-2:45	Ballroom
Zare, Alaa	171	1:45-2:45	Ballroom
Zehnder, Emily	131	9-10	Ballroom

## DISCLAIMER

While the abstracts have consistency, each abstract has been predominantly printed exactly as originally submitted.

Abstract # 1  
Presenter: Ruiz, Martha  
Supervisor: Bhargava, Ravi  
Title: Doppler ultrasound values associated with graft status in children after liver transplantation: A systematic review and meta-analysis  
Authors: Martha Ruiz, Rashid Alobaidi, Michelle Noga, Robin Featherstone, James Shapiro, Ravi Bhargava

## Introduction

Liver transplantation is the only cure for end-stage liver disease in children. Vascular compromise is the leading cause of liver transplant complications. Although vessels are routinely assessed with Doppler ultrasound (DUS), there is no current consensus defining normal values in children. This hampers identification of patients that might benefit from more invasive assessment or a change in management. The purpose of this systematic review is to evaluate the association of various DUS parameters with graft status and to establish normal and abnormal parameters for DUS.

## Methods

We followed the PRISMA-P 2015 guidelines and registered our protocol on PROSPERO (ID: CRD42019119986). We searched multiple databases using a combination of subject headings for liver transplantation, Doppler ultrasound, and children, up to Nov 30th, 2018, with no restriction on the date of publication or language. Studies of all designs were eligible if DUS parameters were obtained in children within one year after liver transplantation and correlated to liver transplant status.

## Results

Forty-one non-randomized studies were included (n=2194). Using the Newcastle Ottawa tool, we found good, moderate and low quality in 41.4%, 17.2% and 41.4% respectively. The twelve studies included for the meta-analysis reported values in the immediate postoperative period.

Grafts with any complication showed a lower hepatic artery resistive index (RI), with a mean difference of -0.15 (95%CI: -0.19 - -0.11, n=540, p<0.001), and a monophasic flow pattern in the hepatic veins (sensitivity=80%, specificity=78%, n=342, p<0.001).

Hepatic artery thrombosis showed a hepatic artery RI <0.6 (sensitivity=83%, specificity=87%, n=797, p<0.001), and/or a hepatic artery peak systolic velocity (PSV) distal to the anastomosis < 37 cm/s (sensitivity=64%, specificity=77%, n=144).

Portal vein stenosis showed a higher portal vein velocity at the anastomosis with a mean difference of 127.82 cm/s (95%CI: 48.26 - 207.39 cm/s, n=83, p=0.002), a threshold >49.6 cm/s (sensitivity=83%, specificity=81%, n=87, p=0.007), and >106 cm/s (sensitivity=100%, specificity=80%, n=61, p<0.001).

Portal vein thrombosis had a portal vein velocity distal to the anastomosis <6 cm/s (sensitivity 75%, specificity = 79.4%, n=105, p=0.036), <10 cm/s (sensitivity = 88%, specificity = 99%, n=105, p=0.036), and a hepatic artery PSV >70 cm/s (sensitivity = 37.5%, specificity = 90.7%, n=105, p=0.027).

## Conclusion

A hepatic artery RI < 0.6, a portal vein velocity distal to the anastomosis <10 cm/s, a portal vein velocity at the anastomosis >49.6 cm/s, or a monophasic hepatic venous flow pattern, are associated with graft complications in pediatric liver recipients.

Funded by Consejo Nacional de Ciencia y Tecnología de México (CONACyT).

The Power of Partnership



Abstract # 2  
Presenter: Durber, Chelsea  
Supervisor: Gokiert, Rebecca  
Title: A student's experience participating in a multi-stakeholder, intesectoral evaluation  
  
Authors: Durber, C.M., Mejia, T., Daniels, J., MacPherson, P., Gokiert, R., & Edwards, K.

### **Introduction**

The All in for Youth (AIFY) initiative is a 5-year pilot project that offers a variety of accessible and integrated mental health, nutrition, and early learning and care supports to children and families at five schools in Central Edmonton. This project reflects a partnership between various non-profit organizations, school boards, and government agencies in order to provide integrated and coordinated services to students and families in these school communities. For these stakeholders, evaluating outcomes is an essential component of the AIFY project; however, the evaluation and engagement aspects of such initiatives is nuanced and complex. For this presentation, a student researcher on the evaluation team will describe the activities undertaken to evaluate year 2 of the AIFY project, discuss strategies used to build and foster participant (i.e., children and parents) and stakeholder engagement in the evaluation, and share reflections on the evaluation experience.

### **Methods**

Using a mixed-method approach, quantitative and qualitative data were collected by the evaluation team using interview, focus group, and online survey methods to learn about children's, families', and other stakeholders' perceptions of the AIFY wraparound supports. This data was integrated with secondary data provided by AIFY partners. Several strategies across the data collection and knowledge mobilization phases of the evaluation were implemented to promote participant and stakeholder engagement, including connecting with participants and stakeholders in ways that were convenient for them, adopting a flexible approach to data collection across groups, and adapting and tailoring the final report to meet the needs of diverse stakeholder groups (e.g., sharing findings in different ways depending on the audience).

### **Results**

The engagement strategies helped meet the varied data collection and reporting preferences across participants and stakeholders. An openness in data collection setting and method was necessary for parent participants, as some parents preferred to meet at their child's school while others preferred to connect by phone. Similarly, a drawing activity was an effective and developmentally appropriate approach to encourage participation from elementary-age children. Finally, partners found it more helpful when evaluation results were organized by stakeholder group, research literature was integrated through the evaluation report, and the report included several high-level takeaway sections.

### **Conclusion**

Being a part of the evaluation team offered insight into the challenges and strengths of evaluating a large, multi-stakeholder, intersectoral project. It was difficult, at times, to access and coordinate data collection from many groups, each with different and sometimes conflicting policies; however, strategies used facilitated the ease and comfort of participants and stakeholders engagement with and use of the AIFY evaluation results.

Funded by Patient and Community Engagement Training (PaCET)

The Power of Partnership



**Presenter: Morris, Heather and Schulz, Petra**

**Supervisor: Hyshka, E.**

**Title: Engaging with bereaved parent advocates on drug policy reform: Reflections on a research and knowledge translation partnership**

**Authors: Morris, H., Schulz, P., Hyshka, E., Jenkins, E. & Haines-Saah, R.**

### **Introduction**

Canada is in the midst of an overdose crisis with over 11,000 Canadians having died from an opioid-related death since 2016 (Government of Canada, 2019). Across Canada, bereaved parents and family members are increasingly visible as stakeholders in public discussions of substance use and drug policy reform, particularly as it relates to anti-stigma and harm reduction efforts. While research and policy initiatives have recently included people who use substances, the involvement of parents and other family members has historically been excluded.

### **Methods:**

In 2016, researchers from the UofA, UofC and UBC embarked on an engaged scholarship project with members of Moms Stop the Harm, mumsDU and the Voice of the Family, three prominent Canadian parent advocacy organizations representing families who have been impacted by substance use. Our team has worked to define a common research and knowledge translation agenda and in 2017, we conducted qualitative interviews with 43 bereaved mothers across Canada, detailing their experience with drug policy advocacy.

### **Results:**

In 2019, we used the findings from this research to inform a public campaign to promote anti-stigma and harm reduction efforts, funded by an **Opioid Awareness Grant to Communities** from the Government of Alberta's Ministry of Health. In this presentation we will reflect on the role of all research team members, the benefits and challenges of partnership and key insights on the meaningful inclusion of family members as stakeholders in substance use research and drug policy reform. We will screen a short segment of our 6 minute film, "See *the Lives*" video series (See-Beyond.ca website) and reflect on the development and evaluation of this knowledge translation tool.

### **Conclusion:**

Our presentation will provide an opportunity for attendees to review and respond to "See *the Lives*" and think critically about the need for community engagement, thereby helping to ensure that the perspectives of people with lived experience be recognized as central to shifting the public discourse in support of harm reduction and anti-stigma efforts.

**Funded By:** WCHRI (Stollery Children's Hospital and Lois Hole Hospital for Women); Social Sciences and Humanities Research Council; Izaak Walton Killam Memorial Scholarship;



Abstract # 4  
Presenter: Palichuk, Airlie  
Supervisor: MacDonald, Shannon  
Title: Immunization coverage of immunocompromised children: A scoping review

Authors: Airlie I. Palichuk, BScN Honors student; Catherine E. Burton, MD, MSc; Linda G. Slater, MLIS; Hailey L. Tripp, BSc; Shannon E. MacDonald, PhD, RN

### **Introduction**

Clinicians work closely with immunocompromised children and their families to manage their conditions. Immunizations are an important component of care for these immunocompromised children, as they have an increased susceptibility to vaccine-preventable diseases. Part of the clinician's role is to counsel families on which vaccines they can safely receive. Little is known about whether this population is receiving the appropriate immunizations necessary to provide protection. The purpose of this scoping review was to determine the current state of knowledge regarding the immunization coverage of children who are immunocompromised. Specifically, we sought to examine the extent, range, and nature of research activity, as well as to identify gaps in the existing literature.

### **Methods**

We searched bibliographic databases and references lists of included studies. We included primary research reporting on the immunization coverage of any vaccine in children with any immunocompromising condition. Records were screened independently by two reviewers. Data were extracted by one reviewer with validation from a second reviewer. Quality appraisal was completed independently by two reviewers. Data were analyzed quantitatively and narratively.

### **Results**

Of the 85 included studies, most were from North America (n=41) and Europe (n=29). Pneumococcal (n=36) and influenza (n=37) were the most commonly studied vaccines, followed by diphtheria/tetanus/pertussis (n=26), measles/mumps/rubella (n=27), and polio (n=21) vaccines. Cross-sectional study designs were the most prevalent study design. Immunocompromising conditions studied included solid organ transplants (n=21), cancer and stem cell transplants (n=22), sickle cell disease (n=17), HIV (n=12), immunosuppressive therapy (n=11), splenectomy (n=4), primary immunodeficiency (n=1), and others unspecified (n=2). Only 24 of 85 studies were of high-quality.

### **Conclusion**

This scoping review emphasizes the need for higher-quality research to be conducted in this field. Future research should expand on the types of vaccines and immunocompromising conditions studied.

Funded by WCHRI Summer Studentship

The Power of Partnership



Abstract # 5  
Presenter: Punjani, Neelam  
Supervisor: Papathanasoglou, Elisavetst  
Title: **Scoping review of the association between adolescents developing sexuality and its impact on psychological: Evidence from lower and middle income countries**  
Authors: Neelam Punjani, Elisavet Papathanasoglou, Kathleen Hegadoren, Saima Hirani, Zubia Mumtaz, Margot Jackson

### **Introduction**

During puberty and sexual debut, adolescents experience important physical, mental, and social transformations. In the process of dealing with these changes, adolescents become potentially vulnerable to mental health problems. The aim was to synthesize published research evidence on sexuality-related mental health stressors among adolescent girls and boys, identify gaps (if any) in current evidence, and contribute to the knowledge about the experiences of stressors related to sexual health among adolescents, to further inform research, practice, and policy initiatives in sexual health.

### **Methods**

A scoping literature review of peer-reviewed articles published between 1990 and 2018. MEDLINE, CINAHL, EMBASE, PsycINFO, Global health, ERIC, and Sociological Abstracts databases were searched for research studies that focused on the experiences of sexual health-related mental health stressors and symptomatology of adolescents. We targeted studies conducted with adolescent populations between ages 11-24 years.

### **Results**

Data from 12 published research papers, including 8 qualitative studies, 3 quantitative studies, and 1 mixed method study, were systematically analyzed. Four major themes and a few sub themes were identified regarding sexual health and mental health of adolescents: 1) Relationship of sexuality and mental health; 2) Myths and misconceptions related to sexuality; 3) Challenges in seeking sexuality information; and 4) Educational needs among adolescents related to sexuality.

### **Conclusion**

Unmet needs for accessible adolescent friendly sexual health services, counselling, and age-appropriate information contributes to several mental health stressors and symptoms, such as sadness, depressive and anxiety symptomatology, regret, fear, embarrassment, low self esteem, guilt, shame, and anger. Therefore, tackling sexuality-related stressors could play an important role in addressing the overall wellbeing of young people. Future studies are needed to generate a deeper understanding of the concept of sexual health and its relation to mental health in diverse contexts.

Health care professionals are encouraged to explore the sexuality-related mental health experiences of adolescent girls by offering effective youth-friendly sexual and reproductive health interventions to improve the quality of life and increase the satisfaction of adolescents.

Funded by WCHRI Graduate Studentship and Izaak Walton Killam Memorial Scholarship

The Power of Partnership



Abstract # 6  
Presenter: Patricny, Nicol  
Supervisor: Pei, Jacqueline  
Title: A systematic review of promotive and protective factors against violence and delinquency in youth and emerging adults  
Authors: Nicol Patricny, Jacqueline Pei

## Introduction

For adolescents, engagement in crime peaks at age 17 years, with 95% of youth going on to display healthy non-delinquent trajectories, and only 5% continuing with antisocial behaviour into adulthood. Most research on youth delinquency has focused on examining negative risk factors for offending rather than exploring healthy strength-based factors that protect the majority of youth from a lifetime of offending. The current review aims to examine which strength-based factors promote healthy developmental trajectories and protect against participation in violence/delinquency.

## Methods

We conducted a systematic review of longitudinal studies by searching the PsychINFO database on October 13, 2018. We used the PRISMA statement for reporting systematic reviews to guide this review. We included original peer-reviewed studies that focused on promotive/protective factors in any population of youth aged 12 to 25 years old with a primary outcome measure of violence or serious delinquency and a follow-up period of at least 2 years. We organized the results into general categories of promotive/protective factors that were supported by two or more longitudinal studies.

## Results

We included a total of 35 articles from 15 longitudinal studies that met the inclusion criteria. The results represent over 90,000 youth, both general and at-risk or vulnerable populations. We identified 22 independent promotive/protective factors that promoted long-term healthy adjustment and reduced the likelihood of participation in violence or serious delinquency in some, but not all youth, and typically not across the youth developmental period. These strength-based factors include: low antisocial attitudes and behaviours; high educational aspirations; school achievement; low ADHD symptoms; non-clinical anxiety; low peer/parental delinquency or attitudes toward delinquency; school engagement/attachment; religious service attendance; caregiver supervision; family management and structure; family bonding and involvement; positive neighborhood; intelligence; social competence/prosocial peer relationships; prosociality; use of non-English primary language; female sex; low use of/exposure to substance use; easy temperament; low parental stress; lack of depressed mood, and higher socioeconomic status. When considering the cumulative impact of multiple promotive/protective factors, we identified strong evidence of promotive and protective effects for both general and at-risk youth populations across the youth developmental period and into adulthood.

## Conclusion

For general populations of youth as well as those at-risk for violence and delinquency, greater cumulative protective factors increase the odds of having a healthy non-delinquent developmental trajectory during adolescence and into adulthood and decreases the odds of participating in violence or serious delinquency. The unique set of promotive/protective factors that act together to protect youth and promote positive outcomes may vary across different youth populations. The results have implications for health care providers in terms of universally promoting positive psychosocial health outcomes, and treatment planning and resiliency-building for youth at-risk of violence and delinquency.

Funded by WCHRI Graduate Studentship

Abstract # 7  
Presenter: Ganguly, Esha  
Supervisor: Davidge, Sandra  
Title: Effects of placenta-targeted treatment with nanoparticle-encapsulated MitoQ (nMitoQ) on fetal cardiomyocyte development in a rat model of prenatal hypoxia  
Authors: E Ganguly, R Kirschenman, F Spaans, TEJ Phillips, CL Cooke, CP Case, ST Davidge  
University of Alberta, Canada and University of Cardiff, University of Bristol, UK.

## Introduction

Chronic fetal hypoxia, associated with placental dysfunction, has been linked to the development of adult cardiovascular disease in the offspring. Prenatal hypoxia leads to increased placental and fetal cardiac oxidative stress, and reduced proliferative growth of myocytes; suggesting increased cardiac mass via hypertrophy (increased myocyte size). We have previously shown that circulating factors released from prenatally hypoxic placentae impaired fetal neuronal development. However, factors impacting cardiomyocyte development are yet to be identified. MitoQ is an antioxidant which, by encapsulation in nanoparticles (nMitoQ), can be used to reduce placental oxidative stress without crossing the placenta to avoid potential off-target effects on the fetus. We hypothesized that circulating factors from placentae of prenatally hypoxic dams will lead to myocyte hypertrophy, and nMitoQ will prevent this effect, thus leading to improved cardiac development.

## Methods

Pregnant rats were exposed to either hypoxia (11% O<sub>2</sub>) or normoxia (21% O<sub>2</sub>) from gestational day (GD) 15-21 (term=22 days). On GD15, rats were intravenously injected with saline or nMitoQ (0.5µM). On GD21, male and female placentae from each of the experimental group were placed in cell culture conditions for 24hr. This conditioned medium, containing factors released from the placenta, was then added to cultured fetal cardiomyocytes for 24 hours. The cardiomyocytes were collected from both male and female fetuses from untreated pregnant normoxia dams in order to control for same sex placental conditioned medium. Using immunofluorescent staining for anti-heavy chain cardiac myosin (cardiomyocyte marker), myocyte binucleation and surface area (marker of terminal differentiation and hypertrophy) were measured.

## Results

Conditioned media from hypoxic placentae significantly enhanced binucleation in myocytes from female fetuses (normoxia:  $6.44 \pm 2.80\%$  vs. hypoxia:  $19.14 \pm 4.52\%$ ;  $p=0.02$ ), which was not affected by nMitoQ. Prenatal hypoxia increased total myocyte size in cultured myocytes from both sexes, while nMitoQ tended to reduce the size of only male myocytes (hypoxia-saline:  $270.5 \mu\text{m}^2 \pm 40.77$  vs. hypoxia-nMitoQ:  $198.5 \pm 22.19 \mu\text{m}^2$ ;  $p=0.07$ ). There was no effect of hypoxia on the size of mononucleated myocytes in either sex. However, in both male and female myocytes, prenatal hypoxia increased the size of binucleated myocytes. nMitoQ treatment reduced the size of binucleated myocytes in males (hypoxia-saline:  $377.4 \pm 36.79 \mu\text{m}^2$  vs. hypoxia-nMitoQ:  $275.8 \pm 21.7 \mu\text{m}^2$ ;  $p=0.02$ ), but not in females.

## Conclusion

Interestingly, terminal differentiation was increased in only female myocytes exposed to conditioned media from hypoxic placentae, suggesting a sex-specific divergence in cardiac development to factors released from prenatally hypoxic placentae. nMitoQ reduced the increase in binucleated myocyte size in hypoxic male fetuses and may thus contribute to preventing cardiac hypertrophy in males. Placental-targeted treatment strategies against oxidative stress could potentially alter circulating factors released from the stressed placenta and optimize fetal cardiac development in a sexually dimorphic manner in offspring born from complicated pregnancies

Funded by CIHR, WCHRI Graduate Studentship

Abstract # 8  
Presenter: Hoffman, Janlyn  
Supervisor: Riddell, Meghan  
Title: **Apical polarization of atypical PKC-? is absent in early first trimester placental epithelium**  
Authors: Janlyn Hoffman, Jasmine Nguyen, Saba Saadat, Meghan Riddell

### Introduction

Apical-basal polarity is a fundamental property of epithelial cells, causing asymmetric localization of membrane proteins, structural development, and specialized functions such as nutrient transport and directional secretion. The placenta is a highly specialized organ of pregnancy, providing an interface between the maternal and fetal circulation. Polarization of this organ is essential for proper function. The outermost layer of the placenta is comprised of placental specific epithelial cells known as trophoblasts. The mononucleate cytotrophoblasts (CT) comprise the inner epithelial layer and fuse together to form the syncytiotrophoblast (ST) - one large, multinucleated, borderless cell comprising the outer epithelial layer. The ST is highly polarized at term and is the primary structure responsible for selective transplacental exchange. Disruption of ST polarity is associated with compromised cell function in placental disorders such as preeclampsia. However, the molecular mechanisms governing ST polarity have never been examined.

The Par complex is an evolutionarily conserved complex of proteins comprised of Par-3, Par-6, and atypical protein kinase C (aPKC), and is known to play an integral role in establishing, maintaining, and altering apical-basal cell polarity. Restriction of aPKC to the apical surface is a key aspect of Par complex function. We hypothesize that the Par complex will be localized at the apical membrane of the ST layer from the early stages of placental development and will regulate ST apical-basal polarity.

### Methods

Tissue samples from the first trimester (6 to 7.5 weeks), and term placenta was collected, fixed, and stained via immunofluorescence with antibodies against aPKC (both aPKC- $\zeta$  and aPKC- $i/\lambda$  isoforms), E-cadherin (a CT marker), ezrin (a sub-apical marker), phalloidin (an actin marker), and Hoechst. First trimester tissue was whole mounted, and third trimester tissue cut into thick (~100 $\mu$ m) sections with a vibratome prior to staining. Images were captured via confocal microscopy.

### Results

Contrary to our hypothesis, aPKC- $\zeta$  does not exhibit apical membrane polarization despite strong actin polarization within the ST during the first trimester. In contrast, apical localization of aPKC- $\zeta$  and aPKC- $i/\lambda$  could be observed in the term ST.

### Conclusion

In conclusion, aPKC- $\zeta$  does not exhibit apical localization within developing placenta in early first trimester ST albeit the apical localization of other structural proteins. This suggests that the function of the Par complex in polarization may not be relevant until the later stages of gestation. Future experiments will attempt to identify a precise time frame of apical polarization of the aPKCs, and potentially identify other functions (i.e. endo- and exocytosis processes) that the Par complex may regulate. Dysregulation of polarity is associated with compromised epithelial cellular functions; hence, dysregulation of the mechanisms governing ST polarity may be associated with development of placental dysfunction and pregnancy complications, therefore effecting lifelong maternal and fetal health.

Funded by Faculty of Medicine and Dentistry

The Power of Partnership

Abstract # 9  
Presenter: Mon Tun  
Supervisor: Piush Mandhane  
Title: Prediction of risk of cesarean section in the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort  
Authors: Radha Chari, Padma Kaul, Mike Paulden, Stuart Turvey, Meghan Azad, Theo Moraes, Malcolm Sears, Padmaja Subbarao

### Introduction

Rising cesarean section (CS) rate is a global concern with CS rates approaching 30% in Canada (2017). Numerous studies have tried to identify factors contributing to increasing CS rates including antenatal and intrapartum obstetric and non-obstetric characteristics. Intrapartum factors cannot be anticipated prior to admission to labour and delivery. As a result, including intrapartum factors in CS prediction models is not practical for obstetricians counselling their patients about the likelihood of CS delivery or planning operating theatre time. We aimed to develop a predictive model for the risk of CS before the onset of labour.

### Methods

We completed a secondary analysis of data collected for the CHILD cohort study. The study sample comprised term pregnant women carrying a singleton fetus with cephalic presentation. Data available included maternal demographics, obstetric history and birth modes. The sample was divided into a training dataset (80%) and validation data set (20%). Variables associated with CS delivery were identified using multiple logistic regression in the training dataset. The predictive ability of our final model, including variables identified in the logistic regression, were evaluated in a validation data set. The accuracy of the models for prediction of CS delivery was measured by the area under the receiver operating characteristic curve (AUC).

### Results

The patient population consisted of 2,626 pregnant women, with a mean age of 32 years, mean BMI of 24.67 kg/m<sup>2</sup>, 47% were nulliparous, and 574 (21.8%) had a CS delivery. Each year of increasing maternal age and each unit increase in BMI increased the odds of cesarean delivery by 6% and 5% respectively (OR 1.06, 1.04-1.09; OR 1.05, 1.03-1.07). In contrast, maternal height was negatively associated with the risk of CS delivery. The best combined predictors of CS delivery included six variables (age, BMI, height, gestational age, pregnancy induced hypertension, antenatal depression score (CES-D) and birth order of the infant. The AUC for our final prediction model was 0.70 (0.66-0.71) in the training set. The validation set showed similar discrimination with an AUC of 0.68 (0.63-0.68).

### Conclusion

We developed a prediction model for clinical estimation of the risk of CS delivery in both nulliparous and multiparous that deliberately did not include intrapartum factors. The validated nomogram to predict the risk of CS could be a potential tool for counselling prospective parents and healthcare planning (e.g. CS operating room scheduling). Further validation of the tool in a larger cohort is warranted.

Funded by

The Power of Partnership



Abstract # 10

Presenter: Hula, Nataliia

Supervisor: Davidge, Sandra

Title: **The effect of a placenta-targeted treatment with a mitochondrial antioxidant (nMitoQ) on later-life cardiac function of male and female offspring exposed to hypoxia in utero**

Authors:

Nataliia Hula, Jennie Vu, Anita Quon, Raven Kirschenman, Christy-Lynn M. Cooke, Tom J. Phillips, C. Patrick Case, Floor Spaans, Sandra T. Davidge

University of Alberta, Canada and University of Cardiff, University of Bristol, UK.

### Introduction

Fetal hypoxia is a major consequence of complicated pregnancies that can negatively affect fetal cardiac programming and impair later-life cardiac function of the offspring. We have previously demonstrated enhanced cardiac susceptibility to ischemia/reperfusion (I/R) injury of adult male and female offspring born from hypoxic pregnancies. Our laboratory has been assessing whether prenatal treatment of the placenta during pregnancy with the antioxidant MitoQ encapsulated into placenta-targeted nanoparticles (nMitoQ) can improve cardiac function of adult offspring. We have previously shown that nMitoQ treatment decreased superoxide levels in hypoxic placentas and fetal hearts, both in males and females. However, the effect of prenatal nMitoQ treatment in hypoxic pregnancies on cardiac function of adult offspring is unknown. We hypothesize that prenatal hypoxia impairs cardiac function by changes in expression of proteins important for calcium cycling, which is ameliorated by nMitoQ treatment.

### Methods

Pregnant Sprague-Dawley rats were exposed to normoxia (21% O<sub>2</sub>) or hypoxia (11% O<sub>2</sub>) and injected with saline or nMitoQ (125 μM) on gestational day 15 (term=22 days). After delivery, male and female offspring were aged to 4 months and cardiac function was assessed ex vivo by subjecting the heart to I/R (20 min of ischemic insult followed by 40 min reperfusion). Afterwards, cardiac left ventricle tissue was assessed for the expression of intracellular proteins involved in cardiac function (SERCA2α, PLN, pPLN, PP2Cε, CaMK II, pCaMK II) using Western blotting. Data was analyzed using two-way ANOVA (n=5-6/group).

### Results

Prenatal hypoxia impaired cardiac recovery after I/R insult, while prenatal nMitoQ treatment during hypoxic pregnancy improved cardiac recovery in adult male (71.5±6.5% vs 96.5±3.5%, p=0.002) and female (62.9±7% vs 84.8±2.3%, p=0.008) hypoxic offspring. In females, hypoxia decreased SERCA2α levels, without effect of nMitoQ treatment, while in males nMitoQ treatment tended to increase SERCA2α levels (68.1±6.2% vs 103.1±10.4%, p=0.08). nMitoQ treatment increased PLN levels compared to saline treatment (156.7±12.7% vs 117.3±12%, p=0.03) in male normoxic and hypoxic offspring but no changes were observed in females. Treatment with nMitoQ increased pPLN/PLN ratio in both normoxic and hypoxic female offspring compared to saline (179.9±27.1% vs 100.7±11.6%, p=0.02) without an effect in males. PP2Cε level was increased in male hypoxic offspring after nMitoQ treatment (75.5±6.9% vs 142.8±9.4%, p<0.0001), but unaltered in females. The level of CaMK II and its activation (pCaMK II/CaMK II) were not affected either by prenatal hypoxia or nMitoQ treatment in both sexes.

### Conclusion

Prenatal placental treatment with nMitoQ improved cardiac function of adult male and female offspring. Improved cardiac function in males may be attributed to increased level of cardiac SERCA2α, while in females this could be due to alleviation of SERCA2α inhibition (increased pPLN/PLN). Our data suggest that the mechanisms by which prenatal nMitoQ treatment improves cardiac function of adult offspring exposed to hypoxia in utero are sexually dimorphic.

Funded by Alberta Innovates Summer Research Studentship, Stefan and Pelagia Wychowanec Graduate Scholarship, WCHRI, CIHR.

The Power of Partnership

Abstract # 11  
Presenter: Skow, Rachel  
Supervisor: Davenport, Margie  
Title: The influence of an aerobic exercise intervention on muscle sympathetic nervous system regulation of blood pressure in pregnancy  
Authors: Rachel J. Skow, Craig D. Steinback, Margie H. Davenport

### Introduction

Healthy pregnancy is associated with augmented basal and reflexive sympathetic nervous system activity and blunted baroreflex gain. Aerobic exercise in non-pregnant populations results in reduced resting and reflexive sympathetic nerve activity and increases baroreflex gain. The influence of exercise on sympathetic regulation has not been explored during pregnancy. We hypothesized that a prenatal aerobic exercise intervention would reduce resting sympathetic nerve activity and maintain baroreflex gain during pregnancy.

### Methods

We conducted a randomized controlled trial of aerobic exercise (3days/week, 50-70% heart rate reserve for 40min) from 16-20 until 34-36 weeks in 59 inactive pregnant women (NCT02948439). Repeated measures of heart rate (ECG), beat-by-beat blood pressure (finger photoplethysmography, Finometer) and direct measures of muscle sympathetic nervous system activity (microneurography; peroneal nerve) were obtained in 9 control and 12 exercising women.

### Results

There were no differences in maternal age, pre-pregnancy BMI, or weight at assessment between groups. Data from ~10min of quiet rest were analyzed. Resting mean arterial blood pressure increased from the second to the third trimester ( $p=0.032$ ) but was not different between groups post-intervention ( $83\pm 8\text{mmHg}$  vs.  $83\pm 9\text{mmHg}$  for control and exercise, respectively;  $p=0.926$ ). The rise in resting heart rate was attenuated in the exercise group ( $p=0.006$  for interaction). There was no difference in systemic vascular resistance across gestation, or between groups ( $p=0.411$ ). Resting muscle sympathetic burst frequency (+11bursts/minute) and burst incidence (+9bursts/100 heart beats) increased in controls, but not in exercisers (+2 burst/minute; +1 burst/100 heart beats) ( $p<0.001$  group\*time interaction for burst frequency and incidence, respectively). Basal neurovascular transduction (the relationship between either blood pressure or systemic vascular resistance and burst frequency) was decreased with gestation in the control group ( $p<0.001$  and  $p=0.005$ , respectively) but not in exercisers. Interestingly, baroreflex gain was not different across gestation or between groups ( $p=0.986$  for interaction).

### Conclusion

These data are the first to show that the previously documented increase in sympathetic nerve activity associated with gestation may be reduced by maternal aerobic exercise training. This reduction occurs without changes in resting mean arterial blood pressure or baroreflex gain suggesting that the communication between the nervous system and blood vessels (neurovascular transduction) is maintained. These data provide evidence that altered sympathetic neurovascular control may be one mechanism by which the risk of gestational hypertension is reduced by prenatal exercise.

Funded by WCHRI, CIHR, Alberta Innovates, NSERC, HSFC NNIA

The Power of Partnership





Abstract # 12  
Presenter: Boparai, Rakhbeer  
Supervisor: Davenport, Margie  
Title: **The effects of moderate-intensity exercise on endothelial function during pregnancy**  
Authors: **Boparai, Rakhbeer; Skow, Rachel; Farooq, Sauleha; Steinback Craig; Davenport, Margie**

### **Introduction**

Poor vascular function is associated with the development of hypertensive complications of pregnancy, however regular prenatal physical activity has been shown to reduce this risk, and as such, has been linked to improved vascular function. The purpose of this study was to assess the impact of a structured aerobic exercise intervention during pregnancy on endothelial function.

### **Methods**

This randomized controlled trial included twenty-seven healthy women with singleton pregnancies in their second trimester. Women were screened for suitability to exercise training using the PARMed-X for Pregnancy. Endothelial function was assessed using flow-mediated dilation (FMD; brachial artery Doppler ultrasonography, normalized for shear stress) in all women at baseline (16-20 weeks) and post-intervention (34-36 weeks). Following the baseline assessment, women were randomized into either a control group (n=11, 32±4 years), or an exercise intervention group (n=16, 31±2 years). The aerobic exercise intervention consisted of 40 minutes of moderate intensity exercise (50-70% heart rate reserve) 3-4 times per week. Women in the control group received standard care. A 2-way mixed model analysis of variance was used to assess differences in FMD variables and physical activity levels between groups, across time and group x time interaction. Holm-Sidak analyses was used to compare multiple means when effects were found to be significant (P<0.05).

### **Results**

Women randomized to the exercise group completed 81% of prescribed exercise sessions. Exercising women experienced an attenuated increase in mean arterial pressure relative to the control group (2±3 mmHg vs. 7±3 mmHg; p=0.044); however, no difference was observed in percent or absolute change in FMD between the groups (P>0.05). The post-occlusion mean flow rate (437 ± 174 vs. 364 ± 112 mL/min; P=0.001) and the post-occlusion antegrade flow rate (438 ± 174 vs. 364 ± 112 mL/min; P=0.001) were both increasingly larger for the exercise intervention group compared to the controls.

### **Conclusion**

Engaging in a supervised aerobic exercise intervention did not alter endothelial functional in healthy pregnant women, however, it did attenuate blood pressure increases across gestation. Therefore, regular exercise contributes to improved cardiovascular health during pregnancy.

### **Keywords**

Physical activity, pregnant women, flow-mediated vasodilation, endothelial function, blood pressure

Funded by **Women and Childrens Health Research Institute (WCHRI) Summer Studentship**

The Power of Partnership



Abstract # 13  
Presenter: van Eeden, Charmaine  
Supervisor: Mandhane, Piush  
Title: Increased behavioral problems at 5 years of age are associated with sleep disordered breathing phenotypes, based on parent-reported symptoms: The CHILD study  
Authors: Charmaine van Eeden, Sukhpreet K. Tamana, Nevin Hammam, Joyce Chikuma, Diana L. Lefebvre, Meghan B. Azad, Theo J. Moraes, Padmaja Subbarao, Allan B. Becker, Stuart E. Turvey, Malcolm R. Sears, Carmen Rasmussen, Jacqueline Pei and Piushkumar J. Mandhane

### Introduction

Sleep breathing problems affect up to 10% of children aged between 2 and 8 years of age. Sleep-disordered breathing (SDB), from habitual snoring to obstructive sleep apnea, in school aged children has been associated with poor learning, adverse executive functioning and, externalizing behavior problems such as ADHD. Our previous investigation found that children with parent-reported SDB up to 2 years of age had greater ADHD symptoms. Our objective was to examine the association between the age of onset and duration of parent-reported symptoms of SDB and behavioral problems at age 5 years.

### Methods

Parent-reported SDB symptoms were assessed quarterly between 3 months and 2 years, and annually from 3 to 5 years of age among 581 CHILD study Edmonton-site participants. Parent-reported SDB symptoms were clustered into phenotypes using trajectory modelling (STATA traj) based on age of onset and duration of symptoms. The Child Behavior Checklist (CBCL) preschool-version (Mean t-score 50, standard deviation 10 points) assessed total, externalizing (attention), and internalizing (anxiety, depression) behaviors at 5 years of age.

### Results

We identified four SDB phenotypes to five years of age: no SDB (77.8%), early onset SDB (10.2%, peak symptoms at 18 months), late onset SDB (6.9%, peak symptoms at 3.6 years) and persistent SDB (4.5%, peak symptoms at 3.2 years). The mean CBCL T-Score for total behavior problems was 42.2 (95% CI 41.4, 42.9) with 1.7% of children having clinically significant T-Scores of  $\geq 65$ . Compared to children with no SDB, those with persistent SDB had the greatest increase in their total behavioral problems score (7.8 points, 95% CI 4.6, 10.9;  $p \leq 0.001$ ). Late onset SDB also had a significant increase in total behavior symptoms (5.0 points, 95% CI 2.4, 7.6;  $\leq 0.001$ ). Early onset SDB had a significant, albeit minimal, increase in total behavior problems (2.1 points, 95% CI 0.03, 4.14;  $p = 0.05$ ). The effects of SDB on behavior exceeded those of any other potential covariate controlled for in this study, including current SDB symptoms, sleep duration, maternal stress and screen time. We found similar results for externalizing behavior for children with persistent and late-onset SDB symptoms.

### Conclusion

Children with persistent or late onset SDB phenotypes have markedly higher behavioral problems than those children with no SDB. These behavioral problems include both externalizing (ADHD-like symptoms) as well as internalizing (anxiety and depression) issues. These findings highlight the need to screen young children for SDB, to try mitigate future mental health problems.

Funded by CIHR, AllerGen and WCHRI

The Power of Partnership



Abstract # 14  
Presenter: Roth, Daniela  
Supervisor: Graf, Daniel  
Title: Connecting altered suture development to midfacial hypoplasia

Authors: Daniela M. Roth, Pranidhi Baddam, Daniel Graf

### Introduction

Midfacial hypoplasia is characterized by insufficient growth of the midface, often associated with breathing problems and various comorbidities in children. Normal growth of the skull is facilitated through fibrous sutures between bones. The midface contains sutures which, if disturbed, likely impact midfacial growth. The current body of knowledge regarding sutures predominantly stems from study of premature fusion of cranial sutures (craniosynostosis). However, little is known about the contribution of midfacial sutures to growth of the midface. We utilize a mouse model of midfacial hypoplasia based on deletion of Bone Morphogenetic Protein 7 (Bmp7) to study suture involvement in midfacial growth. We hypothesize that Bmp7 deletion leads to changes in midfacial sutures, which directly affect midfacial growth. We aim to investigate how Bmp7 organizes sutures of the frontonasal region, identify cell types affected by loss of Bmp7, and describe molecular changes caused by loss of Bmp7 in the frontonasal region.

### Methods

Mice carrying a deletion of Bmp7 in neural crest cells (Bmp7<sup>ncko</sup>) were compared to controls at 2 and 4 weeks of age, corresponding to periods of rapid midfacial growth. Skeletal differences were analyzed using micro-computed tomography ( $\mu$ CT) scans and cellular differences were identified using histology. Molecular differences were demonstrated through immunofluorescence for proteins of interest alongside RT-qPCR for gene expression analysis.

### Results

$\mu$ CT scans of Bmp7 mice indicate malformed frontonasal sutures already at 2 weeks, and more severely at 4 weeks. Histology revealed altered suture architecture in the connection of the frontonasal suture to the nasal septum, suture midline defects, and differences in thickness of sutural mesenchyme. Structural components like collagen were disorganized and deviated from normal expression, as were stem cell and bone progenitor markers. Osteoblast differentiation was altered, osteocytes were disorganized, and osteoclast number was increased alongside the sutures of Bmp7 mice.

### Conclusion

The distinct differences in the frontonasal sutures in Bmp7 mice strongly suggest that alterations to sutures directly contribute to midfacial hypoplasia. More specifically, our data suggests that Bmp7 controls early bone development. Loss of Bmp7 affects bone formation at various levels, ranging from differences in bone progenitor cells to altered bone quality. Thus, changes to suture behaviour is a likely and so far insufficiently considered contributor to midfacial hypoplasia, adding to the complexity of midfacial growth. This insight into the functionality of sutures in midfacial hypoplasia is crucial in a field like pediatrics, where minimally invasive options are mandated.

Funded by WCHRI Innovation Grant

The Power of Partnership



Abstract # 15  
Presenter: Serrano-Lomelin, Jesus  
Supervisor: Ospina, Maria  
Title: Joint effects of adverse childhood experiences on adult onset Asthma

Authors: Jesus Serrano-Lomelin, Sana Amjad, Anne Hicks, Gerald Giesbrecht, Maria B. Ospina

### Introduction

Asthma is a chronic respiratory disease of complex etiology that affects approximately 11% of Canadians. Prenatal and early-life exposures, genetic factors, and environmental hazards have been implicated in asthma causation pathways. Adverse childhood experiences (ACEs) are potentially traumatic events that can have negative and lasting effects on long-term health. They have been independently associated to asthma development in adulthood. Although ACEs frequently co-occur, their combined effects on the likelihood of developing adult asthma have been seldom explored. This study evaluates the effects of variables (latent factors) that combine the relationships among eight types of ACEs on the occurrence of asthma in adulthood by using a parsimonious model based on the underlying correlation structure among the eight ACEs.

### Methods

This study is a secondary analysis of data from a random sample of 1,207 from the 2013-Alberta Adverse Childhood Experiences Survey. The survey gathered information about adversity during childhood and the risk of poor health outcomes in adulthood, including asthma. Exposures to eight ACEs were assessed in the survey: verbal insults, physical abuse, sexual abuse, witnessed violence against mother or stepmother, alcohol or drug use at home, living in a household with someone with depression/mental illness, living in a household with someone with chronic illness or physical disability at home, and living with parents separated or divorced. We applied factor analysis to extract latent factors based on the underlying correlation structure among the eight ACEs. We used multivariable logistic regression models to assess the association between the latent factors and asthma occurrence in adulthood adjusting for sex and born in/out Canada. Odds ratios (OR) and 95% confidence intervals (CI) are reported.

### Results

Among 1,207 study participants, 9% developed asthma. All the eight ACEs were moderately to strongly positively correlated, indicating their high inter-dependence. Three latent factors were identified: relational violence (combining verbal insults, physical abuse, sexual abuse and witnessing violence against mother), negative home environment (combining alcohol/drug use at home, parents separated, and witnessing violence against mother), and illness at home (combining depression/mental illness at home and chronic illness or physical disability at home). Relational violence (OR=2.4, 95%CI 1.4, 4.0) and negative home environment (OR=1.9, 95%CI 1.03, 3.3) were both positively associated with asthma onset in adulthood; whereas the illness at home factor did not show such association (OR=1.60, 95%CI 0.87, 2.94).

### Conclusion

Our study provides evidence that experiences of relational violence against children and negative home environment are important risk factors for adult asthma, and may inform interventions aimed at reducing the lasting negative impact of childhood adversities on adult health.

Funded by Policy Wise for Children and Families, Women & Children Health Research Institute

The Power of Partnership



Abstract # 16  
Presenter: Johnson, Peter Anto  
Supervisor: Schmölzer, Georg  
Title: A heartbeat away from better lifesaving: Novel smartphone technology to improve heart rate assessment during neonatal resuscitation at birth  
Authors: Peter A. Johnson, Po-Yin Cheung, Tze-Fun Lee, Megan O'Reilly, Georg M. Schmölzer

### Introduction

Heart rate (HR) is the most significant parameter to assess a newborn's clinical status at birth. Assessment of HR is used to decide which interventions are performed and in determining its effectiveness during resuscitation. Current neonatal resuscitation guidelines recommend auscultation and palpation along with pulse oximetry and electrocardiography, however every approach has limitations. Most recently, smartphone apps have been proposed as novel technologies to measure HR during neonatal resuscitation. We aimed to evaluate the accuracy and speed of the smartphone app NeoTapLS app (Tap4Life, Stockholm, Sweden) for HR assessment in a porcine model of asphyxia-induced neonatal resuscitation. We hypothesized that the NeoTapLS app will provide a more accurate and faster HR assessment compared to auscultation.

### Methods

Newborn piglets (n=20, 1-3 days, 1.7-2.4kg) were anesthetized, intubated, mechanically ventilated, and subjected to 30 min of hypoxia, followed by asphyxia. Asphyxia was induced by clamping the endotracheal tube and disconnecting the ventilator until asystole was confirmed via carotid blood flow. All HR assessments were performed during asphyxia using: The NeoTapLS app, digital stethoscope (Thinklabs Medical LLC, Centennial, CO), and carotid blood flow. The HR obtained with the NeoTapLS app was derived by tapping a minimum of 3 beats corresponding to heartbeat heard. HR obtained with the digital stethoscope was derived by counting the number of beats over 6 sec and multiplying them by 10 (DS6sec), and by counting for 10 sec and multiplying them by 6 (DS10sec). The time needed to obtain a HR was also recorded. Bland-Altman plots were used to compare HR assessment with the NeoTapLS app, DS6sec, DS10sec, and carotid blood flow.

### Results

During asphyxia, the median (IQR) HR with the NeoTapLS app was 69(56-76) beats per minute (bpm), compared to 60(60-80) bpm, 60(56-74) bpm, and 72(56-81) bpm with the DS6sec, DS10sec, and the carotid blood flow, respectively. Bland-Altman analysis revealed no difference between HR obtained with the NeoTapLS, DS6sec, and DS10sec compared to carotid blood flow. The median (IQR) time to obtain a HR using the NeoTapLS was 3(2-4) sec, compared to 6(6-7) sec and 10(10-11) sec with the DS6sec and DS10sec, respectively. NeoTapLS was faster to assess HR>30 bpm and HR>18 bpm compared to DS6sec and DS10sec, respectively.

### Conclusion

Heart rate assessment using the NeoTapLS is feasible and comparable to carotid blood flow. The NeoTapLS was more accurate compared to the DS6sec and DS10sec with lower HR. Clinical trials using tap-based application are warranted and are currently ongoing.

Funded by Heart and Stroke Foundation of Alberta and WCHRI Graduate Studentship Award

The Power of Partnership



Abstract # 17  
Presenter: Baddam, Pranidhi  
Supervisor: Graf, Daniel  
Title: **Is the cartilage responsible for nasal septum deviation?**

Authors: **Pranidhi Baddam, Mark Nie, Daniela Roth, Daniel Young, Claudine Bussalero, Tiffany Kung, Antoine Dufour, Carlos Flores-Mir, Daniel Graf**

### **Introduction**

Nasal septum is a cartilaginous structure that bilaterally divides the nasal cavity and provides critical structural support and growth for the midface. A relatively frequent abnormality of the nasal septum is nasal septum deviation (NSD), which can result in nasal airway obstruction and consequently sleep disordered breathing (SDB) in children. The etiology of NSD is poorly understood, but it is more prevalent in older children. Since the nasal septum cartilage contributes to the growth of the midface, we hypothesize that nasal septum deviation is a consequence of underlying cartilage growth and differentiation defects. Here we test this hypothesis in a mouse model for midfacial hypoplasia.

### **Methods**

Mice with a neural crest-specific deletion of Bone Morphogenetic Protein 7 (Bmp7) (Bmp7<sup>ncko</sup>) present with midfacial hypoplasia and nasal airway obstruction. We investigated two time-points: 2 weeks, prior to airway obstruction and 4 weeks, established airway obstruction. Skeletal structures were assessed using micro-computed tomography ( $\mu$ CT). Molecular and cellular differences were established using histology, immunofluorescence and gene expression analysis. Quantitative shot-gun proteomics was conducted on isolated nasal cartilage and STRING database was used to identify differentially regulated cellular pathways in the nasal septum.

### **Results**

70% of Bmp7<sup>ncko</sup> mice die between 3-6 weeks, the period of rapid midfacial outgrowth.  $\mu$ CT analysis confirmed a lack of midfacial growth. NSD was evident at 4 weeks but not at 2 weeks. At 2 weeks, a reduction in proliferation and an increase in apoptosis in the nasal septum was detected. The nasal cartilage was histologically inconspicuous at 2 weeks, however, structural changes were evident at 4 weeks. The normally hyaline cartilage showed signs of chondrocyte hypertrophy (expression of IHH, MMP13) at the site of NSD. Molecular changes such as the upregulation of Frzb in the nasal cartilage were already evident at 2 weeks, preceding NSD. Similarly, proteomics and STRING analysis established that extracellular matrix organization and cell metabolism were already de-regulated at 2 weeks preceding NSD.

### **Conclusion**

Loss of BMP7 alters nasal cartilage properties and compromised its growth. The change in cartilage properties was preceded by cellular changes in chondrocytes themselves, placing BMP7 as a critical factor for cartilage growth and differentiation. Our findings suggest that NSD occurs as a consequence of underlying nasal septum growth and cartilage defects, explaining its association with midfacial hypoplasia and relatively late appearance. Thus, NSD might indicate altered cartilage biology in affected children.

Funded by **WCHRI Innovation Grant, NSERC, American Association of Orthodontists Foundation, Gilbert K Winter Fund**

The Power of Partnership



Abstract # 18  
Presenter: Reklow, Robert  
Supervisor: Funk, Gregory  
Title: Postnatal developmental changes in the effects of ATP, adenosine and adenosine clearance mechanisms on activity of the preBötzing Complex inspiratory rhythm generating network  
Authors: Robert J. Reklow, Tucaauê S. Alvares, Megan A. Hansen, Sara M. Frangos, Gregory D. Funk

## Introduction

Breathing in premature infants often stops briefly (apnea) because the brainstem network that controls breathing is immature (apnea of prematurity, AOP). Apneas reduce oxygen levels (hypoxia) triggering the biphasic hypoxic ventilatory response (HVR), which comprises an initial increase in ventilation followed by a centrally mediated depression that can be life-threatening in AOP. The transmitter ATP is released in the preBötzing Complex (preBötC, brain region that generates inspiration), during hypoxia where it excites breathing and attenuates the secondary depression by activating P2Y1 receptors (Rs). However, ATP is metabolized into adenosine (ADO), which contributes to the depression. Thus, the net effect of ATP is determined by a balance between its excitatory actions and the inhibitory actions of ADO. Caffeine, an ADOR antagonist, stimulates breathing in AOP, but new therapies are required because ~20% of infants do not respond to caffeine. Our overall goal is to determine how factors that control the ATP-ADO balance change during development and contribute to the greater hypoxic depression of breathing in prematurity. Here we test during development whether the sensitivity of the preBötC to P2Y1R excitation increases; whether the inhibitory actions of ADO decrease; and whether equilibrative nucleoside transporters (ENTs), which remove ADO from its extracellular site of action, become more effective at terminating the inhibitory actions of ADO.

## Methods

Using medullary slices of mice (0-12 days old, corresponds to ~26-38 weeks human gestation), the inspiratory activity generated by preBötC was recorded from XII nerves and the effects of ATP, ADO, MRS 2365 (P2Y1 agonist) and the ENT inhibitor (NBMPR) on preBötC activity assessed. We also assessed the HVR (10% O<sub>2</sub>) of wild type (WT) and ENT knockout (ENT KO) mice from P0-14 using plethysmography.

## Results

In vitro, ATP (100 µM), which activates P2Y1 and ADORs, increased preBötC frequency ~50% from P0-8; this effect increased to 85% at P9-12. When A1 ADORs were blocked by DPCPX, the ATP excitation was the same at all ages. ADO depressed frequency by 18% and 34% in P0-2 and P3-5 mice, respectively, but only 11% in P9-12 mice. MRS 2365 (100 µM) evoked a 2-fold frequency increase in all age groups. We then compared the HVR of WT and ENT KO mice in vivo. In contrast to WT, in which peak ventilation was depressed by 30%, ventilation fell by 42% in ENT KO mice; most important, at P0-3 ventilation fell more than 100% (below baseline) in the first 40 s. In vitro, the duration of the frequency inhibition evoked by ADO was almost doubled in the KO mice compared to WT, while the ENT-1 inhibitor (NBMPR) significantly increased (10%) baseline frequency in WT mice.

## Conclusion

Data suggest sensitivity of the preBötC network to P2Y1Rs remains constant while sensitivity to ADO decreases through postnatal development, which results in greater ATP-mediated potentiation in juvenile mice. Data also suggest that ENTs set basal ADO tone in the preBötC, but under high ADO loads, as during hypoxia, ENTs help clear ADOe and limit the ADO-depression of the preBötC inspiratory network.

Funded by WCHRI (Graduate Scholarship), WCHRI and FoMD Bridge Funding; CIHR; Lung Association of Alberta & NWT, CFI, NSERC.

The Power of Partnership



Abstract # 19  
Presenter: Wong, Jason  
Supervisor: Lou, Edmond  
Title: Feasibility of using machine learning to aid clinicians to predict curve progression past moderate severity for children with adolescent idiopathic scoliosis  
Authors: Wong, Jason; Lou, Edmond; Reformat, Marek

### Introduction

Scoliosis is a three-dimensional spinal deformity, which involves a lateral curvature coupled with vertebral rotation. Adolescent idiopathic scoliosis (AIS) is the most common form of scoliosis, affecting 1% to 3% of adolescents aged 10 to 18 years old. Determining the risk of curve progression or worsening is challenging in children with AIS. Knowing this risk allows for early initiation of treatment to maximize effectiveness. Individual risk factors to progression have been identified. However, these factors may interact with each other and complicate clinical decision making. This study aimed to investigate the feasibility and validity of using machine learning to predict curve progression past 25° for AIS patients.

### Methods

From the Edmonton scoliosis clinical records, AIS patients who were less than 18 years old, had a Cobb angle less than 19°, and had received no brace treatment were identified. Based on these inclusion criteria, 282 total clinical visits were extracted and split into two parts: 210 visits for a training set and 72 visits for a test set. Random forest models, a machine learning algorithm, were applied to predict whether a patient would progress past the moderate severity threshold of 25°. The predictors consisted of sex, age, menarche, Risser sign, max Cobb angle, number of curves, Cobb angle divided by the number of vertebrae within the curve, body mass index, and time passed between clinical visits. Determining the optimal parameter combinations of the random forests required training multiple models and evaluating them using ten-fold cross validation, a technique for assessing how well a model generalizes to an independent data set. Once the optimal random forest was determined, its performance was evaluated on the 72 visit test set. Among the test set, 32 visits involved prediction 6 months into the future. The classification accuracy, sensitivity, and specificity for both sets of visits were calculated.

### Results

Treating the classifications of an AIS patient into past 25° as positive and less than 25° as negative, the optimal random forest yielded a classification accuracy of 73.6% with a sensitivity of 66.7% and a specificity of 80.6% for the whole 72 visit test set. For the 32 visits that involved a 6 month prediction, a classification accuracy of 65.6% with a sensitivity of 40.0% and a specificity of 77.3% was obtained.

### Conclusion

Applying random forest models to assist clinicians with prediction of curve progression past moderate severity is feasible. However, further study into other machine learning algorithms, including neural networks and support vector machines, still need to be investigated to determine if improvements to classification accuracy can be made.

Funded by WCHRI Graduate Studentship; NSERC Canada Graduate Scholarship - Master's; QEII Graduate Scholarship

The Power of Partnership





Abstract # 20  
Presenter: Chan, Andrew  
Supervisor: Lou, Edmond  
Title: Accuracy of screw placement in 3D-ultrasound (3DUS) based spinal navigation in adolescent idiopathic scoliosis phantom vertebrae  
Authors: Chan, Andrew; Parent, Eric; Mahood, Jim; Lou, Edmond

## Introduction

Adolescent idiopathic scoliosis is a 3D spinal deformity affecting 2-3% of adolescents. In severe cases, surgery is needed to correct the deformity, requiring careful insertion of screws through the two narrow vertebral pedicles which are particularly small in adolescent patients. Although CT-navigation systems can reduce the risk of neurologic injury from screw insertion, pediatric patients are exposed to ionizing radiation and surgical staff may receive scattering radiation. Instead of CT scans, intra-operative 3D ultrasound (3DUS) could be used to capture the vertebral surface and then a pre-op 3D vertebra model could be registered to the surface and displayed for navigation surgery. This study evaluated a custom 3DUS navigator for speed (<1min) and accuracy of pedicle screw placement (<2mm and 5 degrees).

## Methods

A 3DUS navigation system was developed by integrating an ultrasound scanner using a 13.3 MHz transducer with four Optitrack Prime 13W motion capture cameras to generate 3DUS images of vertebral surfaces and localize them in the capture volume.

A T4-T9 vertebral segment was CT scanned, converted into a 3D virtual model, modified to include holes of known trajectory placed through the pedicles, and then 3D printed. The printed model was mounted to a LEGO pegboard (<5µm precision) and ultrasound scanned in a water bath. Each vertebra from T5 to T8 was imaged three times at the capture volume origin (12 scans, 24 screws) to test repeatability. To test accuracy, the phantom was scanned at the volume origin, then rotated in yaw, pitch and roll to 15 degrees in each direction (28 scans, 56 screws). The phantom was then translated 10cm to the north, east, south and west in the volume and scanned in neutral orientation for a total of 16 scans (32 screws). A CT vertebral image was registered to the 3DUS surface in a custom Matlab algorithm for each scan

A 3D environment was created in Unity to display the registered vertebral model for each scan while tracking a surgical probe. Navigation positional accuracy was evaluated by placing the probe into the pedicle hole and then measuring the distance between the probe tip and the hole center as displayed in Unity. Angular accuracy was evaluated by comparing the navigation-acquired angle of pedicle holes to designed hole trajectories. Root-mean squared error and standard deviation were calculated for both.

## Results

Acquisition of each scan required  $25.6 \pm 3.2$ s. Registration required  $15.4 \pm 2.3$ s. Angular repeatability was  $0.3 \pm 0.1$  deg (0.2-0.5 deg) while positional repeatability was  $0.3 \pm 0.2$ mm (0.1-0.6mm). The root-mean-squared angular accuracy was  $1.5 \pm 0.8$  deg (0.0-4.2 deg) while positional accuracy was  $1.2 \pm 0.5$ mm (0.0-2.2mm), with one screw failing the 2mm accuracy criteria (98.9% success from 88 screws).

## Conclusion

Navigation with 3D ultrasound for screw placement in scoliosis surgery is feasible in both speed and accuracy, helping to minimize radiation exposure in pediatric patients. Further study on the effect of surrounding soft tissues on navigation accuracy is needed before for usage in scoliosis surgery.

Funded by Alberta Spine Foundation, Alberta Innovates, NSERC

The Power of Partnership



Abstract # 21  
Presenter: Hurd, Caitlin  
Supervisor: Yang, Jaynie  
Title: **Early, intensive lower extremity training enhances gross motor function in children with perinatal stroke: Results of a randomized controlled trial**  
Authors: **Caitlin Hurd, Donna Livingstone, Kelly Brunton, Allison Smith, Ephrem Zewdie, Monica Gorassini, Adam Kirton, Man-Joe Watt, John Andersen, Jerome Yager, Jaynie F. Yang**

### **Introduction**

Perinatal stroke injures motor regions of the brain during development, thereby reducing activity in motor pathways and motor function. Current interventions for the lower extremity focus on passive approaches, such as stretching, braces and botulinum toxin injections, yet research in other mammals suggests that activity is critical to normal maturation of motor pathways. We hypothesize that intensive, activity-based intervention early in development will improve motor function for children following perinatal stroke. The objective of this study was to determine the efficacy of an early, activity-intensive intervention on gross motor function and walking, as compared to usual care.

### **Methods**

We conducted a two-centre, delay-group, single-blind, randomized controlled trial (RCT), in which one group received intervention immediately (Immediate Group), while the control group received a delayed intervention (Delay Group). In addition, a separate cohort of children living beyond commuting distance was trained by their parents, who were coached by physical therapists (PTs). Participants were 8 months to 3 years old with MRI-confirmed perinatal ischemic stroke and early signs of hemiparesis. The intervention was play-based, lower extremity activity, focused on weight-bearing and walking provided by PTs for 1 hour/day, 4 days/week for 12 weeks. Small foot and ankle weights were also used on the affected lower extremity to enhance activity. The primary outcome was the Gross Motor Function Measure-66 (GMFM-66), which was scored by therapists blinded to the child's group assignment. Secondary outcomes were gait analyses of treadmill walking, motor-evoked potentials from transcranial magnetic stimulation, and patellar tendon reflexes. Follow-up for all children occurred at four years old.

### **Results**

Thirty-three children participated in the study. The change in GMFM-66 score over 12 weeks showed significantly greater improvement in the Immediate Group compared to the Delay Group (change scores of  $6.5 \pm 2.2$  vs  $2.3 \pm 2.6$ , respectively). Continued improvement was seen for the 3 months following training for participants in the Immediate Group. Training intensively for 1 hour/day was feasible, as demonstrated by step counts  $> 1000$  steps/session for all children in the final week of training (range of 1370 – 3750 steps/session). Gross motor function results from parent training were more variable, with GMFM-66 change scores of  $4.2 \pm 2.9$  over the 12 weeks of training. Toe clearance and weight bearing symmetry during treadmill walking showed greater improvement in the Immediate Group than the Delay Group. Motor evoked potentials and tendon reflexes showed changes with maturation but not as a result of training.

### **Conclusion**

Early, activity-intensive lower extremity intervention for children with perinatal stroke is feasible and resulted in improvements in gross motor function beyond usual care. A multi-centre effectiveness trial using a parent-partnership model of rehabilitation is now underway.

Funded by **Women and Children's Health Research Institute, Canadian Institutes of Health Research, Alberta Innovates**

The Power of Partnership



Abstract # 22  
Presenter: Holt, Christopher  
Supervisor: Whittaker, Jackie  
Title: Sticking to it: A Scoping Review of Adherence to Exercise Therapy Interventions in Children and Adolescents with Musculoskeletal Conditions.  
Authors: Christopher J. Holt, Carly D. McKay, Linda K. Truong, Christina Y. Le, Douglas P. Gross, Jackie L. Whittaker

### Introduction

Exercise therapy is a core component of treatment for children and adolescents with musculoskeletal conditions. As exercise therapy effectiveness hinges on adherence, improving exercise therapy adherence is crucial for recovery and reducing long-term consequences. This scoping review consolidates what is known about exercise therapy adherence barriers, facilitators, and boosting strategies for youth with musculoskeletal conditions. In doing so, this review will inform clinical practice and future research.

### Methods

This review was guided by Arksey and O'Malley's 5-stage framework and the PRISMA Extension for Scoping Reviews. Six electronic databases were searched using predetermined search terms and Medical Subject Headings. English studies with original data featuring an adherence barrier, facilitator, or boosting strategy and youth ( $\leq 19$  years) with musculoskeletal conditions treated with exercise therapy were included. Two authors independently conducted title/abstract and full-text reviews. Study quality was assessed using the Mixed Methods Appraisal Tool. Descriptive consolidation and thematic analysis were completed using the Capability, Opportunity, Motivation and Behaviour (COM-B) framework.

### Results

Of 4,930 potentially relevant records, 34 studies representing 1,563 participants (65% female, 2-19 years of age) with 11 different musculoskeletal conditions and multiple exercise therapy interventions were included. Overall, adherence concepts were poorly reported across studies. Reported adherence rates ranged from 15%-99% of prescribed exercises. Time constraints, physical environment (e.g., location), and negative exercise experiences were commonly identified adherence barriers, while social support and positive exercise experiences were frequently identified facilitators. Reinforcement, exercise program modification, and education were commonly used adherence boosting strategies, despite being infrequently reported as barriers or facilitators. Exercise experience (positive/negative), time, and environment (physical and social) emerged as important themes related to exercise therapy adherence for youth with musculoskeletal conditions.

### Conclusion

Despite poor reporting of adherence concepts, a diversity of barriers and facilitators to exercise therapy for youth with musculoskeletal conditions exist. Existing strategies to boost adherence are not consistent with identified barriers or facilitators. Making exercise enjoyable, social, and convenient may be important to maximizing adherence in this population.

Funded by Women and Children's Health Research Institute (Graduate Studentship)

The Power of Partnership



Abstract # 23  
Presenter: Alam, Abrar  
Supervisor: Dyck, Jason  
Title: Resveratrol attenuates Doxorubicin-induced injury and later onset hypertension-induced cardiomyopathy through the inhibition of NLRP3 Inflammasome signalling  
Authors: Abrar S. Alam, Zaid H. Maayah, David D. Eisenstat, and Jason RB Dyck

### Introduction

Anthracyclines, such as doxorubicin (DOX), are very effective anticancer agents that are widely used in pediatric cancer patients. Nevertheless, anthracyclines are known to have adverse cardiotoxic effects that may go undetected but progress to cardiac dysfunction and eventually cardiomyopathy later in life. We have developed a pre-clinical model of occult DOX-induced cardiovascular toxicity in young mice and have demonstrated that juvenile exposure to DOX makes mice more susceptible to the detrimental effects of angiotensin II-induced hypertension later in life. Utilizing this model, we have also shown that co-administration of resveratrol with DOX in young mice attenuates detrimental late-occurring cardiovascular changes. However, the molecular mechanism responsible for protection remains unknown. As growing evidence suggests a central role of cardiac inflammation in the development of myocardial damage induced by chemotherapy, we proposed that a central player in the control of cardiac inflammation, the nucleotide-binding domain-like receptor protein-3 (NLRP3) inflammasome, is involved in both early and delayed DOX-induced cardiac dysfunction.

### Methods

5-week-old male mice were administered a low dose of DOX (4 mg/kg) or saline once a week for 3 weeks and then allowed to recover for 5 weeks. Following the 5-week recovery period, mice were infused with angiotensin II or saline for 2 weeks. In another cohort, mice were fed chow containing 0.4% resveratrol 1 week before, during, and 1 week after the DOX administrations. The gene expression levels of NLRP3 pathway members were determined using quantitative real-time polymerase chain reaction (qRT-PCR).

### Results

1 week after the last DOX administration, NLRP-3, Interleukin-18 (IL-18), and tumor necrosis factor  $\alpha$  (TNF $\alpha$ ) were induced in hearts of DOX-treated mice demonstrating molecular signs of cardiac inflammation and stress. In contrast, mice receiving DOX with resveratrol co-administration displayed low expression levels of IL-18, NLRP-3, and TNF $\alpha$  as well as in response to angiotensin II-induced hypertension later in the life. The inhibitory effect of resveratrol on the NLRP3 pathway was associated with the suppression of cellular redox regulator, thioredoxin interacting protein (TXNIP).

### Conclusion

Our data provides support that resveratrol attenuates DOX-induced injury and later onset hypertension-induced cardiomyopathy through the inhibition of NLRP3 inflammasome signaling and the reduction of cardiac inflammation during DOX treatment. These findings suggest that anti-inflammatory strategies that mitigate the cardiac damage of some chemotherapies but that don't affect the anticancer effects of the chemotherapy could be of therapeutic benefit.

Funded by Stollery Children's Hospital Foundation

The Power of Partnership



Abstract # 24  
Presenter: Beggs, Megan  
Supervisor: Alexander, Todd  
Title: Claudin-2 is necessary for increased intestinal calcium permeability and optimal bone mineralization early in life  
Authors: Megan R. Beggs, Ahsan Raza, Kai Busch, Henrik Dimke, Allen Plain, Vetii Flockerzi, R. Todd Alexander

### Introduction

Infants and children must maintain a net positive calcium ( $\text{Ca}^{2+}$ ) balance in order to achieve optimal peak bone mineral density by early adulthood. Across the small intestine,  $\text{Ca}^{2+}$  is absorbed via transcellular and paracellular pathways although the molecular details of these pathways in early life are not well delineated. Claudins are tight junction proteins that confer selective permeability to epithelia. Claudins-2, and -12 are expressed and have been implicated in paracellular  $\text{Ca}^{2+}$  permeability across intestinal epithelia. To date, the functional contribution of these claudins to  $\text{Ca}^{2+}$  permeability ( $\text{PCa}^{2+}$ ) of small intestine segments and the subsequent effect on bone mineralization has not been defined. The objectives of this study were therefore to 1) determine if  $\text{PCa}^{2+}$  across small intestine segments is increased early in life 2) to assess whether claudin-2 or -12 contribute  $\text{PCa}^{2+}$  and 3) to determine if decreased intestinal  $\text{PCa}^{2+}$  leads to reduced bone mineralization early in life.

### Methods

Wildtype (WT) FVB/N, *Cldn2* KO and *Cldn12* KO mice were used. Infant mice at P14 and adult mice at 6-8 weeks were employed for functional studies. Gene expression was examined by real-time PCR, protein abundance and localization by immunohistochemistry, bone analysis by micro CT and histology.  $\text{PCa}^{2+}$  was measured on ex vivo intestinal segments using bi-ionic dilution potentials in Ussing chambers.

### Results

$\text{PCa}^{2+}$  was 50% greater across of the duodenum and 2-fold greater across the jejunum and ileum at P14 compared to 2 months.  $\text{PCa}^{2+}$  across all segments of small intestine were not different between *Cldn12* WT and KO mice at both P14 and 2 months of age. However,  $\text{PCa}^{2+}$  across jejunum and ileum of *Cldn2* KO mice was 50% less than WT at P14 and no longer different than at 2 months in WT and KO mice. Similarly, *Cldn2* gene expression in the jejunum and ileum was significantly greater from P1 to P14 compared to at 1 to 6 months in WT mice. Immunohistochemical staining of jejunal and ileal segments of WT mice revealed abundant staining in the villi at P14 that disappears at 6 weeks. When femurs of *Cldn2* WT and KO mice at P14 were analyzed, we found significantly decreased bone volume, cross sectional thickness, and bone mineral density in *Cldn2* KO mice.

### Conclusion

Younger mice have significantly increased  $\text{Ca}^{2+}$  permeability along the small intestine relative to older animals, which is mediated by claudin-2 in the jejunum and ileum. This enhanced paracellular calcium permeability contributes to a positive calcium balance enabling normal bone mineralization during postnatal development.

Funded by WCHRI supported by the Stollery Children's Hospital Foundation, NSERC, CRC, DMRC, DFG.

The Power of Partnership



Abstract # 25  
Presenter: Keshavarz-Bahaghighat, Hedieh  
Supervisor: Seubert, John  
Title: **Genetic deletion of soluble epoxide hydrolase preserves cardiac function in aged female mice**  
Authors: **Hedieh Keshavarz-Bahaghighat, K. Lockhart Jamieson, Ahmed. M Darwesh, Deanna Sosnowski, John M. Seubert**

### **Introduction**

Biological aging is an inevitable part of life that has intrigued individuals for millennia. The progressive decline in biological systems impacts cardiac function and increases vulnerability to stress contributing to morbidity and mortality in elderly individuals. Yet, our understanding of the molecular, biochemical and physiological mechanisms as well as sex differences is limited. There is growing evidence indicating CYP450 epoxygenase-mediated metabolites of n-3 and n-6 polyunsaturated fatty acids are active lipid mediators regulating cardiac homeostasis. These epoxy metabolites are rapidly hydrolyzed and inactivated by the soluble epoxide hydrolase (sEH). The current study aims to characterize cardiac function in young and aged sEH null mice compared to the corresponding wild-type (WT) mice.

### **Methods**

Cardiac function was assessed in both young (3 months) and aged (16 months) WT and sEH null male and female mice by echocardiography. Western blotting was done to measure changes in protein expression of phosphorylated Akt, as an indirect marked age-related cardiac hypertrophy and inflammation, acetyl Mn-SOD, sEH and mEH. While the etiology of age-related cardiovascular pathogenesis is poorly understood, it has been shown that deterioration of mitochondria with increased levels of oxidative stress over time plays a critical role in age-related cardiac dysfunction. Indicators of oxidative stress status, protein carbonyl level and SOD activity were determined in the hearts of experimental animals. Citrate synthase activity assay was performed to evaluate the age-related alterations in overall mitochondrial content.

### **Results**

All aged mice had significantly increased body weights compared to young counterparts and significant increases in heart weight:tibia length, marker of hypertrophy, were observed in aged WT and aged sEH null male mice but not in aged female sEH null mice. There was a marked decline in cardiac function in aged WT mice, notably significant decreases in ejection fraction and fractional shortening in both female and males. Interestingly, female aged sEH null mice demonstrated preserved cardiac function compared to aged WT and sEH null males. There was an increase in protein expression level of phosphorylated Akt in all aged mice. Consistent with changes in increased acetyl Mn-SOD expression, Sirt-3 activity significantly decreased over aging in both WT males and females and sEH null males but not sEH null females. Markers of oxidative stress demonstrated age-related increase in protein carbonyl levels in both WT and sEH null males but not females. With aging, the activity level of SOD was decreased significantly in WT animals which was preserved in aged sEH null animals, regardless of their sex. Measurement of citrate synthase activity, revealed no significant age-related alterations in the activity of citrate synthase, suggesting that overall mitochondrial content is not profoundly changed during aging.

### **Conclusion**

Together these data demonstrate genetic deletion of sEH in mice correlates with preserved cardiac function in female mice.

Funded by **Heart and Stoke Foundation; WCHRI (Royal Alexandra Hospital Foundation)**

The Power of Partnership



Abstract # 26  
Presenter: Bilyk, Lena  
Supervisor: Postovit, Lynne  
Title: **Embryonic protein nodal as a potential marker of drug resistance in ovarian cancer**  
Authors: Lena Bilyk, Laura Lee, Dylan Dieters-Castator, Nhu D. Le, Linda Cook, Martin Koebel, Lynne Postovit

### **Introduction**

Ovarian cancer (OC) is the most aggressive gynecological cancer due to the high rate of chemoresistant recurrence. Aggressive cancer cells can exploit normally dormant embryonic stem cell pathways to promote cancer cell plasticity and tumor recurrence following chemotherapy. The objective of this study is to investigate the role of embryonic morphogen Nodal as a potential biomarker of OC cell plasticity, progression and resistance to chemotherapy.

### **Methods**

We applied bioinformatics approach, RNA sequencing and mass spectrometry (MS) to explore the impact of Nodal on OC cells and disease outcome. We conducted in vitro assays designed to assess growth, cancer stem cell like phenotypes and chemoresistance in OC cells with different sensitivity to chemotherapy, wherein Nodal was added with Nodal expression construct, or knockdown with shRNA. IHC staining to evaluate Nodal expression was conducted in 563 high-grade serous OC (HGSOC) tissue microarrays (OVAL-BC study cohort). Survival analysis was performed based on Nodal expression in tissue microarrays in OVAL-BC study cohort and TCGA data.

### **Results**

In vitro, in OC cells sensitive to chemotherapy, Nodal expression significantly increased resistance to cytostatic drugs, tumorigenicity, cancer cell plasticity (EMT, cancer stem cell like phenotype).

By RNA sequencing and MS analysis we discovered that Nodal induces transcriptional reprogramming in OC cells, sensitive to chemotherapy, via altering immune and inflammatory response, metabolism and drug resistance gene expression. More than 3000 genes were up- or down-regulated in response to Nodal overexpression in chemotherapy sensitive OC cells.

In univariate Kaplan-Meier analysis, high Nodal expression was significantly associated with shorter OC specific survival. HGSOC patients with high Nodal expression were less likely to achieve complete debulking after surgery compared to patients with low Nodal expression. In a Cox Hazard model with time dependent coefficient we found that the hazard ratio for high Nodal expression increases over time and becomes significant, as time passes 4 years suggesting that Nodal promotes disease recurrence and progression

### **Conclusion**

Nodal predicts poor survival and aggressive phenotype in patients with most aggressive HGSOC. Nodal likely drives tumorigenic potential and resistance to platinum and taxol in OC cells, sensitive to chemotherapy, by promoting cancer cell plasticity and upregulating target genes involved in immune suppression, inflammation, drug resistance and metabolism. Nodal may hold a promise as a therapeutic target to prevent OC recurrence following chemotherapy.

Funded by CIHR

The Power of Partnership



Abstract # 27  
Presenter: Jamieson, Lockhart  
Supervisor: Seubert, John  
Title: Pharmacological or genetic inhibition of soluble epoxide hydrolase demonstrates cardioprotection following myocardial infarction in aged female mice  
Authors: K. Lockhart Jamieson, Ahmed M. Darwesh, Deanna K. Sosnowski, Mandira Choppella, Tim Lee, Saumya Shah, Hao Zhang, Wang Wang, Pavel Zhabyeyev, Jun Yang, Bruce Hammock, Matthew Edin, Darryl Zeldin, Zamaneh Kassiri, Gavin Y. Oudit, John M. Seubert

### Introduction

Ischemic heart disease accounts for a significant proportion of death and disability in aged individuals. The influence of age and sex on the development and presentation of heart disease is often underestimated in drug development. CYP450 metabolism of polyunsaturated fatty acids (PUFAs) generates numerous metabolites, epoxy lipids, that exhibit a wide range of cellular effects. Previous studies demonstrate epoxy lipids can regulate and protect mitochondria resulting in preserved cardiac function following ischemic injury. The epoxy lipids are further metabolised by soluble epoxide hydrolase (sEH) into corresponding diol products with differing activities. Our first aim was to characterize epoxy lipid metabolism and sEH expression in tissues obtained from the human left ventricle (LV). Second, we aimed to assess whether pharmacologic inhibition or genetic deletion of sEH preserves cardiac and mitochondrial function post-ischemia in aged mice.

### Methods

Human tissues were obtained from male (n=12) and female (n=5) patients with a previous MI as part of the Human Explant Heart Program (HELP) and non-failing control (n=10) heart tissues were obtained from the Human Organ Procurement and Exchange (HOPE) program at the University of Alberta. Male and female C57BL6 (WT) and sEH null mice averaging 15 months old underwent permanent occlusion of the left anterior descending coronary artery (LAD). Pharmacological inhibition of sEH was achieved by giving vehicle (0.1% DMSO) or sEH inhibitor trans-4-[4-(3-adamantan-1-yl-ureido)-cyclohexyloxy]-benzoic acid (tAUCB, 10 mg/ml in 0.1% DMSO) to WT mice in the drinking water four days before or on the day of surgery (n=5-26) and continued ad libitum for 28 days. Cardiac function was assessed at baseline, 7 and 28 days post-MI by echocardiography and electrocardiogram. LV were assessed for changes to protein expression and mitochondrial enzymatic activity; cardiac fibres were used to assess mitochondrial respiration. Human heart tissue was assessed for changes to the PUFA metabolite profile by LC-MS/MS.

### Results

Individuals with a previous MI had significantly elevated levels of sEH expression correlating with changes to the PUFA metabolite profile and decreases in mitochondrial function. In mice, genetic deletion or treatment with the sEH inhibitor tAUCB significantly preserved cardiac function and increased survivability following MI. Importantly, these cardioprotective effects were only observed in aged female mice.

### Conclusion

In summary, these data suggest sEH is a potential pharmacological target for humans who had experienced a previous MI and suffer from heart failure. Moreover, the mouse data indicate an age-dependent sex-difference, suggesting targeting sEH may be more effective in improving post-ischemic heart function in middle-aged females.

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The Power of Partnership





Abstract # 28  
Presenter: Weaver, Olivia  
Supervisor: Vine, Donna  
Title: Fish oil and metformin interventions to target cardiometabolic risk in high-risk women with polycystic ovarian syndrome  
Authors: Olivia Weaver, Mahua Ghosh, Katerina Maximova, Spencer Proctor, Donna Vine

### Introduction

Polycystic Ovarian Syndrome (PCOS) is an endocrine-metabolic disease that affects 15-20% of women of reproductive age and is highly associated with the metabolic syndrome (MetS): obesity, insulin resistance and dyslipidemia, and increases the risk of early development of Type 2 Diabetes (T2D) and Cardiovascular disease (CVD). Atherogenic dyslipidemia occurs in >70% of women with PCOS and includes high fasting plasma triglycerides (TG), LDL-C, non-HDL-C or ApoB, and low HDL-C. Metformin is commonly prescribed to improve glucose sensitivity in PCOS but has been reported to have limited effects on blood lipids. Furthermore, treatments for dyslipidemia are limited due to safety and efficacy. Fish oil (FO) and Icosapentyl ethyl supplementation have been shown to reduce fasting TG, but the effectiveness of FO in combination with metformin is unknown in conditions of the MetS and PCOS. The aim of this pilot study was to determine the effect of FO in combination with metformin on fasting blood lipids and glucose-insulin indices compared to FO and metformin treatment alone in high-risk women with PCOS.

### Methods

Women 18-30 years of age with PCOS (n=30) participated in a randomized clinical trial. Intervention groups included: metformin (Met), FO, or FO+Met treatment for 12 weeks. Inclusion criteria consisted of PCOS diagnosis, BMI >25 kg/m<sup>2</sup>, elevated fasting plasma triglycerides, impaired insulin sensitivity and/or diagnoses of T2D. Fasting (overnight fast 16hrs) plasma lipids, insulin, glucose and endocrine hormones were analysed using standard U of Alberta Hospital calorimetric and ELISA protocols. Data was analyzed using ANOVA (p<0.05) (GraphPad 8.0).

### Results

FO+Met treatment significantly reduced fasting plasma TG from baseline compared to other treatment groups. Met and FO+Met treatment groups tended to reduce LDL-C, and non-HDL-C, as well as blood glucose, fasting insulin and HOMA-IR. However there were no significant effect of treatments on insulin-glucose indices or endocrine hormones.

### Conclusion

FO+Met combination treatment significantly reduces fasting plasma TG levels in women with PCOS. A larger and longer-term trial is warranted to determine the efficacy of fish oil and metformin treatment to improve plasma TG, apoB-lipoproteins and subclinical atherosclerotic CVD risk.

Funded by CIHR, ADI, WCHRI

The Power of Partnership



Abstract # 29  
Presenter: Meah, Victoria L.  
Supervisor: Davenport, Margie H.  
Title: Cardiac responses to incremental resistance exercise in pregnancy: Resistance Exercise in Pregnancy Study (REPS)  
Authors: V.L. Meah, M. Strynadka, C.D. Steinback, M.H. Davenport

Program for Pregnancy and Postpartum Health, Faculty of Kinesiology, Sport, and Recreation, University of Alberta, Edmonton, AB T6G 2E1, Canada.

### Introduction

The 2019 SOGC/CSEP Guideline for Physical Activity throughout Pregnancy provided specific recommendations for aerobic exercise based on demonstrated health benefits. Such recommendations could not be provided for resistance exercise (RE) due to a paucity of information on this modality, including uncertainties regarding the safety of Valsalva maneuver (VM). The aim of this observational study was to determine the acute cardiac responses to different intensities of RE completed with and without VM during pregnancy.

### Methods

Healthy pregnant (n=15; 23±6 weeks gestation; 33±3 years; pre-pregnancy BMI: 22.8±4.5 kg.m<sup>2</sup>) and non-pregnant women (n=15; 32±8 years; BMI: 23.2±2.5 kg.m<sup>2</sup>) were recruited from the local community. Maximal strength over 10-repetitions (10RM) for seated leg press was determined using an incremental protocol (pregnant: 81±24 kg, non-pregnant: 90±31 kg; P=0.364). Women then underwent standardized assessments of cardiovascular function including cardiac output (echocardiography), heart rate (ECG), blood pressure (photoplethysmography) and global longitudinal strain (GLS; speckle tracking echocardiography) at rest, during RE at 20, 40 and 60% 10RM without VM, and during 40%10RM with VM. Significant differences ( $\alpha=0.05$ ) were determined for between-subjects at rest and within-subjects for 40%10RM with and without VM using independent t-tests. A general linear model, with resting value as covariate, was used to identify between- and within-subjects differences during RE.

### Results

Cardiac output and heart rate, but not blood pressure, were significantly greater in pregnant women at rest (4.4±0.9 vs. non-pregnant: 3.3±0.7 L.min<sup>-1</sup>; P=0.003; 71±13 vs. non-pregnant: 61±9 beats.min<sup>-1</sup>, P=0.025). When accounting for resting hemodynamics, there were no significant differences in cardiac output, heart rate or blood pressure responses to RE with and without VM. GLS was not different between groups at rest or during RE without VM, but was significantly greater in pregnant women during VM at 40%10RM compared to without (-17.6±2.8 vs. -16.1±4.1%, respectively; P=0.049), although this difference was not considered functionally relevant.

### Conclusion

These results support that non-pregnant and pregnant women have similar cardiac responses to RE at varying intensities, thereby reinforcing the safety of this exercise modality during pregnancy. Furthermore, our findings support that completion of VM during RE does not have any adverse effect on cardiac function in pregnant women.

Funded by WCHRI Postdoctoral Fellowship, Lois Hole Hospital for Women, Undergraduate Research Initiative, Faculty of Kinesiology Human Performance Fund, Heart & Stroke Foundation

The Power of Partnership



Abstract # 30  
Presenter: Pandya, Vrajesh  
Supervisor: Goping, Ing Swie  
Title: BIK drives an aggressive breast cancer phenotype through sublethal apoptosis and predicts poor prognosis of ER-positive breast cancer  
Authors: Vrajesh Pandya, John Maringa Githaka, Namrata Patel, Richard Veldhoen, Judith Hugh, Sambasivarao Damaraju, Todd McMullen, John Mackey, Ing Swie Goping

### Introduction

Apoptosis is fundamental to normal animal development and is the target for many anti-cancer therapies. Recent studies have explored the consequences of “failed apoptosis” where the apoptotic program is initiated but does not go to completion and does not cause cell death. Nevertheless, this failed apoptosis induces DNA double-strand breaks generating mutations that facilitate tumorigenesis. Whether failed apoptosis is relevant to clinical disease was unknown. BCL-2 interacting killer (BIK) is a stress-induced BH3-only protein that stimulates apoptosis in response to hormone and growth factor deprivation, hypoxia and genomic stress. We have previously shown that high levels of BIK predict poor survival in heterogeneous cohorts of breast cancer patients. It was not known whether BIK actively promoted cancer aggression, and if so, what was the underlying mechanism behind aggressiveness of BIK-high tumors. Furthermore, the relevance of BIK prognostic signature in specific breast cancer subtypes was unidentified. We investigated these issues through a two-pronged approach.

### Methods

We examined BIK levels in primary tumors and generated doxycycline-inducible cell lines that express BIK in a controlled manner. To examine BIK-mediated cancer aggression, we employed in vitro assays that test anchorage-independent growth, stem-cell enrichment, and cell migration. We employed various biochemical and cell biological assays to elucidate the mechanism. To interrogate BIK's association with cancer aggression in vivo, we examined BIK mRNA and protein levels in multiple cohorts of patients in relation to disease relapse and/or death.

### Results

We discovered that BIK induces failed apoptosis with limited caspase activation and genomic damage in the absence of extensive cell death. Surviving cells acquire aggressive phenotypes characterized by enrichment of cancer stem-like cells, increased motility and increased anchorage-independent growth. Furthermore, by utilizing six different cohorts of patients (total n=969), we discovered that high BIK mRNA and protein levels predicted clinical relapse of Estrogen receptor (ER) positive cancers, which account for almost 70% of all breast cancers diagnosed but had no predictive value for hormone receptor-negative (triple-negative) patients.

### Conclusion

Our study demonstrates that BIK actively contributes to cancer aggression through sublethal apoptosis-mediated DNA damage, and identifies high BIK mRNA and protein levels as a prognostic biomarker for ER-positive patients.

Funded by Alberta Cancer Foundation

The Power of Partnership



Abstract # 31  
Presenter: Ferdinands, Alexa  
Supervisor: Raine, Kim D.  
Title: How do young people encounter body size talk on YouTube?

Authors: Alexa Ferdinands, Melissa Bernaldez, Keshinee Moonian, Tara-Leigh F. McHugh, Kate Storey, Kim D. Raine

### **Introduction**

In a world where obesity is often described as a “public health crisis”, young people who live in fat bodies may be stigmatized as “problematic”. We conducted an institutional ethnography to explore the current day social organization of young people’s weight experiences. We learned through interviews how young people (n=16, aged 15-21, self-identifying as fat) regularly use medicalized language, such as the body mass index, in their talk. We were curious about how they acquired such language. Social media, in particular YouTube, surfaced as a probable source in our interviews. This study pursued this line of inquiry by exploring the body size talk that young people encounter as they navigate YouTube.

### **Methods**

A data collection guide was developed with two undergraduate research assistants, both previous interview participants. The guide included factors identified in earlier participant interviews such as age, ethnicity and gender of the people portrayed, terminology used, and viewers’ overall interpretations of the video. Research assistants searched YouTube for videos discussing body size in a way reflecting how they actually use YouTube in their everyday lives. They collected data on n=50 videos, each having >1 million views. Validity was enhanced by having the research assistants and project lead each viewing five of the same videos to observe how and whether interpretations differed. As a team, we then convened to unpack our findings as a means of consciousness-raising.

### **Results**

Data analysis is underway. This presentation will summarize YouTube analytic findings descriptively.

### **Conclusion**

Understanding body size talk on YouTube will help us learn how weight-related discourses are (re)produced among young people. By contributing to knowledge of the social organization of young people’s weight experiences, we can better inform strategies to reduce weight stigma in the places and spaces where young people live, learn, and play.

Funded by Vanier Canada Graduate Scholarship, WCHRI Graduate Studentship, Izaak Walton Killam Memorial Scholarship, Edmonton Community Foundation

The Power of Partnership



Abstract # 32  
Presenter: Tessier, Carmen  
Supervisor: Kosyrskyj, Anita  
Title: **Maternal prenatal depression is associated with infant gut colonization of Clostridium difficile at 3 months of age.**  
Authors: **Tessier CA, Obiakor CV, Vu K, Konya TB, Guttman DS, Lefebvre D, Sears MR, Becker AB, Azad MB, Mandhane PJ, Turvey SE, Moraes TJ, Subbarao P, Scott JA, Kosyrskyj AL; Canadian Healthy Infant Longitudinal Development (CHILD) Study Investigators.**

### **Introduction**

Approximately 30% of healthy infants are asymptotically colonized with Clostridium difficile (C. difficile). Infants colonized with this enteric pathogen have been found to have an increased risk for allergic sensitization, atopic dermatitis, recurrent wheeze, and asthma. Examining risk factors in animal models, researchers found that when mice were induced to present with depressive behaviour they were found to have reduced gut microbiota richness and diversity. Alterations in the gut microbiota increase susceptibility to colonization by C. difficile and other enteric pathogens. This study aimed to examine the impact of maternal prenatal depression on the colonization of C. difficile in infants at 3-months of age.

### **Methods**

This was a substudy of 1,500 term infants from the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort. Maternal reports were used to measure prenatal depression (Center of Epidemiological Studies Depression Scale) and feeding method (formula, mixed, exclusive breastfeeding). Birth mode (vaginal or cesarean section) were retrieved from hospital records. Fecal samples were collected at 3 months after home assessment. Analysis of C. difficile was performed using quantitative polymerase chain reaction (qPCR) with appropriate primers. Logistic regression was used to determine the association between maternal prenatal depression and C. difficile colonization at 3 months of age.

### **Results**

In our sample, one-third (31%) of the infants were colonized with C. difficile at three months of age. During their third trimester of pregnancy, 24% of mothers reported clinically significant depressive symptoms. Relative to no exposure, prenatal depression significantly increased the odds of C. difficile colonization in the infant (Odds Ratio [OR]=1.44, 95% Confidence Interval [CI], 1.11-1.85; p=0.006), adjusted for birth mode and breastfeeding status. Compared to exclusive breastfeeding, the odds of C. difficile colonization (p<0.001) was significantly increased for both formula and mixed feeding methods. Odds of C. difficile colonization was also greater in infants born by caesarean section versus vaginal delivery (p=0.002).

### **Conclusion**

At 3 months of age, infants of mothers who experienced prenatal depression had significantly increased risk of C. difficile colonization in their gut. Our findings further suggest that maternal mood may contribute to alterations in early infant microbiome, in addition to known infant gut microbiota determinants, such as feeding method and birth mode.

Funded by **Canadian Institutes of Health Research (CIHR)**

The Power of Partnership



Abstract # 33

Presenter: Obiakor, Chinwe Vivien

Supervisor: Kozyrskyj, Anita

Title: **The association between early life antimicrobial exposure and *C. difficile* colonization in infants**

Authors: Chinwe V. Obiakor, Jaclyn Parks, Tim Takaro, Hein Tun, Nadia Morales-Lizcano, Theodore Konya, David Guttman, Allan Becker, Meghan Azad, Diana Lefebvre, Piushkumar Mandhane, Theo Moraes, Malcom Sears, Stuart Turvey, Padmaja Subbarao, James Scott and Anita Kozyrskyj

### **Introduction**

Antimicrobial exposure in early life has been associated with gut microbiota dysbiosis and development of allergic diseases in childhood. In adults and older children, *Clostridioides difficile* (*C. difficile*) is the major pathogen responsible for antibiotic-induced diarrhea but the effect of colonization with this bacterium in infants is unclear. About 30% of infants are colonized with *C. difficile* without the presence of clinical symptoms, infection or diarrhea. However, colonization with this bacterium in infancy has been linked to development of asthma and allergic diseases later in life. The aim of this study was to determine the cumulative impact from antibiotics and environmental antimicrobials (household cleaning products) on *C. difficile* colonization in infants.

### **Methods**

This study population comprises of a representative sample of mothers and infants (N=1429) who were successfully enrolled in the Canadian Healthy Infant Longitudinal Development (CHILD) cohort. Infant antimicrobial exposure was obtained from hospital birth chart (maternal intrapartum antibiotic (IAP) and newborn intravenous antibiotic) and standardized questionnaires (infant oral antibiotic and household cleaning product use). Household cleaning product was based on frequency of use and split at median into lower and higher use. Fecal samples were collected at 3 months after home assessment. Analysis of *C. difficile* was performed using quantitative polymerase chain reaction (qPCR) with appropriate primers. Logistic regression analysis was used to determine the crude and adjusted association between antimicrobial exposure and *C. difficile* colonization.

### **Results**

In our study, 44% of infants were indirectly exposed to antibiotics via maternal IAP, 8% directly received an oral or intravenous antibiotic and 47% lived in households with higher use of cleaning product by 3 months. Infants were classified into 4 groups depending on antimicrobial exposure: no antibiotics and lower cleaning products use (NALC), any antibiotics and lower cleaning products use (AALC), no antibiotics and higher cleaning products use (NAHC), any antibiotics and higher cleaning products use (AAHC). Compared to the NALC infants the odds of *C. difficile* colonization was 38% higher (OR:1.38 95% CI:1.00-1.91; p=0.047) in the AALC infants, 52% higher (OR:1.52 95% CI 1.10-2.11; p=0.011) in the NAHC infants and 103% higher (OR:2.03 95% CI 1.49-2.78; p<0.001) in the AAHC infants. After adjusting for covariates, the increased odds of *C. difficile* colonization remained significant in the AAHC infants (aOR 1.50 95% CI 1.03-2.17; p=0.032).

### **Conclusion**

Colonization with *C. difficile* as well as antimicrobial exposure in early infancy has been linked to increased risk of asthma and allergy. Our study suggests that cumulative exposure to antibiotics and higher use of household cleaning products is not without consequence. Hence, the effect of antimicrobial exposure on the infant gut should be considered because colonization with *C. difficile* may be a marker for future health outcomes.

Funded by The lung association Alberta & NWT, Canadian Institutes of Health Research (CIHR) and AllerGen NCE

The Power of Partnership



Abstract # 34  
Presenter: Mander, Inderdeep  
Supervisor: Wine, Eytan  
Title: Finding the relationship between fiber and gut diseases in children

Authors: Inderdeep Mander, Alexandra Petrova, Jeremy Jerasi, Robyn Dickner, Heather Armstrong\*, Eytan Wine\*.

### **Introduction**

The etiology of inflammatory bowel diseases (IBD) remains unknown, although gut microorganisms and diet have been implicated. Interestingly, dietary fibers pass through the bowel undigested, and are fermented within the intestine by gut microbes, typically promoting gut health. Many IBD patients, along with IBS patients, describe experiencing sensitivity to dietary fibers although the reasons remain unclear. We and others have described an altered balance between commensal and pathobiont microbes in IBD. We hypothesize that the loss of fiber fermenting-microbes populating the IBD gut leads to dietary fibers not being efficiently broken down into their beneficial byproducts, resulting in binding of intact fibers to host cell receptors; this can ultimately drive pro-inflammatory responses and a microenvironment that promotes continued dysbiosis.

### **Methods**

ELISAs/qPCR were utilised to evaluate cytokine secretion/production, in response to fiber (5mg/mL) or pre-fermented fibers, cultured with microbes of interest, in both individual cell lines in vitro and biopsy tissues cultured ex vivo. Results were compared to clinical findings.

### **Results**

Whole-fibers induced pro-inflammatory cytokines in select cell types, and specific microbes were capable of fermenting fiber, and reducing the associated inflammation. Results were recapitulated in pediatric IBD biopsy tissues collected during endoscopy, cultured ex vivo; more so in patients with more severe disease. Whole-microbe intestinal washes from severe IBD patients were unable to ferment dietary fibers or reduce inflammatory response in macrophages.

### **Conclusion**

Understanding the relationship between dietary fibers, gut microbes, and intestinal inflammation will aid us in developing tailored dietary intervention to patients most likely to respond through the use of dietary recommendations, prebiotic and probiotic therapies.

Funded by WCHRI, CCC, Weston Foundation, Department of Pediatrics

The Power of Partnership



Abstract # 35  
Presenter: Vu,NgockKhanh  
Supervisor: Kozyrskyj,Anita  
Title: Beyond caesarean birth: Impact of prolonged labour on infant gut microbiota

Authors: Vu NK, Rai U, Chari RS, Guttman DS, Becker AB, Azad MB, Mandhane PJ, Sears MR, Lefebvre DL, Moraes TJ, Turvey SE, Subbarao P, Scott JA, Kozyrskyj AL

### Introduction

Caesarean section delivery is a well-known factor for microbial gut dysbiosis up until mid-infancy. However, little is known about the impact of other birth events such as prolonged labour or rupture of membranes on infant gut microbiota. This study investigates the direct and indirect effects of birth mode, prolonged labour and other perinatal exposures on infant gut microbiota.

### Methods

In a subsample of 999 infants born at or near-term in the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort, stool samples were collected at 3-4 months of age and microbial taxa profiled with 16S rRNA sequencing. Generalized structural equation model was employed to examine directional relationships between birth mode and prolonged stage 2 labour, and microbial diversity (Shannon index) and taxon abundance, taking into account primigravida status, pre-pregnancy obesity, prolonged rupture of membranes, intrapartum antibiotics prophylaxis, gestational age, exclusivity of breastfeeding and infant age at stool collection.

### Results

Four early life factors were associated with reduced total gut microbiota diversity in infants: vaginal birth ( $\beta=-0.10$ ,  $p=0.043$ ), prolonged stage 2 labour ( $\beta=-0.11$ ,  $p=0.01$ ), early term birth ( $\beta=-0.07$ ,  $p=0.056$ ) and exclusive breastfeeding ( $\beta=-0.34$ ,  $p<0.001$ ). Prolonged stage 2 labour mediated the association between reduced microbial diversity and birth mode, prolonged stage 1 labour and rupture of membranes. A first pregnancy was associated with reduced colonization of Bifidobacterium (OR = 0.70,  $p<0.001$ ) in the infant gut via 2 pathways: lower likelihood of exclusive breastfeeding and prolonged stage 2 labour.

### Conclusion

Aside from the physiologic effects of exclusive breastfeeding, prolonged labour and early term birth have the capacity to reduce microbial diversity in the infant gut. Maternal primigravida status is a risk factor for childhood allergic disease. By reducing Bifidobacterium abundance in the infant gut, this study suggests that prolonged labour, which is more common in first pregnancies, could be a pathway to allergic disease.

Funded by Canadian Institutes of Health Research (CIHR)

The Power of Partnership





Abstract # 36  
Presenter: Dijk, Stephanie  
Supervisor: Wine, Eytan  
Title: Microbial & metabolic changes with infliximab therapy in paediatric Crohn disease

Authors: Stephanie Dijk, Rosica Valcheva, Matthew W. Carroll, Zhengxiao Zhang, Juan Jovel, Geraldine H. Huynh, Alexandra Petrova, Karen Madsen, Wael El-Matary, Anne M. Griffiths, Hien Q. Huynh, and Eytan Wine.

### Introduction

By 2030, 1/100 Canadians are predicted to be diagnosed with inflammatory bowel diseases (IBD); approximately 25% of diagnosed cases are children. IBD include Crohn disease (CD) and ulcerative colitis (UC), and manifest with chronic gastrointestinal inflammation. Pathogenesis remains poorly understood but IBD are associated with alterations in microbial recognition and clearance, and an altered intestinal microbiome, including increased numbers of pathogenic organisms. Delineating how current therapies alter intestinal microbes and how the intestinal microbiome is associated with treatment outcomes is critical in understanding disease pathogenesis. Fecal short chain fatty acids (SCFA) are primarily produced through fermentation by beneficial gut microbes, serve as a preferred fuel source for colonocytes, and have multiple beneficial effects (including on gut immune homeostasis). SCFA levels are altered in IBD, and administration shows some therapeutic effect. These and other microbial metabolites have been minimally researched in pediatric IBD, and may explain treatment mechanisms or supply additional therapeutic targets or biomarkers.

### Methods

A multi-centre prospective Infliximab (IFX) dose to level pharmacokinetic study during induction therapy in paediatric Crohn disease patients (IDeaL) was conducted. Thirty-five patients (18 males) were recruited from three Canadian pediatric tertiary-care IBD centres and received five IFX doses over 22 weeks. Biospecimens were collected at drug initiation and completion. Stool was analyzed for SCFA content using gas chromatography, and faecal calprotectin (FCP; as a marker of intestinal inflammation) using ELISA; fecal DNA was extracted for 16s rRNA sequencing. Urine metabolites were analysed using gas chromatography. Findings were correlated with clinical features and treatment outcomes.

### Results

With IFX treatment fecal SCFA concentration increased. The proportion of acetate decreased while total acetate content increased; butyrate and valerate increased in content and proportion. SCFA concentration was negatively associated with disease activity and weighted pediatric Crohn disease activity index (wPCDAI) score. FCP significantly decreased with treatment and correlated positively with wPCDAI and disease activity ( $p < 0.05$ ). 16s microbial sequencing revealed an increase in relative abundance of known SCFA-producing genera (including: Roseburia, Akkermansia, and Ruminococcus). Microbe-associated urinary metabolites (including: 4-hydroxyhippuric and hydroxyphenyllactic acid) were significantly increased with IFX therapy and varied with disease location.

### Conclusion

Disease activity, FCP, and clinical severity decreased with IFX therapy. Associated alterations in microbial composition and function, as evidenced by SCFA and urinary metabolite changes, reflect alterations of host-microbe interactions with IFX therapy. This may indicate mediation of disease severity by microbial activity and may be related to decreasing inflammation or improved dietary intake. Further investigation is required to examine the causal associations between microbial metabolites and host health in pediatric IBD. These findings may lead to novel biomarkers or microbial therapeutic targets.

Funded by WCHRI Graduate Studentship & the Stollery Children's Hospital Foundation, CIHR Canada Graduate - Master's, and the FGSR Walter H. Johns Graduate Fellowship

The Power of Partnership



Abstract # 37  
Presenter: Pagee, Abbey  
Supervisor: Davidge, Sandra  
Title: **Role of LOX-1 in postpartum vascular dysfunction in a mouse model of preeclampsia**  
Authors: **Abbey Pagee, Tamara Saez, Floor Spaans, Anita Quon, Raven Kirschenman, Sandra Davidge**

### **Introduction**

Preeclampsia (PE) is a hypertensive pregnancy syndrome that occurs in 3-7% of all pregnancies and threatens both maternal and fetal health. PE is associated with maternal vascular dysfunction and predisposes women to later-life cardiovascular complications, including those associated with atherosclerosis. It is therefore important to elucidate the mechanisms by which PE negatively impacts maternal vascular health long after delivery. The lectin-like oxidized low-density-lipoprotein (oxLDL) receptor-1 (LOX-1) is a multi-ligand scavenger receptor. LOX-1 is the primary vascular receptor of oxLDL, and LOX-1 expression is increased in the maternal vasculature during PE. The activation of LOX-1 induces pathways leading to oxidative stress, and therefore, to vascular dysfunction. LOX-1 is known to play a role in the progression of cardiovascular disease and atherosclerosis; however, it is unclear as to whether these LOX-1-mediated effects are also involved in the later-life vascular complications after PE. We hypothesized that, via LOX-1 activation, pregnancies complicated by PE lead to vascular dysfunction and atherosclerosis later in life.

### **Methods**

A mouse model of gestational vascular dysfunction was used wherein pregnant C57BL/6 and LOX-1 knockout mice (LOX-1KO, i.e. LOX-1 deficient mice) were fed a high cholesterol diet (HC) (to induce vascular dysfunction as seen in PE) or control diet from gestational day (GD) 13.5 until delivery (GD19). Following delivery, all groups were fed a control diet until three months postpartum (which equals ~10 years in humans). Three months postpartum, vascular function was assessed in abdominal aortas (which are highly susceptible to atherosclerotic changes) on a wire myograph using cumulative doses of phenylephrine and methacholine to elicit vasoconstriction and endothelium-dependent vasodilation, respectively. Thoracic aortas were snap frozen and superoxide levels (an oxidative stress marker) were evaluated using dihydroethidium (DHE) staining. Data were analyzed using a two-way ANOVA.

### **Results**

Abdominal aortas from three-month postpartum C57BL/6 mice that were on a HC-diet during pregnancy showed reduced endothelium-dependent vasodilation compared to all other groups ( $p=0.04$ ). This effect was absent in the postpartum LOX-1KO mice. However, both C57BL/6 and LOX-1KO on the HC, compared to a control diet during pregnancy, showed a decrease in vasoconstriction in response to phenylephrine ( $p=0.03$ ). Superoxide levels were increased ( $p=0.04$ ) in thoracic aortas from C57BL/6 mice that were on a HC-diet during pregnancy, but not in aortas from LOX-1KO mice.

### **Conclusion**

Using a mouse model with complications observed in PE (i.e. a HC-diet during pregnancy) resulted in impaired three-month postpartum vascular function. This occurred only in the aortas from C57BL/6 mice that express basal LOX-1 levels, but not in aortas from LOX-1KO mice, suggesting the role of this receptor in mediating the negative vascular effects seen after PE. Our data suggest that a pregnancy-specific complication (i.e. PE) impairs later-life vascular function via LOX-1 activation.

Funded by **WCHRI Summer Studentship; Alberta Innovates**

The Power of Partnership



Abstract # 38  
Presenter: Holody, Claudia  
Supervisor: Bourque, Stephane  
Title: Sex-specific changes in neonatal cardiac mitochondrial function in response to perinatal iron deficiency  
Authors: Claudia D. Holody, Andrew G. Woodman, Rowan Carpenter, H el ene Lemieux, Stephane L. Bourque

### Introduction

Iron deficiency (ID) during gestation can predispose offspring to chronic disease in later life. Pregnant women are at a high risk for developing iron deficiency and subsequent anemia due to increased iron demands; an estimated 38% of women worldwide and 23% of Canadian women will develop anemia throughout pregnancy. Thus, iron deficiency likely contributes significantly to the global burden of chronic disease. Because the heart quickly becomes mitochondria-dependant after birth and because iron is essential for oxygen transport and oxidative energy production by the mitochondria, we hypothesized that perinatal ID would alter cardiac mitochondrial function through the neonatal period.

### Methods

Female rats were fed either an iron-restricted or an iron-replete diet before and during pregnancy. At birth, all dams were fed standard rat chow. Hearts from male and female offspring were collected at postnatal days (PD) 1, 14, and 28. Electron transport system and fatty acid  $\beta$ -oxidation capacities were assessed in permeabilized cardiac fibers using high-resolution respirometry. Mitochondrial content was measured by citrate synthase activity assay. Cytosolic superoxide anion levels were assessed using dihydroethidium stain visualized by fluorescence microscopy.

### Results

Hemoglobin levels were reduced in ID pups at PD1 ( $P<0.001$ ) and PD14 ( $P=0.008$  for males;  $P=0.02$  for females) but were no longer different at PD28 ( $P=0.85$  for males;  $P=0.58$  for females). Body weights of ID pups were reduced at all ages compared to control pups ( $P<0.05$ ). Heart weight relative to body weight was larger in ID pups at all ages ( $P<0.001$ ). Mitochondrial content and respiratory capacity (oxygen flux per fiber mass) increased with age. ID caused an overall increase in mitochondrial content in both sexes ( $P=0.03$  for males;  $P=0.05$  for females) at all timepoints. When normalized for mitochondrial content, mitochondrial respiration through the NADH-pathway (electron flow through complex I;  $P=0.03$ ), the NS-pathway (electron flow through complexes I and II;  $P=0.06$ ), and the succinate-pathway (electron flow through complex II;  $P=0.02$ ) were reduced in ID male pups only, while complex IV was not affected. These results suggest a defect in complex III in ID males. ID did not change cardiac cytosolic superoxide levels in either sex.

### Conclusion

Male, but not female, neonatal hearts adapt to perinatal ID by producing more mitochondria to compensate for reduced efficiency. Interestingly, this functional change is not accompanied by changes in cytosolic superoxide levels. These results provide insight into the mechanisms linking perinatal ID with long-term cardiovascular dysfunction and may help identify potential therapeutic targets for the treatment and prevention of chronic disease associated with perinatal ID. Furthermore, the study results contribute to the current knowledge on cardiac development and cardiac function in neonates which may be particularly relevant to preterm infants at high risk of iron deficiency.

Funded by NSERC, CIHR, WCHRI, Canada Foundation for Innovation, University of Alberta Dept. of Pediatrics, Faculty of Medicine & Dentistry, and Faculty Saint-Jean

The Power of Partnership



Abstract # 39  
Presenter: Evanchuk, Jenna  
Supervisor: Field, Catherine J.  
Title: A mother's iron stores during second trimester predict infant iron stores at 3 months of age  
  
Authors: Jenna Evanchuk, Susan Goruk, Lauren Brown, Rhonda C. Bell, Catherine J. Field and the APrON study team

### **Introduction**

Iron deficiency anemia and low iron stores during pregnancy can lead to severe complications in the mother and infant. During a gestational deficiency in this vital nutrient, mothers may be at a higher risk for giving birth prematurely, which puts their infant at risk. Low iron stores in the first months of life has been reported to cause lasting neurological and developmental impairments. The objective of this project was to study the relationship between maternal serum ferritin (SF) during pregnancy and the iron storage status of infants at 3 months of age.

### **Methods**

The Alberta Pregnancy and Outcomes Nutrition (APrON) study, a prospective cohort project which gathered information and biological samples from pregnant women, was conducted at local clinics and hospitals in Edmonton and Calgary from 2009 to 2012. All 716 participants in this study, which included 358 mothers and their infants, participated in APrON and were specifically from the Calgary cohort. Maternal blood was collected at each trimester and three months postpartum. Infant blood was collected at a study visit at approximately three months of age. Maternal and infant SF was measured by Chemiluminescent Microparticle Immunoassay (CMIA) on a i2000sr Architect Plus. Maternal SF in each trimester was measured, then the data was ordered from highest to lowest for quartile comparison, where Q4 contained the highest SF concentrations. Statistical methods used included descriptive regression and t-test (paired) analyses.

### **Results**

SF stores decrease during the course of pregnancy to reach a minimum during the third trimester (the mean and standard deviation of SF in the second versus third trimester was 36.85 ng/ml  $\pm$  27.48 and 15.94 ng/ml  $\pm$  12.35, respectively). Mothers who had SF levels in the second and third quartile (Q2 & Q3) in their second trimester had infants with significantly higher SF at three months compared to both Q4 ( $p=0.045$ ) and Q1 ( $p=0.022$ ). Nearly 12% ( $n=43$ ) of infants in the generally healthy population studied were found to be at risk for having low iron stores ( $<50$  ng/ml) at 3 months of age.

### **Conclusion**

The results suggest that there may be an optimal range of SF concentration (17.78 ng/ml to 46.72 ng/ml) during the second trimester of pregnancy that is associated with greater iron storage levels in infants at 3 months of age. Clinical screening of SF during the second trimester may be a useful tool for predicting infant iron status outcomes.

Funded by WCHRI Summer Studentship; NSERC URSA; CIHR project grant and Alberta Innovates

The Power of Partnership



Abstract # 40  
Presenter: Kimber, Miranda  
Supervisor: Meah, Victoria  
Title: Knowledge translation & social media: Twitter data analysis of the 2019 SOGC/CSEP guideline for physical activity throughout pregnancy  
Authors: Miranda L. Kimber, Victoria L. Meah, John Simpson, Margie H. Davenport.

## Introduction

Despite high-quality evidence demonstrating the health benefits of regular physical activity to both mother and baby, less than 15% of pregnant women meet current exercise guidelines. These low rates of physical activity among pregnant women may, in part, be related to inefficient knowledge translation of these guidelines. In recent years, the dissemination of research using social media has been suggested to improve knowledge uptake. As such, the aim of this exploratory study was to examine the impact of the release of the 2019 Guideline for Physical Activity throughout Pregnancy on social media activity related to prenatal physical activity as a metric of knowledge translation.

## Methods

Using the Twitter Application Programming Interface, Tweets containing selected keywords, such as 'pregnancy' and 'exercise' were collected. Tweets published during 1-month prior to (PRE), and 2-months following (POST) Guideline release (Oct-18-2018) were mined using a Jupyter Notebook environment and the Python programming language. Comparisons between the volume and location of Tweets both PRE and POST were analyzed as indicators of research impact and global reach. Sub-analyses (10% of total Tweets, randomly selected) were conducted to identify the relevance of Tweets to prenatal physical activity and/or the Guideline, as well as type of users.

## Results

In total, 19,944 Tweets related to prenatal physical activity were identified during this 3-month period (PRE: 6,735; POST: 13,209). In comparison to PRE, Tweets increased by 12% (n=7,548) in POST month 1, but decreased by 25% (n=5,661) in POST month 2. Analysis identified that the majority of Tweets across the 3-month period originated from North America (38%) and users categorized as 'General Population' (36%). Users Tweeting specifically about the Guideline were largely from academic and health care fields; 'Academic' (27%), 'Exercise Specialists' (24%) and 'Medical Professionals' (19%). While 'General Population' contribution of Tweets was generally low (17%).

## Conclusion

Twitter may be an effective knowledge translation method to a variety of end-users; however, strategies to improve the uptake, longevity and global reach of social media activity are required. Future knowledge translation activities utilizing social media could aim to develop multi-language hashtags or content, as well as produce simple infographics and/or media that could be shared easily by multiple users. Improving knowledge translation of prenatal physical activity research may increase the number of women engaging with and meeting the Guideline recommendations. As such, this could help to improve the health of pregnant women and their babies.

Funded by MLK was recipient of an Undergraduate Research Initiative Stipend. VLM is a recipient of the WCHRI postdoctoral fellowship award.

The Power of Partnership



Abstract # 41  
Presenter: Mitchell, Nikki  
Supervisor: Schmölzer, Georg  
Title: Incidence and risk factors for hypoglycemia during fetal-to-neonatal transition in premature infants  
Authors: Nikki A. Mitchell, Chelsey Grimbly, Elizabeth T. Rosolowsky, Megan O'Reilly, Maryna Yaskina, Po-Yin Cheung, Georg M. Schmölzer

### Introduction

Neonatal hypoglycemia is a common occurrence during the first few days after birth as infants adjust to the extrauterine environment. Hypoglycemia affects 5-10% of otherwise healthy infants, with increasing incidence reported in premature infants. Defining neonatal hypoglycemia remains challenging, as infants can remain asymptomatic at even very low glucose concentrations or be symptomatic with even mild hypoglycemia. The Canadian Paediatric Society guidelines use the widely accepted definition of hypoglycemia as a blood glucose level of  $<2.6\text{mmol/L}$ . Premature infants have lower glycogen stores and deplete them more quickly, putting them at higher risk for hypoglycemia after birth. They may also be exposed to more perinatal stress, leading to their premature delivery. There is a lack of data on the specific incidence and potential risk factors associated with hypoglycemia immediately after birth in premature infants. Our objective was to determine the incidence and risk factors associated with neonatal hypoglycemia in the premature population  $<33$  weeks' gestation.

### Methods

We completed secondary retrospective analysis of premature infants enrolled in two randomized controlled trials carried out at the Royal Alexandra Hospital in Edmonton, Alberta. A total of 255 infants  $<33$  weeks' gestation were born during the study period of seventeen months. Eighty infants were excluded due to missing glucose or maternal data and 175 infants were analyzed. Risk factors examined include gestational age, sex, small for gestational age (SGA, birth weight  $<10\%$ ile for gestational age) large for gestational age (LGA, birth weight  $>90\%$ ile for gestational age), labour at time of delivery, delivery method, maternal hypertension with systolic blood pressure  $>140\text{mmHg}$ , antenatal steroid administration, and antenatal magnesium sulfate. Hypoglycemia ( $<2.6\text{mmol/L}$ ) was determined from blood glucose measured via glucose oxidase method on arterial or venous blood gas collected within 90 minutes of delivery. Participant demographics and clinical information were collected along with maternal data through chart review.

### Results

175 infants  $<33$  weeks' gestational age (89 male, 84 female) were analyzed. Hypoglycemia occurred in 59 infants (33.7%). Maternal hypertension (OR 3.07, 95% CI 1.51-6.30,  $p=0.002$ ) was the sole risk factor for neonatal hypoglycemia. Protective factors for hypoglycemia included labor at time of delivery (OR 4.51, 95% CI 2.29-9.18,  $p<0.0001$ ) and antenatal magnesium sulfate (OR 2.53, 95% CI 1.23-5.50,  $p=0.01$ ). There were no significant differences between hypoglycemic and euglycemic infants in sex, gestational age, SGA infants, LGA infants, antenatal steroids, vaginal birth, or maternal diabetes.

### Conclusion

Premature infants  $<33$  weeks' gestation have increased risk of hypoglycemia. Maternal hypertension increases hypoglycemia risk. Antenatal magnesium sulfate administration or labor at time of delivery decrease hypoglycemia risk.

Funded by WCHRI Research Supports (Biostatistics), Heart and Stroke Foundation/University of Alberta Professorship of Neonatal Resuscitation, Heart and Stroke Foundation Canada

The Power of Partnership



Abstract # 42  
Presenter: Sáez, Tamara  
Supervisor: Davidge, Sandra  
Title: Vascular interaction between lectin-like oxidized LDL receptor 1 (LOX-1) and angiotensin II receptor 1 (AT1) in a mouse model of gestational vascular dysfunction  
Authors: Tamara Sáez, Floor Spaans, Tatsuya Sawamura, Raven Kirshenman, Anita Quon, Sandra T Davidge

## Introduction

Preeclampsia is a hypertensive pregnancy syndrome characterized by maternal systemic vascular dysfunction and increased risk of cardiovascular complications later in life. The lectin-like oxidized low-density-lipoprotein (oxLDL) receptor-1 (LOX-1) is the primary endothelial receptor for oxLDL and is highly expressed in maternal vasculature during preeclampsia. The activation of LOX-1 by oxLDL increases oxidative stress and decreases the bioavailability of nitric oxide (NO), leading to vascular dysfunction. In vitro studies have shown that oxLDL-mediated LOX-1 activation leads to the activation of angiotensin II type 1 receptor (AT1), which is a vascular receptor associated with vascular dysfunction in preeclampsia. Since AT1 inhibitors are contraindicated in pregnancy, LOX-1 could be a possible converging target for vascular dysfunction during preeclampsia. We hypothesized that oxLDL-mediated LOX-1 activation causes activation of AT1, leading to increased oxidative stress and vascular dysfunction in pregnancy.

## Methods

Pregnant LOX-1 overexpressing (LOX-1OE) and wild type (WT) mice were fed a high-cholesterol diet (HC) between gestational day (GD) 13.5 and GD18 (term=GD19), to increase cholesterol levels (oxLDL) and induce vascular dysfunction. Control pregnant mice were fed a standard chow diet. Mice were euthanized at GD18, and pregnancy outcomes were analyzed (n=5-7). Abdominal aortas and uterine arteries were isolated to evaluate ex vivo vascular function by wire myography. Vascular responses to cumulative doses of methacholine (MCh) and angiotensin II (AngII) were evaluated in the presence or absence of oxLDL (50 µg/mL), L-NAME (NO scavenger; 100 µM) or candesartan (AT1 antagonist; 1 nM). Thoracic aortas and uterine arteries were snap-frozen, and superoxide radical levels (an oxidative stress marker) and NO levels were evaluated by DHE and DAF-FM-diacetate staining, respectively.

## Results

HC diet during pregnancy decreased maternal and fetal weight ( $p < 0.05$ ), but did not change placental weight, litter size or food intake. Endothelium-dependent vasorelaxation in response to MCh was reduced in abdominal aortas in both WT and LOX-1OE on HC diet as compared to control groups ( $p < 0.05$ ). In uterine arteries, this effect was only observed in LOX-1OE mice on HC diet. OxLDL impaired vasorelaxation and MCh sensitivity in WT and LOX-1OE control mice in both types of vessels ( $p < 0.05$ ). However, these effects were not observed in the groups on HC diet. The exposure to oxLDL increased vasoconstriction responses to AngII in aortas from WT and LOX-1OE on HC diet compared to control groups ( $p < 0.05$ ). However, this effect was not observed in the uterine arteries. Superoxide levels were increased in aortas and uterine arteries from WT and LOX-1OE mice on HC diet compared to control groups ( $p < 0.05$ ). NO levels were not different between the groups.

## Conclusion

A high-cholesterol diet during pregnancy causes fetal intrauterine growth restriction and maternal vascular dysfunction, as observed in preeclampsia. However, the effect of oxLDL-mediated LOX-1 and AT1 activation differs among vascular beds and needs to be further investigated. Identifying a role for LOX-1-mediated AT1 activation could lead to novel vascular therapeutic strategies for preeclampsia.

Funded by Women and Children's Health Research Institute and Izaak Walton Killam Memorial postdoctoral fellowships. CIHR Foundation grant.

The Power of Partnership

Abstract # 43  
Presenter: Heath, Devon  
Supervisor: Hayward, Dana  
Title: What's in a face? Individual differences in social cognition of women with eating disorders  
  
Authors: Heath, D. S., Jhinjar, N., & Hayward, D. A.

### **Introduction**

Statistics from the National Eating Disorder Information Centre state that 2-3% of Canadians will at some point in their lifetime meet the diagnostic criteria for an eating disorder (ED). These criteria tend to focus on weight and food-related cognitions and behaviours without considering other psychological changes. Recent research suggests that women with EDs may have difficulties with social cognition, such as attending to and remembering social information. If it is difficult to pay attention to people, or remember them, imagine how much harder it would be to navigate every day social exchanges, interpret body language and social rules, or even build meaningful relationships.

### **Methods**

Purpose: to examine a variety of social-cognitive measures in women who were either officially diagnosed with an ED or demonstrated disordered eating (DE) without official diagnosis. Experimental measures included (i) a lab-based task measuring how strongly observing averted gaze shifts attention, (ii) a video-watching task to see where people look using eye tracking technology during complex social interactions, (iii) a face-to-face task to measure social distance and (iv) individual differences measures using various questionnaires. An attentional priority for social information would be seen by shifts of attention/gaze based on the signals presented by the faces.

### **Results**

Using repeated-measures ANOVAs, we found that while control participants shifted their attention based on the eye gaze of another, both the ED and DE participants did not shift their attention based on the eye gaze of another (Task i). When watching the video clip (Task ii), participants with an official ED diagnosis looked at the eyes significantly less than participants with DE. When measuring participant's natural social distance (Task iii), a t-test revealed significant differences in preferred social distance between participants with ED versus those with DE, in that participants with an ED had a preferred social distance that was almost double the distance of those with DE. Finally, using the questionnaire measures we found a negative correlation between number of eating disorder traits (as measured via the Eating Disorder Examination Questionnaire) and degree of attention shifts (from Task i), with fewer ED traits corresponding to greater attention shifts in response to viewing other faces.

### **Conclusion**

In conclusion, we found that women with both an official ED and those with DE present with difficulties across various facets of social cognition. While similar performance was found for the ED and DE groups in Task i, we did find a divergence in behaviours across Tasks ii and iii; those with an official ED diagnosis were less likely to look at the eyes when watching a short video, and were more likely to prefer a larger distance between themselves and others as compared to those with DE. Our study highlights the importance of collecting multiple measures to test a particular construct, along with the importance of treating not just the weight and/or food-oriented compulsions in those with an ED (or DE), but also taking into account how they attend to others and navigate the social environment. Further research will continue to inform how to conduct treatment therapies that incorporate difficulties with social cognition.

Funded by Lois Hole Hospital for Women, Women and Children's Health Research Institute.

The Power of Partnership





Abstract # 44  
Presenter: Maadi, Hamid  
Supervisor: Wang, Zhixiang  
Title: Trastuzumab induce cell cycle arrest in HER2-positive breast cancers with no inhibitory effects on HER receptors' phosphorylation and dimerization  
Authors: Hamid Maadi, Babak Nami, and Zhixiang Wang

### Introduction

HER2 overexpression has been reported in 20-30% of breast cancer (BC) cells and is responsible for lower overall survival rates and differentiation as well as higher malignancy and proliferative index in HER2-positive BC cells. Trastuzumab as a first HER2-targeted therapy for the treatment of HER2-positive BC patients was introduced in 1998. Although trastuzumab has opened a new window toward the treatment of patients with HER2-positive BC and even other types of cancer, some patients do not respond or become resistant to this treatment. So far, several mechanisms have been suggested for the mode of action of trastuzumab; however, the findings regarding these mechanisms are unclear and controversial.

### Methods

To determine the mechanism of action of trastuzumab, two HER2-positive BC cells including BT474 and SKBR3 cells were used. In addition, three different types of CHO and 293T transfected cells were used as cell models to unravel the effect of trastuzumab on HER2 homodimerization, heterodimerization, and HER receptors phosphorylation: 1) cells transfected with HER2 receptors; 2) EGFR and HER2 receptors; and 3) HER3 and HER2 receptors. To assess the effect of trastuzumab on HER2 homo- and heterodimerization, crosslinking assay and immunoprecipitation (IP) followed by immunoblotting were used, respectively. The effect of trastuzumab on cell's viability and cell cycle progression were identified using MTT assay and PI-cell cycle assay, respectively. The phosphorylation of HER receptors and HER2-regulated downstream signaling were evaluated by immunoblotting and immunocytochemistry.

### Results

One of the significant limitations which make it difficult to determine the mode of action of trastuzumab, is uncontrollable formation of HER2 dimers in HER2-positive BC cells. To overcome this limitation, CHO cells transfected with HER2 receptors (CHO-K6) were used to exactly determine the effects of trastuzumab on HER2 homodimer formation and receptors phosphorylation in the absence of other dimers. Our results revealed that trastuzumab has no inhibitory effects on homodimerization and phosphorylation of HER2 receptors. In addition, our results in BT474 BC cells showed that trastuzumab can reduce the viability of the cells and arrest cell cycle in G1 phase. Immunoblotting results demonstrated that trastuzumab can inhibit Akt phosphorylation at both serine and threonine phosphorylation sites. Inhibition of Akt phosphorylation via PI3K inhibitor named LY294002 in BT474 BC cells also arrested the cell cycle in G1 phase which may suggest that trastuzumab exert its antiproliferative effects through inhibition of Akt phosphorylation. In addition, our findings revealed that HER2 overexpression in 293T cells which does not express HER receptors and treatment of BT474 BC cells with HRG and EGF ligands can induce Akt phosphorylation which may indicate that different HER receptors homo- and heterodimerization can induce Akt phosphorylation.

### Conclusion

Our results show that trastuzumab does not suppress Akt phosphorylation through inhibition of HER receptors phosphorylation and HER2 homo- and heterodimer formation.

Funded by Canadian Institutes of Health Research (CIHR), WCHRI Trainee Travel, Faculty of Medicine and Dentistry, University of Alberta

The Power of Partnership



Abstract # 45  
Presenter: Huachen Chen  
Supervisor: Dr. YangXin Fu and Dr. Lynne-Marie Postovit  
Title: Transcription factor ZIC2 promotes tumorigenic phenotypes by regulating the biology of the bulk and cancer stem cells in ovarian cancer  
Authors: Huachen Chen\*, Krista Vincent, Luara Lee, Zhihua Xu, Olena Bilyk, Jiahui Liu, Guihua Zhang, Lynne-Marie Postovit, YangXin Fu

## Introduction

Epithelial ovarian cancer (EOC) is the leading cause of gynecological cancer death in women. Current therapeutic regimen is ineffective in killing cancer stem cells (CSCs), resulting in the recurrence of this disease and acquired chemoresistance. A combined therapy that targets both bulk cells and CSCs would be a more effective therapeutic strategy to manage and/or prevent recurrent and resistant disease. Transcription factor ZIC2 has emerged as an oncogenic factor in various types of cancer. This project aims to investigate the pro-tumorigenic role of ZIC2 in EOC and the underlying mechanisms.

## Methods

Association of ZIC2 expression with survival of EOC patients was determined by analyzing TCGA (The Cancer Genome Atlas) dataset. ZIC2 expression was examined in a panel of EOC cell lines at protein level. ZIC2 knockout via CRISPR or overexpression models were generated in EOC cell lines. The effect of ZIC2 knockout or overexpression on gene expression (real-time RT-PCR, RNA-sequencing, Western blotting and immunohistochemistry (IHC)), the percentage of CSCs (Western blotting and ALDEFLUORTM assay), growth (neutral red uptake assay), migration (Transwell migration assay), anchorage-independent growth (soft agar assay), self-renewal (limiting dilution sphere formation assay), and tumor formation (subcutaneous xenograft model) was examined in EOC cells.

## Results

The TCGA database analysis indicates that higher ZIC2 mRNA expression is associated with shorter survival of EOC patients. Knockout of ZIC2 in the ZIC2-positive EOC cell lines results in decreased cell growth, migration, anchorage-independent growth, ALDH<sup>high</sup> population and sphere-forming ability, and tumor formation in the mouse subcutaneous xenograft model. Mechanistically, ZIC2 knockout dramatically down-regulated the expression of genes critical for multiple biological processes, including CSC (ALDH1A1 and LIN28B), cell cycle (CCND2), EMT (ZEB2), signaling kinases (ROR2 and MAPK4), invasion and metastasis (MMP3 and POSTN), and mRNA binding (IGF2BP1 and LIN28B). Expression of ALDH1A1 and other CSC-associated genes in ZIC2 knockout cells was restored by re-expression of ZIC2, indicating that the phenotypical changes observed in ZIC2 knockout cells are not due to any off-target effect. Western blotting and IHC confirmed that ALDH1A1 and cyclin D2 (CCND2) were only expressed in the ZIC2 wild-type, but not in ZIC2 knockout, EOC cells-derived xenografted tumors.

## Conclusion

Our in vitro and in vivo work indicates that ZIC2 is a pivotal gene regulator and promotes tumorigenic phenotypes through regulating the biology of the bulk cells and CSCs in EOC, suggesting that ZIC2 is a promising therapeutic target for EOC.

Funded by Melterz Tuition Award of Alberta Cancer Foundation; WCHRI foundation; GRAF Funding; Yau Family Foundation Award

The Power of Partnership



Abstract # 46  
Presenter: Githaka, John Maringa  
Supervisor: Goping, Ing Swie  
Title: BAD phosphorylation facilitates mRNA translation during epithelial cell migration in the developing mammary gland  
Authors: John Maringa Githaka, Namita Tripathi, Raven Kirschenman, Namrata Patel, Rachel Montpetit, Lin Fu Zhu, David A. Kramer, Vrajesh Pandya, Richard P. Fahlman, Nika Danial, D. Alan Underhill, Ing Swie Goping

### Introduction

Postnatal development of the mouse mammary gland is dependent on tightly controlled cycles of proliferation, migration, differentiation and apoptosis. Identification of genes driving this normal process is central to understanding signaling pathways that are often dysregulated in cancer. We have previously shown the BH3-only protein BAD is a prognostic marker for survival of breast cancer patients. While this suggests that BAD regulates tissue homeostasis, it is not known whether BAD has a physiological role in the mammary gland. BAD is extensively regulated through coordinated phosphorylation of three key serine (S) residues S112, 136 and 155.

### Methods

We used a mouse genetic model wherein the three S residues are replaced by non-phosphorylatable alanine (3SA) and characterized different stages of postnatal mammary gland development. We combined mouse organoids and human tubulogenesis assay to confirm in vivo observations. We employed mass spectrometry (MS) and reverse phase protein array (RPPA) screens to elucidate the mechanism.

### Results

BAD 3SA mutant animals showed a delay in ductal elongation and decreased primary branching of the mammary gland epithelial tree during puberty. Transplant of mutant epithelium into cleared wild-type mammary fat pads demonstrated that this effect was derived from the epithelial compartment. Ex vivo 3D organotypic cultures of purified mouse mammary epithelium and human mammary epithelial MCF10A cells showed delayed branching and tubulogenesis, confirming the cell autonomous-effect of BAD phosphorylation. MS screen identified differences in actin-binding and focal adhesion components suggesting defects in cell migration. Additionally, RPPA screen identified deficient phosphorylation of the mRNA translational regulator, 4E-BP1. This is intriguing because localized translation in subcellular protrusions has been shown to drive focal adhesion maturation and cell motility in vitro. Consistent with this, BAD phosphomutant 3D organoids generated cell protrusions with decreased mRNA translation and diminished levels of cell migration effectors, actin and paxillin. Importantly, these nascent protrusions were unstable and cells displayed diminished migration.

### Conclusion

Our findings demonstrate that localized translation is critical for cell migration during mammary gland development, identify BAD as a previously unknown regulator of this process and suggest novel pathways to explore in breast cancer pathogenesis

Funded by Alberta Cancer Foundation

The Power of Partnership



Abstract # 47  
Presenter: Myre, Maxine  
Supervisor: Berry, Tanya  
Title: **Body weight diversity in physical activity promotion: Perspectives of women living with obesity**  
Authors: **Maxine Myre, Tanya R. Berry, Nicole M. Glenn**

### **Introduction**

The purpose of this study was to describe the views of women living with obesity about improving body weight diversity in physical activity promotion.

### **Methods**

Women (M=40 years, range 20-59 years) from across Canada were invited to participate in a semi-structured telephone interview. All women had already participated in an experimental study that showed non-stigmatizing images of individuals with obesity being active. The images were from the Obesity Canada, Rudd Center, and World Obesity image banks. Sixteen women who had experienced weight stigma in the context of physical activity shared what they thought about the images, and expressed their perspective on the broader implication of using non-weight-stigmatizing images in physical activity promotion. Qualitative content analysis of the interview transcripts was conducted to produce the findings.

### **Results**

Overall, women liked the images and described them as motivating, encouraging, and relatable. Women welcomed more body weight diversity in images related to physical activity, seeing it as a necessary starting point to reduce weight stigmatizing attitudes in the general public. They hoped that these images could challenge stereotypes perpetuated by unrealistic images currently prevalent in physical activity media, and instead show that individuals living with obesity are willing and capable of being active. Concurrently, they expressed some doubt that individuals from the general public would receive the images positively given that weight stereotypes are so ingrained in our society.

### **Conclusion**

Images portraying diverse body sizes in physical activity promotion may be one strategy to address weight stigma in physical activity.

Funded by **Diabetes, Obesity, and Nutrition Strategic Clinical Network**

The Power of Partnership



Abstract # 48  
Presenter: Elliot, Victoria  
Supervisor: Schulz, Jane  
Title: Obstetrical anal sphincter injuries & the need for adequate care

Authors: Victoria Elliot, MSPH, Obstetrics & Gynecology, UofA, Edmonton, Canada; Maryna Yaskina, PhD, WCHRI, UofA, Edmonton, Canada; & Jane Schulz, MD, Obstetrics & Gynecology, Royal Alexandra Hospital, Lois Hole Hospital for Women, UofA, Edmonton, Canada

### **Introduction**

An estimated 4-6.6% of women delivering vaginally sustain obstetrical anal sphincter injuries (OASI). A distressing consequence of OASI is anal incontinence. Despite the prevalence and negative outcomes associated with OASI, a gap exists in the provision of postpartum care. An OASI rate of 5.5% at the Royal Alexandra Hospital (RAH) from 2000 to 2005 and a gap in formalized care led a multidisciplinary team at the RAH to establish a perineal clinic for the care of women with OASI in 2011. The purpose of this study is fourfold: 1) investigate the literature on the number and structure of perineal clinics specialized in OASI care globally; 2) describe the structure and use of the perineal clinic at the RAH; 3) assess the current prevalence of OASI at the RAH; and 4) assess risk factors for severity of OASI.

### **Methods**

A search of peer reviewed literature was done on Medline; observations and interviews were conducted with the healthcare professionals at the perineal clinic; and a medical chart review was conducted to assess the prevalence of, and associated risk factors for, OASI in 2016. The clinic model of care was reviewed and detailed using interviews conducted with clinic staff. The chart review covered all OASI patients from the site over a 1 year period. Statistical analysis was completed to assess any variables that may impact severity of OASI (3rd versus 4th degree tears). Factors assessed in the chart review included potential risk factors that may impact severity of OASI: length of stages of labor, birthweight, instrumental delivery, chorioamnionitis, presence of female genital cutting, ethnicity, prior OASI, VBAC, gestational diabetes, induction, augmentation, parity, epidural use, and shoulder dystocia.

### **Results**

Descriptions of only 10 perineal clinics specializing in the care of women with OASI were found in the literature, 9 of them in Europe. The clinics are run by physicians, midwives, nurses, physiotherapists, or a combination thereof. The exact structure of the clinics, in terms of the roles of the health professionals, how the clinics are run on a day-to-day basis, and the services provided, varies. Only one of the perineal clinics is physiotherapy-led like the RAH perineal clinic, which offers education and Pilates classes to all women with OASI, as well as one-on-one physiotherapy sessions and access to other experts including nurse practitioners, urogynecologists, and a dietician. In 2016, 6.9% of women having vaginal deliveries at the RAH experienced OASI. Of those women, 65% with third degree and 94% with fourth degree tears were referred to the perineal clinic. Length of stages of labor, time pushing and ethnicity were found to be not statistically significant risk factors for increased severity of OASI. Other factors, such as parity, prior OASI, operative vaginal delivery, gestational diabetes, and birthweight were not significant risk factors.

### **Conclusion**

There is limited published literature on perineal clinics specializing in OASI care globally, which, along with the varying nature of the clinics, hinders the establishment of a standard of care. Despite the creation of a local perineal clinic and increased education of care providers, the rates of OASI have failed to improve at the RAH, and referral rates are suboptimal. None of the reviewed clinical risk factors for severity of OASI were statistically significant. Further research and literature in this area is needed.

Funded by David & Beatrice Reidford Research Scholarships and the Women & Children's Health Research Institute

The Power of Partnership

Abstract # 49  
Presenter: Nielsen, Charlene  
Supervisor: Osornio-Vargas, Alvaro  
Title: A medical macroscope for children's environmental health: The ChEHC map collection  
Authors: Charlene Nielsen, Osnat Wine, Lesley Brennan, Irena Buka, Carl Amrhein, Alvaro Osornio-Vargas

### **Introduction**

Many childhood diseases and health conditions are due in part to such environmental risks as air pollution, water pollution, hazardous wastes, radiation, and climate change. In our research, we have brought the geographic perspective to air pollution and adverse birth outcomes, childhood cancer, congenital heart defects, infant gut microbiota, asthma, and autism. While our research is ongoing, we wish to share resources with clinicians and the public.

### **Methods**

Geographical Information Systems (GIS) helped us to define study population locations, identify potential pollution sources, assign exposure estimates, and analyze spatiotemporal patterns. And as part of the Data Mining and Neonatal Outcomes (DoMiNO) Project, we generated new hypotheses on the co-location of industrial air pollution and adverse birth outcomes. We harnessed the power of visual storytelling through the web-based application ArcGIS StoryMaps to help create awareness of our pediatric environmental health research.

### **Results**

We have created and curated environmental health maps and our current collection highlights air pollution from traffic and industry. We illustrate the spatial relationships of where one lives and the characteristics of air pollution sources that are within user-specified distances. Users can also explore the areas of chemical mixtures associated with adverse birth outcomes from the DoMiNO research. Our ongoing efforts are incorporating greenness and other environmental factors.

### **Conclusion**

A map can be a medical macroscope to help clinicians and their patients better “see” their outdoor environment. We designed this knowledge translation tool for use by the Children’s Environmental Health Clinic, but it can also inform both clinicians and the public about modifiable environmental hazards which can be reduced to mitigate exposure by children.

NOTE: If this abstract is chosen as a poster presentation, we wish to have a poster station near an electrical outlet so we may display a touch-screen computer for the audience to interact with the online map collection.

Funded by CIHR and NSERC

The Power of Partnership



Abstract # 50  
Presenter: Lim, Kenji Rowel Q.  
Supervisor: Yokota, Toshifumi  
Title: **Developing antisense gapmers to knock down DUX4 for the treatment of facioscapulohumeral muscular dystrophy**  
Authors: **Kenji Rowel Q. Lim, Rika Maruyama, Yusuke Echigoya, Quynh Nguyen, Hunain Khawaja, Sen Chandra Sreetama, Takako Jones, Peter Jones, Yi-Wen Chen, Toshifumi Yokota**

### **Introduction**

Facioscapulohumeral muscular dystrophy (FSHD) is the third most common inherited neuromuscular disorder, with a prevalence of 1:8000-1:22000 worldwide. FSHD patients present with muscle wasting on the upper body, which descends to the lower extremities with age. Age of onset is variable, but typically begins in childhood. An infantile form of the disorder also exists, characterized by a greater severity of symptoms. There is no cure for FSHD. FSHD is caused by the aberrant expression of DUX4 in muscle. DUX4 is normally expressed in early embryos but is then silenced in most tissues, including muscle, upon differentiation. We aim to develop a therapy for FSHD using antisense oligonucleotides called gapmers. Gapmers act by binding mRNA targets through sequence complementarity, and then degrading them via RNase H1. By designing gapmers to target DUX4, its expression can be reduced in muscle and could potentially serve as a treatment for FSHD.

### **Methods**

We used two gapmer chemistries: locked nucleic acid (LNA) and 2'-O-methoxyethyl (2'-MOE). Seven LNA and three 2'-MOE gapmers were designed to target different locations of the DUX4 mRNA. In vitro testing of the gapmers was done by transfecting them into immortalized FSHD patient-derived muscle fibers at various doses (100, 10, and 1 nM) and extracting total RNA the next day. Quantitative real-time PCR was performed to assess DUX4 expression changes, as well as those of the DUX4 downstream target genes ZSCAN4, MBD3L2, and TRIM43. RNA sequencing was also used to evaluate changes in the expression of FSHD signature genes. Muscle fusion and apoptosis assays were then performed to evaluate effects on the muscle cell phenotype. For the next phase, in vivo testing of a candidate LNA gapmer was done in FLEXDUX4 FSHD model mice. The gapmer or saline was injected thrice, every other day, into the tibialis anterior muscle of FLEXDUX4 mice. Total RNA from muscles collected 24 hr after the last injection was used for quantitative PCR assessment of changes in DUX4 expression.

### **Results**

Significant knockdown of DUX4 mRNA expression was observed following treatment with 100 nM of all gapmers, except for LNA#2. Nearly 100% DUX4 knockdown was achieved on average. Corresponding significant knockdown of ZSCAN4, MBD3L2, and TRIM43 expression levels were observed. Gapmer activity was dose-dependent, with significant knockdown observed at 10 nM but not 1 nM of the transfected gapmers. RNA sequencing analysis revealed that LNA#4 gapmer treatment reduced the expression of 86% of genes significantly upregulated in FSHD. While LNA treatment significantly improved muscle fusion, no effect was found on apoptosis. Finally, significant knockdown of DUX4 expression was observed in LNA gapmer-treated muscles in vivo compared to saline-injected controls.

### **Conclusion**

Our designed LNA and 2'-MOE gapmers could significantly reduce DUX4 expression in vitro and, in the case of one of our LNA gapmers, in vivo as well. Further testing and development of these gapmers should help lead to a clinical trial drug candidate for therapy, which will be of great benefit to patients with FSHD in the future.

Funded by **Canadian Institutes of Health Research, Alberta Innovates HS, FSH Society, Women and Children's Health Research Institute, Muscular Dystrophy Canada**

The Power of Partnership



Abstract # 51  
Presenter: Khodaei, Mahdieh  
Supervisor: Lou, Edmond  
Title: **Prognostic factors for curve progression in adolescent with idiopathic scoliosis: A systematic review**  
Authors: Mahdieh Khodaei, Eric Parent, Lawrence H Le, Edmond Lou

### **Introduction**

Adolescent Idiopathic Scoliosis (AIS) is a 3D spinal deformity recognized by lateral curvature of the spine coupled with axial vertebral rotation. Curve progression is monitored by measuring curve severity on radiographs every 6 months. However, 85% of cases do not progress and unnecessary radiographs increase the risk of cancer. The literature reports that scoliosis curve progression may be predicted by different parameters including demographic information, radiographic measurements, and physiological parameters. However, controversy exists about the best prognostic factors. This systematic review aimed to identify the best predictors of curve progression in children with idiopathic scoliosis.

### **Methods**

MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, and CINAHL were searched. The search strategy combined synonyms for AIS deformity, potential prognostic factors, the outcome curve progression, and prognostic statistical terms. A medical librarian assisted tailoring search for each database. Eight independent reviewers were involved for abstracts and full-texts screening, data extraction and risk of bias assessment (RoB). The eligibility criteria for the articles were: 1) human participants, 2) diagnosis of AIS, 3) participants' age between 10 and 18 years old, 4) follow-up studies, 5) initial Cobb  $\geq 10^\circ$ . Full-text screening also confirmed: 7) report on the prediction of curve progression. For each stage, the main reviewer reviewed all references which were divided among the other reviewers for a second review. The Quality in Prognostic Studies (QUIPS) quality appraisal tool was used to assess the RoB. The QUIPS domains include study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis. An overall score as high, moderate, and low risk of bias was assigned to each article for each domain. The level of evidence (strong, moderate, limited, no, and inconclusive evidence) was classified based on the risk of bias of the cohort studies and the consistency of the research findings.

### **Results**

A total of 1448 unique references was included for abstract screening and 615 articles remained for full-text screening. Sixty-three articles were extracted, of which 12 (19%), 48 (76%), and 3 (5%) presented low, moderate, and high RoB respectively. From the 12 low RoB articles, the level of evidence and the number of studies reporting the predictive factors (Yes/No) are as follows: Conflicting evidence: Age (3/3); body mass index (BMI) (1/1); gender (1/4); Risser sign (4/2); weight (1/2); baseline Cobb angle (2/4); lumbar spine and femoral neck of the hip bone mineral density (BMD) (2/1). Strong evidence: menarche (3/0%) as a predictor and curve pattern (1/4) as a non-predictor.

### **Conclusion**

Only 12 prognostic articles presented low RoB. The best predictor of curve progression with the most support was absence of menarche. For the rest of identified predictors, there was conflicting evidence available. A meta-analysis study is in progress to quantify the prediction value of different parameters.

Funded by WCHRI, Scoliosis Research Society

The Power of Partnership





Abstract # 52  
Presenter: Saurette, Matthew  
Supervisor: Alexander, R.Todd  
Title: **Intestinal phosphate absorption: Claudin-12 attenuates paracellular phosphate absorption**  
Authors: **Saurette M, MacDonald T, Alexander RT**

### **Introduction**

Hyperphosphatemia is a near ubiquitous finding of children with renal insufficiency. Treatment consists of binding phosphate in the diet. This requires upwards of 20 tablets per day, which is poorly tolerated. In order to design better, more targeted therapies for increased plasma phosphate in children with kidney disease we seek to understand how phosphorus is absorbed from the intestine. Claudins are a family of tight-junction proteins that regulate epithelia permeability to an ion and claudin-12 is a tight junction protein located between intestinal enterocytes. Preliminary work suggests that inorganic phosphate (Pi), ubiquitous in the Western diet, is absorbed predominantly via the paracellular pathway and that claudin-12 decreases absorption via this pathway. Changes in oral Pi bioavailability on a diet of predominantly inorganic Pi, therefore, reflects changes in paracellular Pi transport. Despite the importance of the paracellular pathway in Pi absorption under most conditions, it is unknown which claudins are involved in paracellular Pi transport. Given that a global KO of claudin-12 increases urine Pi excretion, we hypothesized that claudin-12 is a paracellular Pi blocker and sought to test this with our study.

### **Methods**

Pi homeostasis was characterized in-vivo by placing wild-type and claudin-12 KO mice in metabolic cages and feeding them organic and inorganic Pi diets, absorbed primarily via the transcellular and paracellular route respectively. Urinary and fecal Pi excretion, and Pi bioavailability were determined for each diet to assess the role of claudin-12 in mediating intestinal Pi absorption.

### **Results**

Both wild-type and claudin-12 KO mice had increased oral Pi bioavailability and urine Pi excretion on the inorganic Pi diet, consistent with enhanced intestinal absorption. In contrast, potassium, another ion absorbed by the paracellular route in the gut, did not display differences in oral bioavailability or urinary excretion between the different diets. Further, claudin-12 null mice had significantly greater oral Pi bioavailability, serum Pi and urine Pi excretion relative to wild-type mice on the inorganic but not organic Pi diet.

### **Conclusion**

Our data confirms that inorganic Pi is more bioavailable than organic Pi and is consistent with i) claudin-12 forming a paracellular Pi barrier that inhibits inorganic but not organic Pi absorption and ii) inorganic Pi being absorbed through the paracellular pathway. Ultimately this work provides a putative pharmacological target for increasing paracellular Pi absorption in children with kidney disease.

Funded by **CIHR (PI Grant)**

The Power of Partnership



Abstract # 53  
Presenter: MacDonald, Tate  
Supervisor: Alexander, Todd  
Title: **Towards an understanding of the difference in organic and inorganic phosphate bioavailability**  
Authors: MacDonald T, Saurette M, Alexander T

### **Introduction**

Impaired bone mineralization is implicated in deficient bone integrity, which is seen largely in postmenopausal osteoporosis in women. As sufficient phosphate (Pi) absorption from the small intestine is a prerequisite for adequate bone mineralization, we sought to delineate the pathway(s) by which dietary Pi is absorbed. Inorganic-based dietary Pi is recognized to have a higher fractional absorption from the intestine than its organic counterpart. We hypothesized that inorganic Pi is predominantly absorbed from the intestine via the unsaturable paracellular epithelial pathway conferring its high degree of absorption, and that organic Pi is predominantly absorbed via the transcellular pathway. Specifically, we predicted that a knockout of the intestinal tight junction protein Claudin-12 (Cldn-12) would influence the absorption of inorganic Pi with nonsignificant effects on organic Pi absorption.

### **Methods**

To investigate our hypothesis, wild-type (WT) mice, and Cldn-12-null mice were generated. Mice were fed an organic Pi-based diet for 72 hours, and were transferred thereafter to an inorganic-Pi based diet for 72 hours. Euthanasia was performed prior to tissue extraction. To determine fractional Pi absorption from the intestine, urinary and fecal Pi was measured for each respective dietary treatment.

### **Results**

Consistent with our hypothesis, a higher fraction of inorganic Pi was absorbed in Cldn-12-null mice than WT mice. The null mice also had higher urinary Pi excretion on an inorganic diet than the WT animals. Also consistent with our hypothesis was the nonsignificant difference in organic Pi absorption or urinary Pi excretion between WT and Cldn-12-null mice.

### **Conclusion**

Given that manipulation of the tight junction influenced inorganic but not organic Pi absorption, our results are consistent with inorganic Pi absorption occurring primarily paracellularly with organic Pi absorption occurring predominantly transcellularly. Our findings are instructive to future research purporting to discover pharmacological means of upregulating intestinal Pi absorption in so far as the paracellular pathway should be specifically targeted.

Funded by WCHRI, The Kidney Foundation of Canada

The Power of Partnership



Abstract # 54  
Presenter: Ladak, Zeenat  
Supervisor: Persad, Sujata & Yager, Jerome Y  
Title: **A therapy to prevent neurodevelopmental disabilities: Protection of brain cells by sulforaphane**  
Authors: Ladak, Z., Garcia, E., Armstrong, EA., Yoon, J., Yager JY., Persad, S.

### Introduction

Perinatal brain injury results in neurodevelopmental disabilities (NDDs) including cerebral palsy, autism, and attention deficit disorder among others. Many factors can contribute to perinatal brain injury, one major factor being placental insufficiency which is the inadequate transportation of nutrients and oxygen to the fetus, causing a hypoxic-ischemic environment in-utero. Over 80% of perinatal brain injuries lead to NDD prior to birth. Therefore, preventive approaches are needed, as opposed to 'rescue' therapies which take place after the injury has already occurred. Sulforaphane (SFA), derived from cruciferous vegetables such as broccoli sprouts (BrSps), is a phase-II enzyme inducer that indirectly enhances the production of anti-oxidant enzymes. We previously showed a profound neuro-protective effect of BrSps, on newborn brain pathology and behavior when given as a dietary supplement to pregnant rats in our model of placental insufficiency, compared to control. The aim of this study is to explore how SFA affects different brain cell types and the dosing range of SFA for neuronal and glial protection and toxicity in normal and oxygen/glucose deprived (OGD) cell cultures.

### Methods

OGD simulates in-vitro, the conditions of in-vivo HI. We developed a newborn rodent cell culture of primary cortical neuronal, astrocyte, and combined cell cultures (co-cultures). Cell culture purity is evaluated by presence of cell specific markers in Western blot and immunofluorescence (IF). Cultures are exposed to an OGD environment for different durations of time to achieve 50% cell death (LD50). Using the LD50, cultures are exposed to varying doses of SFA. Control cultures are not exposed to OGD. Cell viability is assessed by a Live/Dead assay using IF/high content and cytotoxicity by Alamar blue. One Way ANOVA and Dunette's Multiple Comparison are used for statistics.

### Results

Primary cortical neuronal, astroglial, and co-cultures have been established. We determined the LD50 to be 2 hours for neurons, 4 hours for astrocytes, and 10 hours for co-cultures. At the previously determined LD50, SFA was protective at 2.5uM ( $p < 0.05$ ) in both neurons and co-cultures, and at 5uM ( $p < 0.001$ ) in astrocytes. Significant toxicity of SFA in control cultures was seen at doses  $\geq 100\text{uM}$  ( $p < 0.01$ ) for neurons, and  $\geq 50\text{uM}$  ( $p < 0.05$ ) for both astrocytes and co-cultures.

### Conclusion

These findings suggest that SFA shows promise as a preventative agent for fetal ischemic brain injury and that dosing parameters are required for safety. Future studies include determining the safety and efficacy of SFA in a rat animal model of placental insufficiency.

Funded by WCHRI Innovation Grant & MatCH (Maternal and Child Health Scholarship Program)

The Power of Partnership



Abstract # 55

Presenter: Amanda Yaworski

Supervisor: Janani Kassiri

**Reduction in emergency department visits and improved diagnoses through implementation of a rapid access neurology clinic**

Yaworski, A., Yager, J., Mailo, J., Richer, L., Rajapakse, T., & Kassiri, J.

**Introduction**

Pediatric neurology referral wait times are increasing, often interfering with neurologists ability to diagnose and treat conditions in a timely manner. This often leads to increased utilization of emergency department (ED). Approximately 5% of ED patients present with neurological symptoms and 35% of ED neurological diagnoses are revised after specialist neurological review. In an attempt to improve these issues we have created a Stollery Rapid Access Neurology (RAN) clinic. Our goal was to decrease wait time for issues deemed more urgent, and to create a more efficient referral and follow up process.

**Methods**

This study occurred at the Stollery Children's Hospital in Edmonton, Alberta. This was a prospective study approved by the University of Alberta ethics board. The RAN clinic ran once a week from March 2018 until April 2019. Patients were referred to this clinic through the emergency department or other subspecialties. Inclusion criteria was met prior to the referral being accepted. It was intended that all patients being referred had to be discussed with the on-call neurologist. Patient satisfaction was evaluated through anonymous parental survey.

**Results**

Ninety-one patients were assessed in the RAN clinic, approximately half of the referrals were from the Stollery ED. Average triage time was 5 days, with an average wait time for patients of approximately 6 weeks. Three months prior to RAN appointments, 64% of patients visited the ED at least once, whereas only 9% returned in the following three months. The referring diagnosis was consistent with neurologist diagnosis in 66% of RAN patients. The most frequent diagnoses were seizures and headache. Patient satisfaction was ranked highly, with all families seen having a good understanding of the management and follow up plan. Overall satisfaction was ranked on average 9.7/10.

**Conclusions**

Emergency department and hospitalizations of neurologic patients are a significant cost to our healthcare system. Managing referrals and seeing urgent patients in a timely manner is essential for quality outpatient care and can prevent unnecessary ED visits. The RAN clinic created an effective urgent triage method for pediatric neurology patients. A significant portion of referring diagnoses were modified by specialist review. This study reveals that a RAN clinic can significantly reduce visits to the ED following appointment and initiate appropriate follow up. Discharge from appointments without patient understanding of symptoms and uncertainty in diagnoses is one of the most common causes for return visits to the ED. Studies have revealed that urgent clinics can increase patient attendance rate due to short wait time. This was reflected in our study with an almost 99% attendance rate. Limitations of this study include the lack of data collected on admission rates of neurology patients and time spent waiting in ED for specialist review. Areas to improve include triaging time, wait time and better access to investigation. Future evaluation to understand cost effectiveness and long distance appointments via telehealth are needed to improve urgent neurology care for rural patients.

Abstract # 56  
Presenter: Novak, Chris  
Supervisor: Davies, Dawn  
Title: Peripherally-acting mu-opioid antagonists for treatment of opioid-induced constipation in children  
Authors: Chris Novak, MD, Amanda Hogg, MD FRCP(C), Kyle Sue, MD, MHM, CCFP(PC), Dawn Davies MD MA FRCP(C)

### Introduction

Opioid-induced constipation (OIC) is a common and important problem in pediatric palliative care, critical care and post-operative settings. Treatment for OIC is often ineffective and limited by enteral intake. A new class of drugs called peripherally-acting mu-opioid receptor antagonists (PAMORAs) have been shown to be effective treatments of OIC in adults, including the agents methylnaltrexone and naloxegol. Data in children is limited to several small case reports, mostly in the palliative care setting. The goal of this study was to evaluate the effectiveness and safety of methylnaltrexone and naloxegol in hospitalized children, including those with critical illness.

### Methods

We conducted a retrospective study of all children admitted to the Stollery Children's Hospital in Edmonton (Canada) who received either methylnaltrexone or naloxegol for OIC. The primary outcome was time to first BM after the first dose of PAMORA. Secondary outcomes included the proportion of patients to have a BM in the first 24 hours after the first dose of PAMORA, differences in the number of BMs in the week before and after the first dose of PAMORA, and adverse events. We completed subgroup analysis comparing outcomes for patients receiving PAMORAs for palliative care, critical care, or post-operative pain indications.

### Results

A total of 27 patients were included in the study. Patients had trialed an average of 3.3 laxative agents prior to PAMORA administration. Kaplan-Meier survival analysis showed the median time to the first bowel movement after the first dose of PAMORA was 15.5 hours. Seventeen (63%) patients had laxation within 24 hours of first dose. Patients had a mean of 2.6 more BMs in the week after receiving their first dose of PAMORA than in the week prior, which reached statistical significance. Comparing palliative care, PICU and post-operative subgroup showed no statistically significant difference in the number of BMs in the week after receiving the first dose of PAMORA. No significant adverse events were observed.

### Conclusion

OIC is an important condition that causes significant distress to many hospitalized pediatric patients. PAMORAs represent a promising new treatment modality for OIC. This study is the largest to date to evaluate efficacy and safety of PAMORAs in children. The results of this study suggest that PAMORAs are highly effective for children with refractory OIC. The study was likely under-powered to evaluate subgroup differences. Future studies should be prospective and include larger numbers of patients with critical illness and post-operative OIC as indications for treatment.

Funded by WCHRI Resident Research Grant

The Power of Partnership



Abstract # 57  
Presenter: Bitar, Eyad  
Supervisor: Hyderi, Abbas  
Title: The value of early echocardiographic parameters to predict chronic pulmonary hypertension in extreme premature infants  
Authors: Eyad Bitar, Renjini Lalitha, Kumar Kumaran, Maryna Yaskina, Abbas Hyderi

### Introduction

Extremely low gestational age newborns (ELGANs) are at high risk of developing bronchopulmonary dysplasia (BPD). Pulmonary hypertension (PH) is a significant complication in ELGANs who develop BPD and is associated with considerable morbidity and mortality. Early screening using echocardiographic markers for such bronchopulmonary dysplasia associated pulmonary hypertension (BPD-PH) may help caregivers to modify management practices that could result in reduction in both chronic lung disease and pulmonary hypertension. This study aimed to test the predictive ability of early echocardiographic markers (pulmonary artery acceleration time and interventricular septal flattening) for subsequent development of BPD-PH in extreme low gestational age infants.

### Methods

This is a retrospective matched case control study. All preterm infants < 29 weeks admitted to the Neonatal Intensive Care Unit (NICU) at Royal Alexandra Hospital (RAH) between June 1, 2013 and May 31, 2017 were screened to identify infants who had an echocardiogram at 2 time points, 7-21 days of life and after 36 weeks corrected gestational age. Infants with BPD-PH were identified based on their 36 weeks or later echocardiogram and matched with infants without BPD-PH at 1 to 2 ratio. PH markers from early echocardiograms (pulmonary artery acceleration time/right ventricle ejection time (PAAT/RVET) ratio and Eccentricity index (EI)) and their relationship to subsequent development of BPD-PH were analyzed for the two groups. Infants with congenital heart disease (other than patent ductus arteriosus, persistent foramen ovals /atrial septal defect) and multiple congenital anomalies were excluded.

### Results

A total of 588 preterm infants < 29 weeks admitted to the NICU at RAH for the study period, 133 infants were found to have an echocardiogram at the 2 time points. 9 infants were excluded as per criteria. Out of 124 eligible infants, 26 were found to have BPD-PH and were matched with 52 infants without BPD-PH for gestational age. The mean gestational age at birth for the BPD-PH and non BPD-PH groups were 25.27 and 25.30 weeks respectively. Mean PAAT/RVET ratio for PH and non-PH group were 0.34 (95% CI 0.31-0.38) and 0.43 (95% CI 0.4-0.45) respectively, OR for 0.1 unit increase is 0.33 (95% CI 0.17-0.66, P value: 0.0015), the area under the ROC curve (AUC) is 0.73 (95% CI 0.61, 0.85). Mean Eccentricity index for BPD-PH and non BPD-PH groups were 1.24 (95% CI 1.14-1.35) and 1.06 (95% CI 1.01-1.11) respectively, OR for 0.1 unit increase is 1.63 (95% CI 1.19-2.23, P value: 0.002), the AUC is 0.76 (95% CI 0.65, 0.88). A multi-variate analysis combining both PAAT/RVET ratio and eccentricity index resulted in an AUC of 0.79 (95% CI 0.66, 0.91).

### Conclusion

Pulmonary artery acceleration time and Eccentricity index are useful screening tools for subsequent development of chronic pulmonary hypertension in extremely low gestational age infants. Their predictive ability is better when they are considered together.

Funded by Funded by the Women and Children's Health Research Institute (WCHRI)

The Power of Partnership

Abstract # 58  
Presenter: Catena, Gina  
Supervisor: Davies, Dawn  
Title: Medical assistance in dying and minors: Views of the Canadian pediatrician

Authors: Gina Catena BSc MD PGY-4, Dept. of Pediatrics, University of Alberta  
Dawn Davies MD MA FRCP(C), Associate Professor, Dept. of Pediatrics, University of Alberta

### Introduction

Medical Assistance in Dying (MAID) has been available to Canadians meeting specific eligibility criteria since the Royal Assent of Bill C-14 in 2016. As part of this Act, an independent review was initiated to evaluate requests made by mature minors for MAID and ultimately possible inclusion in further iterations of the Act. Limited Canadian data exists on the role of MAID in mature minors or the views of health care practitioners on this topic.

### Methods

A survey was disseminated to members of the Canadian Pediatric Society, collecting information on attitudes surrounding MAID as it applies to minors, specifically mature minors, those with intractable pain, intolerable disability and mental illness. The survey also assessed demographics of respondents, including type of practice and patient population. The results were analyzed using logistical regression to determine if there were correlations between practice variables and opinions surrounding MAID.

### Results

A 29% response rate was achieved (574/1979), with 487 participants completing all questions. Of the respondents, 46% favoured that MAID should be eligible for mature minors experiencing progressive or terminal illness/intractable pain; 29% felt patients with intolerable disability should be eligible, while only 8% favoured extension in cases of intolerable mental illness. Lastly, 33% felt that MAID should never be extended to minors. There was no correlation between attitudes towards MAID and the respondents' type of practice, or if they work with minors suffering from life-threatening illness. There was a statistically significant correlation ( $p < 0.00001$ ) between those who allow religious/spiritual beliefs to influence their views on MAID and opinions on eligibility. Those who allowed religious beliefs to guide their opinions were more likely to disapprove of the extension of MAID to mature minors. There was a correlation between practitioners who had the experience of discussing MAID with parents or minors and support for extending MAID to mature minors ( $p = 0.046$ ). The clinical significance is unclear as only 101 out of 487 had such conversations.

### Conclusion

There exists a great variability in viewpoints amongst pediatric healthcare practitioners as it relates to extension of MAID to minors. Opinions may vary based on factors including spiritual beliefs and conversations pertaining to end of life care with patients.

Funded by WCHRI Resident Research Grant

The Power of Partnership



Abstract # 59  
Presenter: Huie, Michelle  
Supervisor: Forbes, Karen  
Title: Preferred pediatric resident learning styles: From junior to senior resident

Authors: Huie, Michelle  
Forbes, Karen

### **Introduction**

Medicine is a career that encompasses life-long learning. Studies in medical trainees have shown that individual learning styles (LS) change during the progression from medical school to residency (Bitran, 2012). Further, LS differ across varying sub-specialties with limited literature in non-surgical specialties such as Pediatrics. We sought to evaluate LS in our Pediatric residents, and how they may change throughout residency.

We hypothesized that Junior residents will represent more abstract and reflective LS as this style is most consistent with the lecture-based formal instruction in medical school. Further, as Junior residents progress through residency and become Senior residents, they will adapt more concrete and active LS as the learning in residency is less formal instruction and more experienced based.

### **Methods**

The Kolb Learning Style Inventory (LSI) is a well-established and validated 12-item tool used to classify learning styles. There are four classifications: 1) Diverger, 2) Assimilator, 3) Accommodator and 4) Converger. In September 2018, 22 Pediatric residents completed the Kolb LSI and in September 2019, 27 Pediatric residents completed the Kolb LSI.

### **Results**

In the first year of data collection, 12 Year 1 Pediatric residents and 10 Year 2 Pediatric residents participated in the study. LS ranged among the Pediatric residents and among years with each of the 4 LS represented; Convergers and Assimilators were most common (9 and 7 residents respectively) with fewer Divergers and Accommodators (3 residents each). In the second year of data collection, 7 Year 1 Pediatric residents, 10 Year 2 Pediatric residents and 10 Year 3 Pediatric residents participated in the study. Similar to the previous year, LS ranged among residents and years with 10 Convergers, 7 Assimilators and 4 Divergers and 6 Accommodators. Of the residents who participated in both years of the study, 12 residents had changed their LS while 7 residents had the same LS as the previous year.

### **Conclusion**

In contrast to LS of other subspecialty programs previously studied, there is a variety of LS among Pediatric residents with a diversity of LS among junior and senior level of training. This may suggest a diversity of learning needs within the Pediatric residency group at the University of Alberta. Further, for some Pediatric residents, learning styles are dynamic and change over time.

These findings may be used to cater to the different academic learning needs of Pediatric residents (e.g. didactic vs small group vs simulation). By allowing for a variety of teaching formats aligning with a diversity of preferred LS, learning environments may be more conducive to the learners and curriculum planning can be more effective.

Funded by This research has been funded with a resident grant by the generous support of the Stollery Children's Hospital Foundation through the Women and Children's Health

The Power of Partnership





Abstract # 60  
Presenter: Giffin, Nicholas  
Supervisor: Sivarajan, Venkatesan  
Title: **Impact of early surgical correction/palliation of congenital heart defects in infants with viral respiratory tract infections in the current era**  
Authors: **N.A. Giffin and V. Sivarajan**

### **Introduction**

The development of viral respiratory tract infections (RTI) represents a significant portion of acute care provided to the pediatric population and disproportionately affects those with congenital heart disease (CHD).(1) As increased operative and post-operative risks in adults with active viral RTI undergoing cardiac surgical interventions was established in the 1990's,(2) the standard of practice has been to wait 4-6 weeks after a symptomatic, viral RTI to correct CHD in the pediatric population. The Stollery Children's Hospital Cardiac Surgery Program is the primary surgical centre for Western Canada with a high volume of urgent, complex surgeries that can necessitate surgical intervention before resolution of active respiratory tract infections. The outcome literature available for infants with CHD undergoing surgical repair/palliation with active viral RTI symptoms is limited to one, uncontrolled study which analyzed the post-operative course of children with an active, or recent (< 6 months) RSV infection.(3) This retrospective study aims to investigate the post-operative impact of active viral RTI using a case control methodology. Our goal for this study was to either support the 4-6 week waiting period before surgery, or should the outcomes be similar, to spur further research into identifying cases at higher risk of post-operative complications. References: (1) MacDonald, NE et al. N Engl J Med 1982; 307, 397-400. (2) Feldman, RJ et al. J Thorac Cardiovasc Surg 1994; 108, 1152. (3) Khongphatthanayothin, A et al. Crit Care Med. 1999; 27, 9, 1974-1981.

### **Methods**

This retrospective study design was performed in a case control manner identifying infants less than 6 months of age undergoing surgical repair/palliation of CHD and were divided into two groups: (i) those infants with active viral RTI confirmed on nasopharyngeal aspirates (NPA) analysis and with documented, corroborating clinical symptoms peri-operatively (Group 1); and (ii) no recent, or ongoing symptoms of viral RTI (Group 2). The individuals from the two groups were matched based on age, congenital heart defect and surgery type in a 1 active viral RTI to 2 control case fashion. The post-operative outcomes were compared statistically in a case control manner between the two groups.

### **Results**

We identified 22 infants (< 6 months of age) who had surgical correction/palliation between 2014-2017 and with active viral RTI symptoms and positive NPA from the PICU electronic record, or from paper charts. 5 patients had to be excluded as no controls could be identified from our surgical registry. The remaining 17 cases were compared to matched controls in a 2:1 fashion.

### **Conclusion**

To our knowledge, this is the first study investigating the post-operative outcomes of infants undergoing surgical repair/palliation for CHD in the setting of active viral respiratory infections in a retrospective, case-control manner.

Funded by **WCHRI Application in Progress**

The Power of Partnership



Abstract # 61  
Presenter: Valji, Rafiaa\*  
Supervisor: MacLean, Joanna\*  
Title: **A comparison of long-term non-invasive ventilation use in Down syndrome and non-Down syndrome children**  
Authors: Rafiaa Valji\*, Maria L. Castro-Codesal\*, Melanie Lewis<sup>^</sup>, Joanna E. MacLean\*<sup>#</sup>  
\*Division of Pediatric Respiriology, University of Alberta  
<sup>#</sup>Women & Children's Health Research Institute, University of Alberta  
<sup>^</sup>Division of General and Community Pediatrics, University of Alberta

## Introduction

Long-term non-invasive ventilation (LT-NIV) has become a standard therapy for a range of diseases leading to respiratory insufficiency or sleep related breathing disorders. From 2004-2015, the number of children started on LT-NIV tripled, leading to a five-fold increase in the number of children using LT-NIV in Alberta. Children with Down syndrome are one of the largest single groups using LT-NIV, comprising 20% of the Alberta pediatric LT-NIV clinic population. As a group, children with Down syndrome have a high rate of comorbidity and neurodevelopmental impairment, which may add to the challenge of using LT-NIV. The objective of this study is to compare the characteristics, use, and outcomes of LT-NIV for Down syndrome and non-Down syndrome children.

## Methods

This study is part of a longitudinal, retrospective regional cohort study of children in Alberta initiated on LT-NIV over a ten-year period (N=622). Data was collected from medical and sleep laboratory records, including sleep study reports and NIV downloads. Primary diseases leading to LT-NIV were grouped into five primary disease categories: upper airway, central nervous system, musculoskeletal, cardiorespiratory, and other, when a single primary disease could not be identified. Children with Down syndrome (Ds) were matched in a 1:2 ratio with non-Down syndrome (nDs) children based on age and therapy start date. Groups were compared using Student's t-test, Chi-square, and Fisher exact test where appropriate.

## Results

A total of 314 children (106 Ds, 212 nDs) were included in the analysis; sufficient matches were identified for inclusion of 88% of the Ds children from the cohort. The age at initiation ( $7.1 \pm 5.3$  y) and male: female ratio (67%:33%) did not differ between groups. The distribution of the primary diagnostic category leading to LT-NIV initiation did differ between groups with upper airway accounting for 90% of Ds children in comparison to a greater spread in nDs children (50% upper airway, 24% central nervous system, 15% musculoskeletal,  $p < 0.001$ ). The groups did not differ by number of comorbidities ( $3.4 \pm 1.7$  vs  $3.4 \pm 4.5$ ,  $p = ns$ ) or apnea-hypopnea index at baseline (12.3 (IQR 20.7) vs 12.0 (IQR 25.0) events/hour,  $p = ns$ ). The trigger for starting Ds children on LT-NIV was more often a sleep study compared to nDs children (80% vs 66%,  $p < 0.05$ ). While the follow-up period was longer for Ds compared to nDs children ( $2.7 \pm 2.0$  vs  $2.0 \pm 1.8$  y,  $p < 0.01$ ), the outcome of LT-NIV at the most recent follow-up visit (remained on, stopped, transfer to another clinic, lost to follow-up, death) did not differ between groups, with 49% of Ds and 44% of nDs continuing on LT-NIV. Overall mortality rate was low (4%) with no difference between Ds and nDs children (2.8% vs 4.2%,  $p = ns$ ).

## Conclusion

Down syndrome children show some differences in clinic characteristics when compared to other children using LT-NIV, though do not differ with respect to continued use at most recent follow-up or mortality. A more detailed assessment of factors related to LT-NIV technology, adherence, and outcomes will help determine if a tailored approach is needed to support Down syndrome children using LT-NIV.

Funded by The Respiratory Health Strategic Clinical Network, Alberta Health Services

The Power of Partnership



Abstract # 62  
Presenter: Bhaloo, Zafira  
Supervisor: Kherani, Tamizan  
Title: Improving the efficiency of handover in pediatrics: A resident-led quality improvement project  
Authors: Zafira Bhaloo, Nichole Pereira, Chrystale Champigny, Jennifer Walton, Tamizan Kherani

### **Introduction**

Handover is a major preventable cause of patient harm. Residents are responsible for handover throughout their training and handover is a new key CanMEDS competency. In our institution, despite initiating the I-PASS curriculum for pediatric resident handover, residents still feel that handover is inadequate. This resident-led quality improvement (QI) project aims to improve the efficiency of pediatric resident handover by identifying challenges and employing QI methodologies for improvement. By improving handover, we hope to enhance the quality of care and patient safety for our pediatric patients.

### **Methods**

A qualitative thematic process based on resident perceived challenges was conducted. Resident handover was observed. Resident focus groups reflecting on the thematic process while engaging residents in the Model of Improvement were conducted. QI tools including root cause analysis (eg. Ishikawa diagrams) and process mapping were employed to develop an aim statement, outcome measures and change ideas. These informed plan-do-study-act (PDSA) cycles and change ideas were implemented by the residents. Handover was observed in a controlled before and after study design to evaluate the interventions.

### **Results**

The qualitative thematic process identified content (73%), structure (55%), interruptions (36%) and late starts (36%) as major challenge themes. The resident focus groups prioritized interruptions, content and structure as challenges to address. Change ideas implemented included staggered handover times, reminding staff to refrain from paging during handover time unless urgent and adding another computer for handover. Time the handover lists are printed, the start and end time of handover, the duration of handover, and the number of interruptions during handover were recorded.

### **Conclusion**

This QI project engages pediatric residents in QI methodology to improve handover, a daily component of pediatric patient care. Handover, QI, and patient safety are reflected in the CanMEDS competencies and framework as residency goals. Improved handover efficiency can lead to improved patient safety and quality of care for our pediatric patients.

Funded by Alberta Health Services Quality Innovation Fund

The Power of Partnership



Abstract # 63  
Presenter: Burnett, Mervin  
Supervisor: Sergi, Consolato  
Title: Graphene oxide nanoparticles on induced apoptosis in osteosarcoma

Authors: Mervin Burnett, Yasser Abuetaab, Ania Wronski, Fan Shen, Sujata Persad, Roger Leng, David Eisenstat, Consolato Sergi

### Introduction

Osteosarcoma is the most common primary bone tumor in children, adolescents and young adults and comprises about 20% of primary bone sarcomas. There has been an improvement in the survival rate for persons diagnosed with osteosarcoma due to advancements made in diagnosis and treatment. However, there is a need to improve management for osteosarcoma, as traditional therapeutic approaches are limited by non-specificity and systemic toxicity. Nanoparticles can provide an effective treatment for cancer as it can specifically target cancer cells while reducing undesired side effects. One such nanoparticle with anti-cancer properties is graphene oxide. We hypothesized that graphene oxide has a toxic effect on human cancer cells while not affecting non-cancerous cell lines. The aim of this study was to evaluate the toxicity and underlying mechanism of graphene oxide on osteosarcoma in vitro

### Methods

In this study human osteosarcoma cell lines, U2OS and SAOS2; and the normal osteoblast cell line hFOB1.19 were used. IGF1 and IGFBP3 were deleted using CRISPR/Cas9. These cells were cultured and then treated over a time course with graphene oxide at concentrations of 0, 25 and 50 µg/ml. Apoptosis and ROS were analysed using the Annexin V-FITC apoptosis detection kit and Invitrogen total reactive oxygen species (ROS) assay kit respectively using a Muse cell analyser. Morphology of the cells was investigated using digital photomicroscopy. Western blotting was used to analyse for expression of the NRF-2 antibody.

### Results

There was an increase in apoptosis for cells treated with graphene oxide when compared to untreated cells. A significantly higher rate of apoptosis was detected in the osteoblastoma cell lines compared to the normal osteoblast cell line, especially in U2OS cells in which IGF1 and IGFBP3 were knocked out. ROS increase due to graphene oxide exposure was time and concentration dependent. Based on the rate of apoptosis, ROS and morphological changes, graphene oxide had a greater cytotoxic effect on the osteosarcoma cell lines; U2OS and SAOS2 than on the normal osteoblast cell line of hFOB1.19. Minimal morphological changes were observed in the normal osteoblasts treated with graphene oxide.

### Conclusion

When considering the biological properties of graphene oxide, our data support further preclinical development towards its potential use as a treatment option for osteosarcoma. Furthermore, targeting the IGF1 and IGFBP3 signalling pathway in osteosarcoma in combination with graphene oxide therapy may potentiate cytotoxicity.

Funded by

The Power of Partnership



Abstract # 64  
Presenter: AL Riyami, Hilal  
Supervisor: Escudero, Carolina  
Title: Does a smartphone-based ECG recording system in pediatric patients with palpitations improve diagnostic yield?  
Authors: Dr. AL Riyami Hilal Dr. Escudero Carolina Dr. L. Hornberger Dr. J.Atallah Dr. J.Y. Coe Dr. A. Ohinmaa

### Introduction

Palpitations are a common occurrence in children and a frequent indication for referral to pediatric cardiology. Palpitations are defined as the feeling of a rapid, irregular, or abnormal heart beat, and can be caused by many different types of heart rhythms. There are several types of diagnostic equipment that can be used to obtain symptom-rhythm correlation, including Holter monitor (applied for 24-48 hours), event recorder, and the more invasive option of an internally implanted loop recorder. Event recorders are most commonly used for documentation of intermittent palpitations. Limitations to use of an event recorder include the limited time duration of prescription of the recording unit, potential for poor quality recordings, need for a landline and the need for the patient to have the recording device available and applied to the chest at the time of experiencing symptoms.

The AliveCor Kardia monitor is a newer generation device which is much smaller and more easily portable than the CardioCall event recorder. To record an electrocardiographic tracing, the user must open the associated application on their mobile device and place two fingers from each hand onto the electrodes of the recording device. The patient can indicate their symptoms at the time of the recording and the tracing can be emailed immediately to the physician. The cost of a Kardia monitor is \$130/unit.

### Methods

Objectives:

Primary objective of this prospective randomized trial is to determine the diagnostic utility and time to diagnosis using the AliveCor Kardia monitor compared to the current standard of care (Cardiocal event recorder).

The secondary objectives are to determine the cost of obtaining a diagnostic transmission and related cardiologic health care costs, patient satisfaction and tracing interpretability between the AliveCor Kardia and CardioCall groups.

Study Design:

A prospective, randomized trial of pediatric patients presenting for pediatric cardiology consultation for investigation of palpitations.

Inclusion and Exclusion Criteria:

Inclusion criteria are: age 5-18 years; parent or patient ownership of a smartphone compatible with use of the AliveCor Kardia Application; estimated palpitation duration of at least 1 minute; and consistent symptoms of palpitations with the need for symptom-rhythm correlation using an event recorder, as determined by the consulting pediatric cardiologist. Patients will be excluded for refusal to consent.

### Results

The study still the progress, so far we have 4 participant.

### Conclusion

Clinical Impact: If the AliveCor smart phone device is found to be clinically diagnostic, accepted by patients/parents and cost effective for pediatric arrhythmia diagnosis associated with palpitations, it would impact our local practice immediately but could also change the standard of arrhythmia surveillance practice nationally and internationally.

Funded by University of Alberta

The Power of Partnership

Abstract # 65  
Presenter: Pajunen, Kiera  
Supervisor: Tham, Edythe  
Title: CMR assessment of aortopathy in pediatric Turner syndrome

Authors: Kiera Pajunen, Somjate Suntratnpiat, Elizabeth Rosolowsky, Rose Girgis, Joseph Pagano and Edythe Tham.

## Introduction

Turner Syndrome (TS) is associated with aortopathy and a risk of aortic dilation. Thresholds for risk of aortic dissection are reported at an aortic size index (ASI) of 2-2.5 cm/m<sup>2</sup>. Clinical assessment using static 2-dimensional measurements of aortic size does not reflect vascular function. Cardiac MRI (CMR) allows for evaluation of ventricular and vascular properties, thus we sought to evaluate the aortic properties of strain, compliance and ventriculoarterial (VA) coupling in pediatric patients with TS.

## Methods

Patients with Turner syndrome underwent CMR to evaluate the aortic anatomy, flow and ventricular function. Systolic blood pressure (SBP) and pulse pressure (PP) were obtained and the end systolic pressure (ESP) calculated as  $0.9 \times \text{SBP}$ . Aortic root diameters were obtained from cine images. Magnitude images from phase-contrast imaging of the ascending aorta in cross-section was used to calculate: relative area change (RAC = max-min area); and ASI (maximum diameter) from the same image. Vascular properties were calculated as such: aortic strain = RAC/min area; aortic compliance = RAC/PP; aortic elastance ( $E_a = \text{ESP}/\text{SV}$ ); LV elastance (Ees) =  $\text{ESP}/\text{ESV}$ ; and VA coupling (VAC) =  $E_a/E_{es}$ . Pearson correlation coefficient examined the associations between aortic size and vascular properties.

## Results

CMR was performed in 27 patients, age  $14 \pm 3$  years, height  $139 \pm 12$  cm, BSA  $1.34 \pm 0.32$  m<sup>2</sup>, SBP =  $116 \pm 13$  mmHg and DBP  $76 \pm 13$  mmHg. Seven (26%) had bicuspid aortic valve, 1 aortic coarctation repair, 1 PAPVR, and 3 LSVC. All patients had normal LV volumes, LVEF ( $62 \pm 5.6\%$ ), and aortic root size ( $Z = -0.08 \pm 1.2$ ). Mean ASI was  $1.8 \pm 5$  cm/m<sup>2</sup> ( $Z = +1.48 \pm 1.27$ ), and 6 patients had a dilated ascending aorta ( $>2$  cm/m<sup>2</sup>). Aortic elastance was  $2.28 \pm 0.62$  mmHg/ml and LV elastance  $3.88 \pm 1.56$  mmHg/ml, resulting in VAC  $0.63 \pm 0.15$ .

Increased ASI was associated with increased aortic compliance ( $r = 0.69$ ), increased aortic elastance ( $r = 0.37$ ), decreased aortic strain ( $r = -0.34$ ) and increased LV elastance ( $r = 0.34$ ) but not Ees. Higher max aortic area was associated with increased aortic compliance ( $r = 0.69$ ), and increased aortic root diameter was associated with increased aortic elastance ( $r = 0.38$ ). None of the parameters had any relationship to blood pressure.

## Conclusion

While larger aortas displayed increased compliance, they also demonstrated decreased strain suggestive of increased aortic stiffness, which was not due to hypertension. The corresponding increased aortic elastance, accompanied by increased LV elastance, is consistent with preserved myocardial contractility in order to maintain optimal coupling (VAC  $<1$ ). Evaluation of the biophysical properties of the aorta in Turner syndrome may provide early detection of patients at risk for dissection, which may be present even without aortic dilation.

Funded by

The Power of Partnership



Abstract # 66  
Presenter: Mackie, Andrew  
Supervisor: Mackie, Andrew  
Title: **Randomized controlled trial of a transition intervention program for young adolescents with congenital heart disease**  
Authors: Andrew Mackie, Kathryn Rankin, Maryna Yaskina, Jody Gingrich, Michelle Schuh, Elina Williams, David Nicholas, Gwen Rempel

### **Introduction**

Adolescents with congenital heart disease (CHD) require lifelong specialized cardiology follow-up and the knowledge and self-management skills needed for chronic disease management. Prior studies have demonstrated the benefit of educational transition interventions for older adolescents. However, the American Heart Association has recommended that transition interventions begin by age 13. We hypothesized that a nurse-led transition intervention will result in improved self-management skills and CHD knowledge among 13-14 year olds with moderate or complex CHD.

### **Methods**

Single center randomized controlled trial. Participants were randomized to a transition intervention or usual care. The intervention group received a 1-hour individualized session with a cardiology nurse, focusing on CHD education and self-management. The primary endpoint was change in transition readiness score between baseline and 6 months, using the validated TRANSITION-Q, a 14-item instrument. The secondary endpoint was change in MyHeart score (CHD knowledge) between baseline and 6 months.

### **Results**

We enrolled 60 participants to intervention (n=30) or usual care (n=30). Mean baseline TRANSITION Q scores (range 0-100) were  $47 \pm 14$  (usual care) vs.  $49 \pm 10$  (intervention). At 6 months, TRANSITION Q scores were  $44 \pm 14$  (usual care) vs.  $54 \pm 9$  (intervention). Adjusted for baseline score, TRANSITION Q scores at 1 and 6 months were higher in the intervention group (OR 5.9, 95% CI 1.3-10.5,  $p=0.01$ ). Mean MyHeart score (range 0-100) increased from  $54 \pm 24$  to  $57 \pm 22$  (usual care) vs.  $48 \pm 24$  to  $71 \pm 16$  (intervention). Adjusted for baseline score, MyHeart scores at 1 and 6 months were higher in the intervention group (OR 18.5, 95% CI 11.5-25.5,  $p<0.0001$ ). Participants age 14 had a greater increase in TRANSITION Q score at 6 months compared to 13 year olds ( $p=0.046$ ).

### **Conclusion**

A nurse-led transition intervention resulted in improved transition readiness and CHD knowledge among young adolescents.

Funded by

The Power of Partnership



Abstract # 67  
Presenter: Tham, Edythe  
Supervisor: Tham, Edythe  
Title: Cardiac magnetic resonance parameters associated with surgery in a pediatric and young adult population with chronic aortic regurgitation  
Authors: Amol Moray, Joseph Pagano, Michelle Noga & Edythe Tham

### Introduction

The timing for intervention in patients with significant chronic aortic regurgitation (AR) is based on symptoms and 2-dimensional echocardiography measurements of LV diameters and function. However, threshold dimensions in adults do not apply to children. Because of its high accuracy and reproducibility cardiac magnetic resonance imaging (CMR) is being increasingly used in the evaluation of AR. However there is limited data on the use of CMR parameters to guide surgical decision making in pediatrics. We examined associations between CMR quantification of AR and left ventricular (LV) volumetric function and the need for surgical

### Methods

Forty-one children and young adults with aortic regurgitation who had undergone CMR at our institution were retrospectively divided into two groups, based on subsequent need for aortic valve surgery. CMR consisted of bSSFP cine imaging for assessment of ventricular volumes, mass, and ejection fraction, and phase contrast imaging for quantification of aortic regurgitant fraction (RF) and indexed regurgitant volume (RVi). Left ventricular (LV) dimensions were taken in end diastole (LVEDD) and end systole (LVESD) from the 3 chamber view to compare with ventricular volumes using Pearson correlation coefficient. For patients in the surgical group, the CMR immediately prior to the intervention was included, while the most recent CMR was used for those in the non-surgical group. Differences in CMR parameters between the 2 groups were compared using unpaired t-tests. Receiver operating characteristic (ROC) analysis identified CMR parameters with discriminatory ability towards primary end point of surgery (area under the curve AUC >0.7). Cutoff values were determined using the Youden index.

### Results

Of 41 patients with chronic AR, 20 (14±5y) underwent surgery and 21 had no interventions (16±5 y). Patients who underwent surgery had significantly larger ventricular dimensions, volumes and aortic regurgitant fraction than those without surgery. Results of ROC analysis demonstrated that aortic RF and RVi had the highest discriminatory power (AUC of 0.93 and 0.92 respectively). Indexed LV volumes had good but slightly reduced discriminatory power (AUC 0.85 and 0.89 for indexed end diastolic and end systolic volume respectively) towards surgery. 2D measurements showed moderate correlation with ventricular volumes (LVEDD vs LVEDV,  $r=0.5$  and LVESD vs LVESV  $r=0.57$ ).

### Conclusion

Guidelines for surgical intervention in children with chronic aortic regurgitation are lacking. Furthermore, adult 2D echo measurements of LV dimensions and AR quantification may not apply to the pediatric population. Our study highlights the significant differences in CMR parameters between patients who underwent aortic valve surgery and those who were managed conservatively. We identified potential threshold values for surgery and this provides an opportunity for further research to formulate guidelines for aortic valve surgery in children with chronic AR.

Funded by

The Power of Partnership





Abstract # 68  
Presenter: Sacrey, Lori  
Supervisor: Zwaigenbaum, Lonnie  
Title: Physiological measurement of emotion from infancy to preschool

Authors: Lori-Ann R. Sacrey, Sarah Raza, Vickie Armstrong, Azadeh Kushki, Jessica Brian, Isable M. Smith, & Lonnie Zwaigenbaum

## Introduction

Emotional regulation, the ability to regulate emotional responses to environmental stimuli, develops in the first years of life and plays an important role in the development of social competence, personality, and problematic behaviours. Responses to positive and negative stimuli may be difficult to assess in young children who do not yet have the ability to communicate verbally. As such, physiological measurement is a method that can allow us to better understand age-related changes and individual differences in response to environmental challenges. Unfortunately, there are currently no standard practices for measuring cardiac physiology for very young children.

## Methods

We completed a review of the literature to provide an in-depth examination of research that has measured physiology during emotion-evoking tasks in neurotypical preschool children to provide recommendations for (1) normative values of respiratory sinus arrhythmia (RSA) for baseline and emotion-evoking tasks, and (2) variability in responses to positive and negative tasks. A systematic literature review was completed in accordance with the PRISMA checklist. Searches were performed in PsycINFO, Web of Science, CINAHL Plus, and Ovid MEDLINE(R) using the following terms: emotion, physiology, and preschooler. Of the 2,598 articles found, 64 were included in the in-depth analyses of the various methodologies.

## Results

Tasks: Baseline tasks were highly variable in duration, from as brief as 2 seconds up to 420 seconds, and fell within five categories, sitting quietly, sedentary task, play episode, between-tasks break, watching a video, and an unknown category described as 'baseline period.' The emotion-evoking tasks probed for distress, anger, disappointment, frustration, fear, 'positive', multiple emotional responses, or guilt.

Mean Changes by Age: Analyses of mean RSA showed an increase with age. This was supported by Spearman's correlation ( $\rho(29) = .81, p = .001$ ). When change from baseline was correlated with age (task mean – baseline mean; i.e., adjusted score removing baseline values), this was no longer significant ( $\rho(29) = .21, p = .28$ ), suggesting the age-related changes are due to changes in baseline heart rate.

RSA Normative Values: (i) 0-6 months: baseline = 2.70-3.70 ms<sup>2</sup> and task = 2.60-3.50 ms<sup>2</sup>, (ii) 7-12 months: baseline = 3.17-4.27 ms<sup>2</sup> and task = 3.65-4.27 ms<sup>2</sup>, (iii) 13-24 months: baseline = 3.20-5.36 ms<sup>2</sup> and task = 3.13-5.02 ms<sup>2</sup>, (iv) 25-48 months: baseline = 5.66-5.76 ms<sup>2</sup> and task = 5.76-5.66 ms<sup>2</sup>, and (v) 49 months and older: baseline = 5.95-6.20 ms<sup>2</sup> and task = 5.65-6.34 ms<sup>2</sup>.

## Conclusion

Having a good understanding of age-related changes of neurotypical children, for both baseline and emotion-evoking tasks, as well as the different methodologies used to assess and analyze responding, is vital when examining emotional regulation in populations of children who are at-risk or diagnosed with developmental disorders.

Funded by Women and Children's Health Research Institute, Canadian Institutes of Health Research (CIHR), Brain Canada, and the Azrieli Foundation

The Power of Partnership



Abstract # 69  
Presenter: Buschmann, Robert  
Supervisor: Mayan, Maria  
Title: **Southside Mother's Day out: Understanding one child care's struggle to improve early learning and care in Edmonton**  
Authors: Buschmann, Robert; Wicks, Shea

### **Introduction**

Child care is increasingly seen as a social determinant of health. Access to high-quality, affordable child care has been shown to have direct and indirect health benefits for the children who attend such programs as well as their families. That access, however, is not assured in Canada. To address this problem, the newly formed Edmonton Council for Early Learning and Care (ECELC) has been tasked with developing an integrated system of child care in Edmonton. Recently, the ECELC came across the story of Southside Mother's Day Out (SSMDO), a high-quality, community-based child care struggling to keep its doors open. It soon became obvious that understanding the maze of barriers that SSMDO has faced—and continues to face—could be used to better understand the larger forces determining the quality, affordability, and accessibility of child care in Edmonton.

### **Methods**

A case study describing SSMDO's situation was co-created in several steps. First, a meeting was held with the director of SSMDO and several members of the ECELC to understand the basic elements of the story. Second, that story was synthesized into a narrative and combined with a review of the relevant public policies impacting SSMDO. This document was then revised and edited multiple times by both a subset of members of the ECELC and the director of SSMDO, ultimately resulting in the final case study, which was presented to the entire ECELC.

### **Results**

The case study described the barriers that SSMDO faced, including municipal and provincial policies, demographic pressures in Edmonton, and a sometimes surprising set of private market forces. Most interesting, however, was how these individual barriers inadvertently combined to create an environment that could threaten to change the landscape for child care in Edmonton. Just as important as the technical results of the written case study, however, have been some of the unexpected impacts of its creation. For example, the case study of SSMDO is becoming a shared common story for the ECELC that has become a focus of both formal and informal discussion and debate.

### **Conclusion**

Research in recent years has shown the health benefits of high-quality, affordable child care. Focused case studies, such as the one presented here, can be valuable in understanding the forces that affect such social determinants of health. In addition, the very act of creating such case studies can help those who seek to improve child care focus their energies and form lasting connections.

Funded by WCHRI Patient and Community Engagement Training (PaCET) program; Edmonton Council for Early Learning and Care

The Power of Partnership



Abstract # 70  
Presenter: Shillington, Jessica  
Supervisor: McNeil, Deb and Raffin, Shelley  
Title: Feeding and readiness: The transition from hospital-to-home with a late-preterm infant

Authors: Jessica Shillington, Deb McNeil, Shelley Raffin, Shahirose Premji, and Jeanne Scotland

### **Introduction**

Parents of late-preterm infants have identified inadequate preparation to manage their newborn's unique needs at home, yet little is known about their hospital discharge experience. This study aims to describe the perspectives of parents surrounding their transition from hospital-to-home with their late preterm infant (born between 34 weeks and 36 weeks and 6 days gestation).

### **Methods**

Twelve parent participants, nine mothers and three fathers, were recruited from Calgary, Alberta, and shared their experience through in-person interviews and one focus group. Interpretative description was used to guide the study, and data was analyzed through interpretive conceptual analysis and description.

### **Results**

Key themes from parents' experiences are "Feeling ready" and "Fed is best". These two themes illustrate parents' transition home with their late-preterm infant and are influenced by "Previous parenting experience" and their "Discharge care setting". Parents described verbal approval from healthcare professionals, early community follow-up, and discharge teaching specific to their late-preterm infant's unique characteristics to increase their feelings of readiness to transition home. Feeding was parents' most significant challenge, and they expressed a "fed is best" stance indicating that breastmilk is nutritionally superior yet feel the most important thing for their newborn is to feed and grow.

### **Conclusion**

With a "fed is best" mind-set, parents feel that they should be supported to choose a feeding method or combination of methods that is best for them and their family. Mothers and fathers of late-preterm infants must be supported to take care of themselves and their infant. In hopes of reducing feeding challenges, parents require education on the behavioral characteristics of their late-preterm infant in hospital and the community. With the late-preterm infant population growing globally, quality late-preterm infant care is becoming increasingly important, and the education and wellbeing of parents of late-preterm infants is essential to improving health outcomes for these infants.

Funded by Health Outcomes Improvement Fund from the Maternal Newborn Child and Youth (MNCY) Strategic Clinical Network

The Power of Partnership



Abstract # 71  
Presenter: Tulli, Mia  
Supervisor: Salami, Bukola  
Title: Immigrant children in Canada: Mothers' perspectives on barriers to mental health care  
Authors: Tulli, M., Salami, B., Begashaw, L., Meherali, S., Yohani, S., Hegadoren, K.

### **Introduction**

Data on newcomers' access to services in Canada typically focus on adult populations generally but not children specifically. To fill this gap, this study explored barriers faced by immigrant and refugee mothers in accessing mental health services for their children in Edmonton, Alberta, Canada

### **Methods**

In this qualitative descriptive study, researchers conducted 18 semi-structured interviews with immigrant and refugee mothers who live in Edmonton, Alberta, self-identify as women, and have children living in Canada

### **Results**

Barriers included financial strain, lack of information, racism/discrimination, language barriers, stigma, feeling isolated, and feeling unheard by service providers. Facilitators to mental health services included schools offering services, personal levels of higher education, and free services

### **Conclusion**

Health professionals can improve access to mental health services by addressing issues related to racism within the health system and creating awareness related to mental health, and by providing trained interpreters to help bridge barriers in communications

Funded by This research has been funded by the generous support of the Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute.

The Power of Partnership



Abstract # 72  
Presenter: Qureshi, Mosarrat  
Supervisor: Aziz, Khalid Aziz  
Title: Prophylactic indomethacin: The impact on brain and gut injury may be gestational age dependent  
Authors: Mosarrat Qureshi, Prakesh S. Shah, Dalal Abdelgadir, Xiang Y. Ye, Jehier Afifi, Ryan Yuen, Sara Calderon, Barbara Taylor, Khorshid Mohammad, Bruno Piedboeuf, Khalid Aziz on behalf of the Canadian Neonatal Network

### Introduction

Extremely low gestational age newborns (ELGAN) have higher rates of mortality and brain or gut injury. Prophylactic indomethacin (PI) has been shown to reduce severe neurological injury (SNI); however, studies suggest an association of indomethacin with spontaneous intestinal perforation (SIP). Our objective was to evaluate association of PI on early mortality (<10 days of age) or SNI and early mortality or SIP across gestational age groups in babies born at <29 weeks' (w) GA.

### Methods

Data from the Canadian Neonatal Network (CNN) database were reviewed for neonates born at GA 23 - 28 weeks and admitted to participating Neonatal Intensive Care Units (NICU) in Canada during 2010 – 2017. Infants with major malformations and moribund on admission were excluded. Infant characteristics were compared between groups with and without receipt of PI. The impact of PI on the primary outcomes (early mortality/SNI and early mortality/SIP) across GA was assessed using multivariable logistic regression model with Generalized Estimating Equations (GEE) approach to account for the clustering of infants within each site, after adjustment for confounders.

### Results

Of 12515 included eligible infants, 1,435 were exposed to PI. The rate of receipt of PI was 28.79% at 23w, 26.59% at 24w, 18.82% at 25w, 9.76% at 26w, 5.68% at 27w and 2.35% at 28w GA. The PI group were of lower GA, lower birth weight, and had higher severity of illness (Score for Neonatal Acute Physiology with Perinatal extension, SNAP II PE score) on admission (Table 1). Univariate analysis showed PI was associated with significantly lower early mortality/SNI in infants born at 23w GA and lower early mortality/SIP at 23-24w GA but increased early mortality/SIP at 28w (Table 2). Multivariable analysis revealed that PI was associated with reduced early mortality/SNI, early mortality/SIP and death before discharge at 23-25w, 23-24w and 23-24w GA respectively. PI was associated with increased risk of early mortality/SIP at 26-28w GA (Table 3; Figure 1).

### Conclusion

In a large national cohort of ELGANs, and after adjustment for known confounders, PI for neonates at 23-25w GA was associated with lower mortality with SNI or SIP. Use of PI at 26-28w GA, was associated with harm.

Funded by The Canadian Neonatal Network Coordinating Centre is supported by funding from the Canadian Institutes of Health Research and Mount Sinai Hospital.

The Power of Partnership



Abstract # 73  
Presenter: Assi, Ali  
Supervisor: MacDonald, Shannon  
Title: **The childhood immunization reminder project (ChIRP): A pilot intervention to improve uptake of children's 18-month immunizations**  
Authors: Ali Assi, Shannon MacDonald, ChIRP Academic Advisory Committee

## **Introduction**

In order to adequately protect children from infectious diseases, vaccine coverage needs to be maintained at or above 95% for most vaccines. Thus, it is concerning that vaccine coverage levels routinely drop 10-15% between the 12-month and 18-month immunizations. This drop is often the difference between achieving community immunity for a vaccine-preventable disease and having coverage so low it can put the population at risk of a disease outbreak. The Childhood Immunization Reminder Project (ChIRP) aims to improve the uptake of 18-month immunizations in Alberta. The project will achieve this by piloting an immunization appointment reminder system and providing immunization information to parents in languages other than English. The goal is to support healthcare providers (HCPs) by alleviating the burden of recalling children who miss appointments and to support parents by reducing forgetfulness of scheduled appointments and improving access to immunization information.

## **Methods**

In collaboration with two participating health centres in Alberta, the project launched an immunization reminder service along with a website containing pre-school immunization information in 9 different languages. As part of ChIRP, parents receive two routine reminders: (1) a reminder when the child turns 15 months old to book or reschedule the 18-month immunization visit, along with a link to a website with immunization information; and (2) a reminder sent 3 days prior to the scheduled 18-month visit with the date and time of the appointment. At the 12-month visit, nurses are recruiting parents to evaluate the reminder service after their child's 18-month visit. When the child turns 19 months old, recruited parents receive a link to an online survey to evaluate the intervention. They also have the option to complete the survey over the phone. Interpretation services will be available for participants who choose to answer the survey in a language other than English. ChIRP will also evaluate the public health program leaders and HCPs' acceptability of the intervention, as well as the effectiveness of the intervention in terms of the change in appointment "no shows" and vaccine coverage pre- and post-intervention.

## **Results**

ChIRP launched the recruitment phase at the Lethbridge Community Health Centre in AHS South zone (March 2019) and at the Mill Woods Public Health Centre in AHS Edmonton zone (May 2019). We also developed a website that hosts the AHS pre-school immunization information that we had translated into 8 different languages. ChIRP recruited 479 participants between March and August 2019, with recruitment continuing until February 2020. The reminder phase launched in May 2019 and will continue until August 2020. The evaluation phase began in September 2019 and will conclude in September 2020.

## **Conclusion**

As a result of the intervention, we aim to present public health program leaders and HCPs with improved and efficient processes for providing appointment reminders and immunization information. We also aim to support parents in remembering appointments. Access to immunization information in a language of choice has the potential to provide consistent and timely information to improve parents' knowledge of vaccines, in order to facilitate discussion with HCPs and ultimately improve immunization uptake.

Funded by Public Health Agency of Canada (PHAC), Alberta Health

The Power of Partnership



Abstract # 74  
Presenter: Petrova, Alexandra  
Supervisor: Huynh, Hien Q.  
Title: Infliximab clearance during and post induction predicts clinical and endoscopic outcomes at 1 year in children with Crohn's disease  
Authors: Petrova A., Wine E., Griffiths A.M., El-Matary W., Huynh G.H., Prosser C., Kluthe C., Mould D.R., Carroll M.W., Huynh H.Q

### Introduction

IFX clearance (CL) is varied in children with CD, and CL is increased relative to body weight in those under 30 kg at induction. Our aim was to determine if CL at and post induction can predict 1 year outcomes in children treated with IFX.

### Methods

IDEAL study was conducted at 3 Canadian Children IBD Network sites. We prospectively followed 35 pediatric CD patients who initiated IFX. 88% required dose optimization. NONlinear Mixed Effects Modelling was used to develop a population PK model. 1 year follow-up data for 26 patients were available. Non-responders were defined as Weighted Pediatric CD Activity Index (wPCDAI)  $\geq 12.5$ , persistently elevated CRP  $> 4$ , intestinal surgery, discontinuation of IFX, or steroid use during the 6 months prior to 1 year follow-up. Fecal Calprotectin (FCP), CRP, ESR, and Simple Endoscopic Score for CD (SES-CD) were also collected. Correlation analysis, Fisher exact test, and logistic regression were used to identify predictors of clinical, endoscopic and biomarker response at 1 year. ROC curve was used to estimate cut-off points for predicting a response.

### Results

The median follow-up was 12.8 months [11.8;14.98]. 20 patients were responders (11 males) and 6 non-responders (2 males). Age, weight and gender had no effect on 1 year outcomes. Of the 6 non-responders - 1 switched to a new class biologic, 1 remained on IFX, 4 required intestinal surgery (2/4 remained on IFX post intestinal resection), 21/26 patients had a follow-up colonoscopy and 13/21 achieved mucosal healing (SES-CD $<4$ ). CL at doses 1 and 5 predicted clinical and endoscopic response at one year ( $p=0.03$ ,  $r=0.474$  and  $p=0.005$ ,  $r=0.592$ , respectively). Dose 1 CL  $\geq 0.321$ L/day and Dose 5 CL  $\geq 0.305$ L/day were associated with poor outcome (AUC[95%]=0.78[0.56;0.99]) (AUC[95%] = 0.85[ 0.66;1.00]) respectively. The non-responders had higher IFX trough at dose 5 compared to the responders (10.1 [7.3;13.5] and 4.9 [3.4;7.4], respectively,  $p=0.028$ ). All non-responders were dose optimized with median dose 6.0mg/kg [5.4;9.0] and frequency 4.3 weeks [4;6] at dose 5 as compared to 7.2mg/kg [6.9;7.8] and 6 weeks [4;6] in responders ( $p>0.1$ ). wPCDAI  $< 12.5$  at doses 4 and 5 predicted clinical response, with dose 5 being the better predictor ( $p<0.0001$ ,  $r=0.697$ ). The odds of a dose 5 non-responder to respond at one year were 3 in 100, or 0.03 [0.02;0.39]. Dose 5 FCP $\leq 221$  mcg/g was a predictor of remission and mucosal healing (AUC[95%]=0.78[0.48;1.00]). FCP for non-responders were Dose 5 - 1140 mcg/g [219;2416], Year 1 - 518 mcg/g [152;1808]. FCP for responders were Dose 5-95 mcg/g [55; 343], Year 1-73 mcg/g [28;276].

### Conclusion

IFX CL at dose 1 and 5 are predictors of clinical and endoscopic response in children with CD. Increased CL suggests inadequate response to IFX treatment. Low wPCDAI and FCP at dose 4 and 5 are also predictors of response. With dose optimization, IFX trough at dose 5 was no a longer predictor of better clinical or endoscopic outcome at 1 year. 1 year analysis indicates that with dose optimization at induction, the medium-term response to IFX can be predicted as early as Doses 4 and 5 and effort should be made to alter treatment earlier if inadequate response was observed

Funded by This research has been funded by WCHRI Capacity Grant.

Abstract # 75  
Presenter: Sample, Dory  
Supervisor: Turner, Justine  
Title: AGY for patients with symptomatic Celiac disease: Protocol for a randomized, placebo-controlled phase II trial  
Authors: Dory Sample, Justine Turner, Leo Dieleman

### **Introduction**

AGY is an oral anti-gliadin antibody made from the yolks of immunized laying hens. An open label pilot study was completed with 10 adults with celiac disease (CD), to determine safety of 500mg AGY taken with meals for 4 weeks, and to explore potential efficacy related to symptoms, anti-tissue transglutaminase antibody (aTTG) levels, and lactulose/mannitol excretion ratios (LMER) at baseline and after treatment. No safety concerns were identified, and participants had improvements in symptoms, aTTG, and LMER. Due to the positive pilot observations, a phase II study was designed to test both efficacy and safety in a larger trial. The primary objective is to determine the efficacy of AGY as measured by the Daily Celiac Symptom Index (CSI). Secondary objectives include safety, quality of life assessment, monthly symptom scores, aTTG, and LMER.

### **Methods**

We plan to conduct a 16 week, double-blind, placebo-controlled crossover trial, for individuals age 10-65 years, with symptomatic CD at least 1-year post diagnosis. Because AGY has not yet been tested in pediatric patients, we have incorporated an innovative strategy to mimic the previous pilot study, but in a pilot pediatric cohort imbedded in a larger trial. Total enrollment in the study will be 149, allowing 80% power and 5% alpha. Participants will be stratified by age and screening aTTG levels at study entry.

### **Results**

We plan to begin enrollment in spring 2019.

### **Conclusion**

A non-toxic, food source based natural health product that could neutralize the gliadin in food, thus preventing gliadin absorption and subsequent gliadin-induced pathogenesis, could dramatically improve the quality of life for individuals with CD.

Funded by Vetanda Group Ltd,  
MNCY SCN HOI Fund, Women and Children's Health Research Institute (WCHRI)

The Power of Partnership





Abstract # 76  
Presenter: O'Neill, Marcus  
Supervisor: Ball, Geoff  
Title: **Using the social ecological model to improve pediatric ambulatory appointment scheduling**  
Authors: Tink L, Perez A, O'Neill M, Holt NL, Bruce A, Childs M, Davison ME, Kane Poitras S, Kherani T, Ladha T, Majaesic C, Webber M, Ball GDC

### **Introduction**

To ensure interventions account for the complexity of the ambulatory scheduling, it is important to emphasize the inter-relationships between different domains. By identifying the problem fields associated with pediatric ambulatory scheduling at a children's hospital in Alberta, Canada, we sought to develop a multi-level model that recognizes the importance of the individual, social, contextual, and environmental factors that influence ambulatory scheduling systems.

### **Methods**

This study represents the first phase of a larger quality improvement (QI) project. Focus group interviews were conducted with three groups of stakeholders who use the pediatric ambulatory scheduling system on a day-to-day basis and could identify areas for improvement. Perceptions were elicited about the areas where improvements could be made (i.e., the existing problem fields). The study design was guided methodologically by qualitative description. The social ecological model for health was used as a theoretical framework throughout the analysis. Data were analyzed using deductive content analysis.

### **Results**

Parents (n=11), administrative professionals (n=23), and clinicians (n=13) discussed areas of improvement related to the pediatric ambulatory scheduling system. These perceived problem fields were grouped according to three categories: 1) individual knowledge, skills and behaviors, 2) communication processes, 3) organizational structures and processes. Each category directly reflects a level of the social ecological model.

### **Conclusion**

Emphasizing the need to distinguish between the level of an intervention and the target of an intervention, our multi-level model provides a framework for other quality improvement projects that aim to support interventions across three separate, yet interacting, levels: intrapersonal, interpersonal, and institutional.

Funded by This research was supported by an Innovation Grant from the Women and Children's Health Research Institute

The Power of Partnership



Abstract # 77  
Presenter: Wingert, Aireen  
Supervisor: Hartling, Lisa  
Title: Clinical interventions that influence vaginal birth after cesarean delivery rates: Systematic review & meta-analysis  
Authors: Wingert A, Hartling L, Sebastianski M, Johnson C, Featherstone R, Vandermeer B, Wilson RD

### **Introduction**

To systematically review the literature on clinical interventions that influence vaginal birth after cesarean (VBAC) rates.

### **Methods**

We searched Ovid Medline, Ovid Embase, Wiley Cochrane Library, CINAHL via EBSCOhost; and Ovid PsycINFO. Additional studies were identified by searching for clinical trial records, conference proceedings and dissertations. Limits were applied for language (English and French) and year of publication (1985 to present). Two reviewers independently screened comparative studies (randomized or non-randomized controlled trials, and observational designs) according to a priori eligibility criteria: women with prior cesarean sections; any clinical intervention or exposure intended to increase the VBAC rate; any comparator; and, outcomes reporting VBAC, uterine rupture and uterine dehiscence rates. One reviewer extracted data and a second reviewer verified for accuracy. Meta-analysis was conducted using Mantel-Haenszel (random effects model) relative risks (VBAC rate) and risk differences (uterine rupture and dehiscence). Two reviewers independently conducted methodological quality assessments using the Mixed Methods Appraisal Tool (MMAT).

### **Results**

Twenty-nine studies (six trials and 23 cohorts) examined different clinical interventions affecting rates of vaginal deliveries among women with a prior cesarean delivery (CD). Methodological quality was good overall for the trials; however, concerns among the cohort studies regarding selection bias, comparability of groups and outcome measurement resulted in higher risk of bias. Interventions for labor induction, with or without cervical ripening, included pharmacologic (oxytocin, prostaglandins, misoprostol, mifepristone, epidural analgesia), non-pharmacologic (membrane sweep, amniotomy, balloon devices), and combined (pharmacologic and non-pharmacologic). Single studies with small sample sizes and event rates contributed to most comparisons, with no clear differences between groups on rates of VBAC, uterine rupture and uterine dehiscence.

### **Conclusion**

This systematic review evaluated clinical interventions directed at increasing the rate of vaginal delivery among women with a prior CD and found low to very low certainty in the body of evidence for cervical ripening and/or labor induction techniques. There is insufficient high-quality evidence to inform optimal clinical interventions among women attempting a trial of labor after a prior CD.

Funded by Maternal, Newborn, Child and Youth Strategic Clinical Network (AHS); Alberta Strategy for Patient-Oriented Research SUPPORT Unit Knowledge Translation Platform

The Power of Partnership



Abstract # 78  
Presenter: Gates, Allison  
Supervisor: Not applicable.  
Title: A systematic review of the factors that influence the acceptability of childhood vaccines among Canadians  
Authors: Allison Gates, Michelle Gates, Jennifer Pillay, Robin Featherstone, Sholeh Rahman, Samantha Guitard, Tara MacGregor, Lisa Hartling

## Introduction

The National Advisory Committee on Immunization (NACI) develops vaccine recommendations for Canadians. In 2016, NACI's mandate expanded to include considerations for ethics, equity, acceptability, and feasibility when developing recommendations. To inform considerations for acceptability, we completed a systematic review of evidence for: (a) factors that influence the acceptability of vaccines among the Canadian public, healthcare providers, and policymakers, and (b) interventions aimed at improving the acceptability of vaccines. Herein, we describe our findings related to childhood vaccines.

## Methods

On 10-11 October 2018 we searched 4 bibliographic databases, the Theses Canada Portal, and ClinicalTrials.gov for studies published in the past 5 years in English or French. Two reviewers screened the candidate records and agreed on those included in the review. From each study, we extracted information related to the participants, intervention or exposure, comparator, and setting, and relevant outcomes. We appraised risk of bias in each study and synthesized the findings narratively due to heterogeneity in the reported factors and acceptability outcomes. We appraised the certainty of evidence for each acceptability factor using the GRADE approach.

## Results

We screened 3316 records and included 152, accounting for 135 unique studies. The studies investigated 13 vaccines or groups of vaccines, of which six were relevant to children: childhood vaccines (as a group) (n = 13 studies; 10,944 participants), the human papillomavirus vaccine (n = 24; 170,909), measles-containing vaccines (n = 3; 5,495), the meningococcal vaccine (n = 2; 914), the pertussis vaccine (n = 3; 4,411), and the rotavirus vaccine (n = 1; 12,525). Across vaccines, there was at least low certainty evidence for the influence of 48 factors on the acceptability of childhood vaccines for parents. Among these, 19 were common to multiple vaccines: attitudes about vaccination, number of injections, perceived alternatives to vaccination, perceived effectiveness, perceived need or importance, perceived safety, knowledge (measured), receipt of information, social support, religious or moral beliefs, trust in healthcare providers, public health authorities, and scientific evidence, vaccination history, receiving a recommendation from a doctor, perceived disease severity, costs, awareness of the vaccine, and receiving a recommendation from a family member or friend. We identified little evidence for high-risk groups, healthcare providers, and policymakers. The certainty of evidence was very low for the effectiveness of all interventions (n = 19; 1,181,194), except for reminders for parents to have their infant vaccinated and universal vaccination programs for the rotavirus vaccine. For these, we found low certainty evidence of a positive influence on vaccine uptake and coverage, respectively.

## Conclusion

Among the array of factors investigated across studies, we identified those that are most important to consider during the development of vaccine recommendations. Although some factors were common to multiple vaccines, many were relevant only to specific vaccines. Future research should focus on lesser-studied vaccines and population groups (i.e., high-risk, healthcare providers, policymakers).

Funded by The National Advisory Committee on Immunization (Public Health Agency of Canada), contract #4600001536.

The Power of Partnership

Abstract # 79  
Presenter: Meherali, Salima  
Supervisor: Meherali, Salima  
Title: **A systematic review: Interventions and strategies to improve sexual and reproductive health outcomes of adolescents living in low and middle-income countries**  
Authors: Dr Salima Meherali, Neelam Punjani

### **Introduction**

Globally, approximately 1.2 billion people are under the age of 25 and 90% of whom live in low-middle-income countries (LMICs). Adolescence is a critical period in life. Adolescents' sexual and reproductive healthcare (ASRH) needs are distinct from adults'. Neglect of specific ASRH needs can pose serious challenges and affect their physical and mental health, future employment, economic well-being and ability to reach their full potential. Presently, adolescents living in LMICs suffer disproportionately from negative SRH outcomes, such as early/unintended pregnancy, unsafe abortions, sexual violence, and sexually transmitted infections, including HIV. The literature identifies a number of interventions that help to improve SRH of adolescents living in LMICs; however, many questions remain about what interventions work, how they are designed, carried out, and evaluated, and how these interventions can be sustainable and potentially scalable.

The aim of this systematic review is to identify and evaluate the effectiveness of interventions designed and implemented to improve SRH outcomes for adolescents living in LMICs.

### **Methods**

This systematic review followed a comprehensive scientific process using rigorous methodological guidelines and is register it with PROSPERO. We will include Randomized Controlled Trials (RCTs), Quasi-RCTs, and controlled before-after studies (CBA). Studies without any control arm will not be included. Study outcome data were aggregated and analyzed according to the type of intervention(s) that aim to improve ASRH in LMICs.

### **Results**

The systematic review has a high potential to be transformative as it will be the first comprehensive systematic review of the literature to evaluate the effectiveness of interventions employed to improve ASRH outcomes in LMICs.

### **Conclusion**

The findings of this review will provide policymakers, funders, and other decision-makers a detailed assessment of the current state of evidence on ASRH programming in LMICs that they can use to best prioritize future investments in research in this area.

Funded by Killam Research Operating Grant

The Power of Partnership



Abstract # 80  
Presenter: Gates, Michelle  
Supervisor: Hartling, Lisa  
Title: Effectiveness of digital technologies as a distraction for acute pain in children: A systematic review and meta-analysis  
Authors: Michelle Gates, Lisa Hartling, Jocelyn Shulhan-Kilroy, Tara MacGregor, Samantha Guitard, Aireen Wingert, Robin Featherstone, Ben Vandermeer, Naveen Poonai, Janeva Kircher, Shirley Perry, Timothy AD Graham, Shannon D Scott, Samina Ali

### Introduction

Digital distraction is being integrated into pediatric pain care, but its efficacy is currently unknown. We conducted a systematic review to determine the effect of digital technology distraction on pain and distress in children experiencing acutely painful conditions or medical procedures.

### Methods

We searched eight online databases (MEDLINE, Embase, Cochrane Library, CINAHL, PsycINFO, IEEE Xplore, Ei Compendex, Web of Science), grey literature sources (clinicaltrials.gov, Google), scanned reference lists, and contacted experts for quantitative studies where digital technologies were used as distraction for acutely painful conditions or procedures in children. Study selection was performed by two independent reviewers with consensus. One reviewer extracted relevant study data and another verified it for accuracy. Appraisal of risk of bias within studies and the certainty of the body of evidence were performed independently in duplicate, with the final appraisal determined by consensus. The primary outcomes of interest were child pain and distress.

### Results

Of 3247 unique records identified by the search, we included 106 studies (n=7820) that reported on digital technology distractors (e.g., virtual reality; videogames) used during common procedures (e.g., venipuncture, minor dental procedures, burn treatments). We located no studies reporting on painful conditions. For painful procedures, digital distraction resulted in a modest but clinically important reduction in self-reported pain (SMD -0.48, 95% CI -0.66 to -0.29, 46 RCTs, n=3200), observer-reported pain (SMD -0.68, 95% CI -0.91 to -0.45, 17 RCTs, n=1199), behavioural pain (SMD -0.57, 95% CI -0.94 to -0.19, 19 RCTs, n=1173), self-reported distress (SMD -0.49, 95% CI -0.70 to -0.27, 19 RCTs, n=1818), observer-reported distress (SMD -0.47, 95% CI -0.77 to -0.17, 10 RCTs, n=826), and behavioural distress (SMD -0.35, 95% CI -0.59 to -0.12, 17 RCTs, n=1264) compared to usual care. Few studies directly compared different distractors or provided subgroup data to inform applicability.

### Conclusion

Digital distraction provides modest pain and distress reduction for children undergoing painful procedures; its superiority over non-digital distractors is not established. Healthcare providers and parents should strongly consider using distractions as a pain-reduction strategy for children and teens during common painful procedures (e.g., needle pokes, dental fillings). Context, child preference, and availability should inform the choice of distractor.

Funded by WCHRI Innovation Grant and (SPOR) SUPPORT Unit Knowledge Translation Platform, which is funded by Alberta Innovates and the CIHR

The Power of Partnership

Abstract # 81  
Presenter: Golden-Plotnik, Stevi  
Supervisor: Ali, Samina  
Title: Caregiver perspectives on children's functional experiences after fracture: A qualitative study  
Authors: Stevi Golden-Plotnik, Mackenzie Moir, Michael Van Manen, Amy Drendel, Naveen Poonai, Samina Ali

### **Introduction**

Fractures are a common childhood injury. While the pain associated with fractures has been well-described, the related functional impact is less understood. When a child's function is impaired due to fracture, his or her ability to participate in day-to-day life is restricted. Eighty percent of children with fractures experience compromise in at least one domain of daily function. While there is clear value in measuring function, no studies have provided an in-depth assessment of functional limitations related to childhood limb fractures. Furthermore, none have identified the specific outcomes that are important from the perspective of patients and families.

### **Methods**

We performed a qualitative study employing interviews of caregivers of children (5 to 11 years) who received care for acute, non-operative long bone fractures at the Stollery Children's Hospital emergency department (ED). Audio-recorded, semi-structured, one-on-one telephone interviews were completed one to two weeks following the ED visit. Open-ended interview questions focused on areas of function identified by existing literature and expert opinion. Qualitative analysis was completed using content analysis theory. Our aim was to describe the phenomenon of functional change following fracture. Transcripts were read and coded by two researchers concurrent with data collection.

### **Results**

Twenty-five interviews were included in our final analysis. Most children (23/25) were diagnosed with upper extremity fractures, and most participants were female and mothers (21/25). All caregivers reported a change in their child's function. The most commonly affected areas included: sleep, activities of daily living, and play. Caregivers reported that their children were also impacted by pain and related negative emotional responses. All children required additional help or effort from their caregivers to carry out day-to-day tasks; this required adaptive strategies such as planning, changes to household routine and missing work. Key concerns from caregivers included pain management, fracture healing or complications, and regression of their child's independence.

### **Conclusion**

Function is universally impaired in younger children with fractures. Caregivers were also impacted by these limitations and often had to provide significant support in order to successfully adapt. Caregiver impact was often described within the context of a disrupted family dynamic. Successful healing, child wellbeing, and adaptation to disruptive changes were described as important goals. The impact of a fracture on a child's function (including sleep, activities of daily living, play), and improvement thereafter, should be a key patient-oriented outcome for pediatric fracture research.

Funded by WCHRI Resident Research Grant

The Power of Partnership



Abstract # 82

Presenter: Morrison, Ellen

Supervisor: Ali, Samina

Title: Validation of the Stoplight Pain Scale tool in the Canadian emergency setting

Authors: Ellen Morrison MD, Seyara Shwetz MD, Maryna Yaskina PhD, Manasi Rajagopal BSc MBT, Andrea Estey MD, Amy L Drendel DO MS, Samina Ali MDCM

### Introduction

More than half of all children presenting to an emergency department have a painful complaint, but less than half of these children will receive analgesia. Documentation of a pain score is associated with increased provision of analgesia. A variety of children's pain assessment tools exist; however, none of the current scales are specifically designed for family use nor provide direct guidance regarding pain treatment. This study aimed to validate a novel, three faced, colour coded pain tool: the Stoplight Pain Scale (SPS).

### Methods

A prospective observational cohort study was conducted at a Canadian pediatric emergency department from November 2014 to February 2017. Patients 3-12 years and their caregivers were asked to rate pain using the SPS and the Faces Pain Scale-Revised (FPS-R). Pain was measured at presentation, immediately following painful procedures, and thirty minutes after analgesia administration.

### Results

A total of 227 patients were included for analyses; 26.9% (61/227) were 3-5 years old while 73.1% (166/227) were 6-12 years old; 23.3% (53/227) had been previously hospitalized. Using Kappa Statistics, correlation for SPS and FPS-R was 'fair' for both children (0.28, 95% CI 0.20-0.36) and caregivers (0.14, 95% CI 0.07 – 0.21) at presentation. The SPS had 'fair to moderate' correlation between child and caregiver scores (0.37, 95% CI 0.27-0.47), compared to FPS-R which showed 'poor to fair' agreement between child and caregiver scores (0.20, 95% CI 0.12-0.29). Overall, 85.8% (139/192) of children and 60% (118/196) of caregivers preferred SPS over FPS-R.

### Conclusion

SPS demonstrates fair correlation with FPS-R and good correlation between children and caregivers. SPS is simple and easy to use, and offers both a rating of children's pain and guidance regarding analgesia. This may have a role in empowering family involvement in pain management. Future research should focus on at-home study of the tool.

Funded by WCHRI Resident Research Grant (Stollery Children's Hospital Foundation)

Abstract # 83  
Presenter: Hartling, Lisa  
Supervisor:  
Title: **Pediatric parent advisory group evaluation: Assessing meaningful involvement and identifying future directions**  
Authors: Hartling L, Elliott SA, Gates M, Brooks HM, Scott, SD

### **Introduction**

The Pediatric Parent Advisory Group (P-PAG) was established at the University of Alberta in 2016. Parents volunteer their time and engage in monthly meetings to provide advice, guidance and knowledge from a parent perspective on various child health research activities. The objective of this engagement evaluation was to understand parents' needs and expectations about the P-PAG, and how it is run.

### **Methods**

All P-PAG members (n=26) were invited to participate. The evaluation consisted of an anonymous online questionnaire about their experiences and engagement with the group, as well as an optional one-on-one interview. Data were analyzed using standard quantitative and qualitative approaches. Results were then illustrated graphically and presented to the P-PAG for feedback.

### **Results**

Fifteen members (58%) completed the survey and five respondents were interviewed. Most members understood the purpose of the P-PAG and appreciated its organic development over time. Members agreed that their views and efforts were valued and respected by the research team; they enjoyed seeing the results of their input. Several members felt they contributed to research that was important to them and that the outputs would be helpful for other parents. Some areas for improvement included: considering tools and processes to be more inclusive of remote participants; ensuring that enough context is given before feedback is sought, discussion around tool dissemination activities is had early on, and communication about shared learning opportunities and special interest activities takes place. Balancing group size with group diversity was considered a challenge: members wanted to maintain the small group trust and comfort, yet ensure the group was representative of a diverse community.

### **Conclusion**

These results will help guide our relationship with the P-PAG to foster meaningful engagement and ensure that the group meets its members' expectations. The results will be helpful for researchers or organizations interested in involving parents/patients in research.

Funded by Stollery Science Lab, Distinguished Researchers and Canadian Institutes of Health Research (CIHR)

The Power of Partnership





Abstract # 84  
Presenter: Plesuk, Tabatha  
Supervisor: Scott, Shannon D.  
Title: Comparing the usability evaluation results of two parental tools for urinary tract infection  
  
Authors: Tabatha Plesuk, Samantha Louie-Poon, Alyson Campbell, Hyelin Sung, Anne Le, Hannah Brooks, Lisa Hartling, Shannon Scott

### **Introduction**

Urinary tract infections (UTI) are a common source of acute illnesses in infants and children. Most infections can be treated with antimicrobial therapy although some children may develop lifelong consequences such as hypertension and decreased renal function. UTIs are often difficult to identify as pediatric symptoms differ from adult symptoms. Furthermore, the wide variation in treatment may compound to increased confusion for parents. Evidence has provided support for the use of digital knowledge translation (KT) tools in providing parents with information regarding their child's health.

### **Methods**

We worked with parents of children with UTI to develop and evaluate two digital tools on UTI (whiteboard animation video and interactive infographic). Following prototype completion, usability testing was conducted using iPads in two Alberta Emergency Department waiting rooms. Parents were randomized to either the video (n=30) and infographic (n=30) and asked to complete a 9-item, 5-point Likert scale survey that assessed usability, aesthetics, language, length, and future use. Data were analyzed using SPSS.

### **Results**

Both tools were highly rated, with parents providing scores of 4.07-4.77 (out of 5.00) on each usability item. Unpaired t-tests were conducted to compare usability item scores between tools. Results showed a significant difference in parents' scores for usefulness ( $p < 0.00$ ), with the infographic being rated 4.10 compared to the video, with a score of 4.77. There were no significant differences for the other usability items.

### **Conclusion**

Results from this study suggest that both videos and infographics are useful in delivering complex health information to parents.

Funded by NCE, CIHR

The Power of Partnership



Abstract # 85  
Presenter: Goonaskera, Michelle  
Supervisor: Kirkham, Amy  
Title: A biopsychosocial perspective: Relationships among quality of life, treatment symptoms and cardiorespiratory fitness in women receiving chemotherapy for breast cancer  
Authors: Michelle Goonasekera, Richard Thompson, Kerry Courneya, Carla Prado, John Mackey, Ian Paterson, Edith Pituskin, Amy Kirkham

### Introduction

Although studies examining biomedical factors in cancer are prevalent, the interaction of physiological, psychological and social factors in the experience of chemotherapy is limited. Chemotherapy treatment for breast cancer is associated with reduced health-related quality of life (QoL), a number of treatment symptoms and a reduction in cardiorespiratory fitness (VO<sub>2</sub>peak). This study aimed to examine the relationship between QoL, treatment symptoms and cardiorespiratory fitness among women receiving chemotherapy for breast cancer.

### Methods

Women with early stage breast cancer were assessed prior to the first chemotherapy treatment and 2-3 weeks after the mid-point of chemotherapy. All participants performed a maximal cardiopulmonary exercise test to assess VO<sub>2</sub>peak and completed questionnaires assessing cancer-related quality of life (Functional Assessment of Cancer Therapy (FACT)-General) and fatigue (FACT-Fatigue subscale) and patient-reported symptoms (Rotterdam Symptom Checklist – Physical Distress). Baseline values and change scores in QoL were compared with VO<sub>2</sub>peak, fatigue and symptoms using correlation.

### Results

Fifty-one women completed all assessments. Prior to chemotherapy, QoL was moderately correlated with physical symptoms ( $r=0.65$ ,  $p<0.001$ ) and fatigue ( $r=-0.50$ ,  $p<0.001$ ) and trended toward a positive correlation with VO<sub>2</sub>peak normalized to body weight ( $r=0.23$ ,  $p=0.09$ ). Prior to treatment, VO<sub>2</sub>peak was correlated with fatigue ( $r=0.27$ ,  $p=0.05$ ). Over the course of chemotherapy, absolute VO<sub>2</sub>peak (1.91plus/minus0.34 to 1.76plus/minus0.31 L/min,  $p<0.001$ ) and quality of life (88plus/minus13 to 80plus/minus17 points,  $p<0.001$ ) decreased, while patient-reported fatigue (43plus/minus7 to 38plus/minus10 (lower is worse),  $p<0.001$ ) and physical symptoms (11plus/minus7 to 23plus/minus11 (higher is worse),  $p<0.001$ ) increased. However, there was no relationship between the change in QoL and the change in absolute VO<sub>2</sub>peak ( $r=-0.06$ ,  $p=0.68$ ). A decrease in QoL was moderately correlated with an increase in physical symptoms ( $r=-0.51$ ,  $p<0.001$ ) and fatigue ( $r=0.45$ ,  $p<0.001$ ).

### Conclusion

Prior to the receipt of chemotherapy for breast cancer, women with higher QoL also have higher cardiorespiratory fitness and less fatigue. However, the extent of the impact of chemotherapy on QoL does not appear to be related to the extent of deterioration in cardiorespiratory fitness. Rather, the extent of fatigue and physical symptoms both prior to and during chemotherapy appear to be important determinants of QoL in women with breast cancer. Future studies are needed to elucidate how psychological resilience affects the experience of chemotherapy symptoms and their resulting relationship with QoL in women undergoing chemotherapy for breast cancer.

Funded by Susan G. Komen Foundation

The Power of Partnership

Abstract # 86  
Presenter: Crosley, Powel  
Supervisor: Hitt, Mary  
Title: Preclinical evaluation of TRAIL combined with PAC-1 to control granulosa cell tumour

Authors: Crosley, Powel; Potts, Kyle; Agopsowicz, Kate; Noyce, Ryan; Evans, David; Fu, YangXin; Hitt, Mary

### Introduction

Granulosa cell tumor (GCT) is a malignant sex-cord stromal cell form of ovarian cancer that constitutes ~5% of ovarian neoplasms. Current chemotherapy regimens are not effective enough in controlling recurrent GCT and ~80% of women who relapse will die of disease. Pro-caspase-activating compound 1 (PAC-1) is a small-molecule activator of procaspase-3 that has been extensively studied both in vitro and in vivo but never on GCT. Tumour necrosis factor-related apoptosis-inducing ligand (TRAIL) has failed to replicate in vitro efficacy in the clinic due to inadequate delivery methods; a short half-life; and inherent or acquired resistance to TRAIL therapy. Vaccinia virus (VACV) is an ideal vector for use in viral gene therapy. It has a short lifecycle, rapidly spreads cell-to-cell, has strong lytic ability, and a large cargo capacity. Here we report on the development of a recombinant, tumour-selective VACV expressing TRAIL (VACV-TRAIL) that generates effective levels of soluble TRAIL during the viral replication cycle and combines with PAC-1 to control GCT, in vitro.

### Methods

PAC-1 and rhTRAIL interaction was assessed with in vitro cytotoxicity assays and high content analysis using GCT cell line KGN. We then designed a plasmid encoding a secretable form of the extracellular domain of TRAIL targeting insertion into the viral thymidine kinase (J2R) locus of VACV. The recombinant virus (VACV-TRAIL) was then used for growth and cytotoxicity assays, and secreted TRAIL was measured in viral supernatant by ELISA and western blot.

### Results

PAC-1 combination with TRAIL displays cytotoxic synergy in KGN cells with strong activation of caspase-3 within 24 hr of treatment. Importantly, PAC-1/TRAIL combination is similarly effective on patient-derived GCT cells while being much less cytotoxic to normal cells. VACV-TRAIL replicates effectively in KGN and virus-mediated cytotoxicity is greater than that of VACV WT, and is potentiated by combination with PAC-1. VACV-TRAIL generates effective levels soluble TRAIL that combined with PAC-1 controls KGN cells as well or better than rhTRAIL.

### Conclusion

To our knowledge, this is the first attempt to combine oncolytic vaccinia gene therapy with PAC-1, and the first study looking at viral gene therapy for treatment of GCT. VACV-TRAIL is an efficient vector for gene therapy and combined with PAC-1 effectively controls GCT, a disease with few current treatment alternatives. The combination provides a three-pronged strategy for cancer control through activation of caspase-3, increased death signaling, and self-amplifying replication of oncolytic virus.

Funded by Women & Children's Health Research Institute, Sladjana M. Crosley Fund for GCT Research, Cancer Research Society

The Power of Partnership



Abstract # 87  
Presenter: Richter, Solina  
Supervisor: Last Name, First Name  
Title: Intersection of place, social connectedness, income, culture and health: Experiences and perceptions of female economic migrants in Canada  
Authors: Solina Richter & Helen Vallianatos

## Introduction

The proportion of migrants who are women are increasing, commonly referred to as the feminization of migration, due in large part to an increased demand of women in the care professions. Migration frequently contributes to greater autonomy, human capital and self-esteem among women. International conventions like the Convention on the Elimination of Discrimination Against Women, stipulate that gender disparities against migrant women require attention, including access to life-saving and health protective care (Economic Commission for Africa, 2009; UN 1996). However, it is clear that health of women migrants does not uniformly improve post-migration. The purpose of this study was to explore the intersections of place with aspects of identity including age, socioeconomic status, etc. to learn how the health of women migrants to Canada is impacted by migration and settlement. Findings will support the goal of improving the health of this growing sub-population through a better understanding of the ways in which social, environmental, occupational, economic and culture factors determine health and access to health care of female economic migrants.

## Methods

We employed a focused ethnography design using an intersectionality approach as our theoretical framework. Intersectionality refers to the interactions between categories as gender, race, and other aspects of identity that shape individual lives, as well as social practices, institutional arrangements, and cultural ideologies and outcomes. We used purposive sampling and interviewed 28 economic migrant women from Ghana, Nigeria and South Africa. Thematic analysis were conducted to analyse the data with the support of Atlas Ti software.

## Results

Women decided to move to Canada for different reasons, some with their families. Adapting to the Canadian context were discussed in depth, and it was clear that the intersection of various factors created challenges, including individual-level factors such as women's reasons for migration, community-level factors such as discrimination and lack of social supports, and structural-factors, such as employment policies – in addition to Canadian winters.

All of the challenges affected participants' physical and mental health, as participants complained about the fragmentation of the Canadian health care system, physical symptoms that were connected with overwork, and mental health challenges related to the confluence of the aforementioned factors that created ongoing stress.

## Conclusion

Our findings have clear policy implications. The development of integration courses and support groups for immigrant women must expand. Support groups have the potential to impact the health outcome, particularly mental health and wellbeing of immigrant women. Cultural sensitivity training for employees are proposed to encourages diversity through the identification and removal of barriers and biases, and the creation of workplaces and learning environments that are free of harassment and discrimination.

Funded by Women & Children Research Institute

The Power of Partnership



Abstract # 88  
Presenter: Janes, Tara  
Supervisor: Kinkead, Richard  
Title: Panic, stress and sex: Orexin 1 receptors are necessary for enhancement of the hypercapnic ventilatory response in female rats subjected to neonatal stress  
Authors: Janes, Tara; Lopes, Luana; Gulemetova, Roumiana; Drolet, Guy; Bretzner, Frédéric; Kinkead, Richard. Centre de Reserche du CHU de Québec / IUCPQ/ Université Laval, Québec, QC, Canada.

### Introduction

Panic disorder (PD) is a debilitating anxiety disorder affecting ~3x more women than men. Key respiratory symptoms can include increased sensitivity to inhalation of high CO<sub>2</sub> (hypercapnia). PD typically emerges following puberty, suggesting that ovarian function contributes to the onset of PD in females. Exposure to early-life stress is a risk factor for PD and we have previously shown that neonatal maternal separation (NMS), a clinically relevant stressor, augments ventilatory responses to high CO<sub>2</sub> in female rats following puberty. However, a neural mechanism linking NMS with CO<sub>2</sub> sensitivity has been elusive. Hypothalamic orexin neurons (ORX) are involved in fear and anxiety responses, modulate respiration and recent data support a role for these neurons in CO<sub>2</sub> sensing. Based on these observations, we tested the hypothesis that orexin 1 receptors (OX1-Rs) are necessary for stress-related enhancement of the ventilatory response to hypercapnia in post-pubescent female rats.

### Methods

NMS pups were isolated from their mother in an incubator for 3 h/day from postnatal days 3 to 12. Control pups remained undisturbed. Female rats were reared to adulthood (P60-70) and ventilatory responses to hypercapnia measured by whole-body plethysmography (FICO<sub>2</sub> = 0.05, 10 min). The OX1 antagonist (SB334867; 15mg/kg) or vehicle was injected (i.p.) 45-60 minutes before the start of recordings. Estrus cycle phase was determined by vaginal smear in order to determine any interactional effects of circulating hormones on the ventilatory response.

### Results

In controls, the ventilatory response to hypercapnia was not affected by estrus cycle phase or pharmacological inactivation of OX1-Rs. The hypercapnic ventilatory response of NMS females was higher than controls and was phase-dependent, with the greatest responsiveness observed during proestrus. Inactivating OX1-Rs in NMS females reduced the ventilatory response to hypercapnia, with the most important effects observed during the proestrus and metaestrus phases.

### Conclusion

Based on the phase-dependent effects on hypercapnic ventilatory responses of NMS females, we postulate that stress interferes with the influence that ovarian hormones exert on respiratory control. These effects may involve the activity of ORX neurons, since activation of OX1-Rs was necessary for stress-related enhancement of the hypercapnic ventilatory response in NMS females. These results provide new insights into the pathophysiology of PD.

Funded by Canadian Institutes of Health Research (CIHR); CNPq - Brazil; Quebec Respiratory Health Network

The Power of Partnership



Abstract # 89  
Presenter: Krysa, Jacqueline  
Supervisor: Proctor, Spencer  
Title: **Non-fasting remnant cholesterol in Alberta's tomorrow project: Implications for CVD risk prediction in women**  
Authors: Jacqueline A Krysa, Ming Ye, Dean T. Eurich, Spencer D. Proctor

### **Introduction**

Circulating fasting low-density lipoprotein cholesterol (LDL-C) has been a cornerstone of CVD risk assessment in Canada. In adults, males have been found to have an increased risk of CVD over the lifespan compared to females. Therefore, the majority of lipid lowering studies have focused on reducing CVD-risk in males, primarily through statin-based therapies. Premenopausal females appear to be relatively protected from CVD, yet, following menopause, the risk gap narrows between sexes and females become more prone to CVD. Despite this, there is little understanding of CVD-risk prediction in post-menopausal females. Recent studies from Europe have demonstrated that non-fasting remnant cholesterol (RC) is causally associated with CVD, and in some circumstances is a better risk predictor than LDL-C. These findings have resulted in many European countries to change their clinical guidelines to include measurements of non-fasting lipids to assess CVD risk. In Canada, the lipid guidelines for physicians were also updated in 2016 and included the importance of recognizing this new measurement. However, in Canada we currently do not have any studies that can determine normal reference ranges for non-fasting lipids and RC. Alberta's Tomorrow Project (ATP) is a large, Canadian prospective cohort that is predominantly female. The purpose of this study is to generate non-fasting lipid and remnant cholesterol values in ATP and determine the relationship between non-fasting remnant cholesterol and LDL-C with CVD prevalence in males and females. CVD prevalence is defined as the number of CVD cases reported in the ATP cohort.

### **Methods**

Non-fasting lipid data and CVD events were assessed in ATP participants (n=5,294 males; n=10,957 females; age  $62.3 \pm 9.7$  years). Non-fasting RC was calculated as: total cholesterol – (LDL-C + high-density lipoprotein cholesterol). Differences between sexes were determined by student's T-test and one-way ANOVA, differences in statin use was determined by chi-squared analysis, and the relationship between non-fasting RC and LDL-C with CVD was determined by logistic regression.

### **Results**

Non-fasting LDL-C was significantly elevated in females compared to males ( $2.73 \pm 0.89$  mmol/L versus  $2.88 \pm 0.85$  mmol/L) while non-fasting RC was significantly higher in males ( $0.89 \pm 0.41$  mmol/L versus  $0.75 \pm 0.36$  mmol/L). Statin use was also significantly higher in males (35.1% versus 18.6%,  $p < 0.0001$ ). Non-fasting RC was significantly elevated in females with CVD prevalence compared to those without CVD ( $0.73 \pm 0.36$  mmol/L versus  $0.83 \pm 0.38$  mmol/L,  $p < 0.001$ ) but was not significantly different for males. Conversely, non-fasting LDL-C was significantly lower in both males and females with CVD prevalence (males:  $2.82 \pm 0.85$  mmol/L versus  $2.42 \pm 0.92$  mmol/L; females:  $2.90 \pm 0.83$  mmol/L versus  $2.80 \pm 0.94$  mmol/L).

### **Conclusion**

Non-fasting RC may be a more effective CVD-risk predictor for post-menopausal women than LDL-C.

Funded by WCHRI graduate studentship, ADI graduate studentship

Abstract # 90  
Presenter: Moray,Amol  
Supervisor: Hornberger,Lisa  
Title: 3rd trimester umbilical arterial blood flow is associated with neurodevelopmental outcomes at 2 years  
Authors: Amol Moray, MBBS, Charlene M.T. Robertson MD, Angela McBrien, MBBS Gwen Y. Bond MN, Jayani B. Abeysekera, MD and Lisa K. Hornberger MD.

### Introduction

Congenital heart disease (CHD) necessitating surgical intervention in infancy is associated with altered neurodevelopmental (ND) outcomes. Some of the contributing insults begin before birth. In support of this, we have recently discovered an inverse relationship between 3rd trimester umbilical artery (UA) pulsatility index (PI) and growth and ND outcomes at 2 years in hypoplastic left heart syndrome (HLHS) and d-transposition of great arteries. In the present study we investigated relationships between UA-PI and middle cerebral artery (MCA) PI in other major fetal CHD with 2-year growth and ND outcomes.

### Methods

All children with major structural CHD including non-HLHS single ventricle pathologies (SV) and CHD requiring repair at <6 weeks who had a 3rd trimester fetal echocardiogram between 2007-2017 and underwent 2-year ND and biometric assessments were identified. Those with genetic syndromes and those without 3rd trimester UA-PI and/or MCA-PI measures were excluded.

### Results

74 children, including 34 with SV and 40 with biventricular (BV) CHD (22/40 with conotruncal lesions) were included. Mean age of fetal echo was  $34.2 \pm 2.7$  (SD) weeks and mean UA-PI and MCA-PI were  $1.7 \pm 0.3$  and  $1.6 \pm 0.4$ , respectively. Two-year Bayley III mean cognitive, language and motor scores were  $91.2 \pm 14.7$ ,  $85.2 \pm 15.2$  and  $84.2 \pm 16.9$ , respectively. Linear regression analysis of all CHDs and for SV and BV groups showed no association between UA-PI and MCA-PI with growth and ND. Analysis of those with conotruncal defects alone, however, showed an association between UA-PI and language (ES -37.44(95%CI -69.608, -5.279), $p=0.025$ ) and motor scores (ES -18.244(95%CI -35.837, -6.51), $p=0.043$ )

### Conclusion

An altered 3rd trimester fetal circulation as reflected by increased UA-PI is associated with abnormal language and motor development in conotruncal lesions. Further work examining a larger cohort of specific CHD subgroups is needed to better understand these relationships.

Funded by

The Power of Partnership



Abstract # 91  
Presenter: Amjad, Sana  
Supervisor: Maria Ospina  
Title: **Association between maternal wildfire exposure and the risk of adverse birth outcomes: A systematic review**  
Authors: **Sana Amjad, Dagmara Chojecki, Alvaro Osornio-Vargas, Maria Beatriz Ospina**

### **Introduction**

Maternal wildfire exposure is associated with poor pregnancy outcomes potentially mediated through air pollution and psychosocial stress. We conducted a systematic review that evaluated the evidence on the association between wildfire exposure during pregnancy and the risk of adverse birth outcomes (PROSPERO # 42018094103).

### **Methods**

Comprehensive searches in nine databases were conducted up to July 2019. Observational epidemiological studies that evaluated the relationship between adverse birth outcomes and exposure to wildfire during pregnancy were included in the review. Screening of retrieved articles, data extraction and methodological quality assessment was performed by two independent reviewers. Data were analyzed descriptively.

### **Results**

Seven studies published from four countries (U.S [n=4], Indonesia [n=1], Australia [2] and Brazil [1]) involving 1,255,291 births met the inclusion criteria for the review. Heterogeneity in study populations, timing of exposure (first/second/third trimester), duration of exposure, and exposure ascertainment methods precluded data pooling. In-utero exposure to wildfire smoke was assessed by measurement of wildfire-generated air pollutants (particulate matter 2.5 [n=1], particulate matter 10 [n=1], aerosols [n=2]) and proximity of maternal residence to disaster area (n=3). The methodological quality of primary studies was fair. Maternal wildfire exposure was consistently associated with birth weight reductions (range 3.3 gm -18.0 gm), particularly when mothers were exposed to wildfire smoke in the second and third trimesters. Sex differences in birth weight were also reported with baby boys being heavier than girls and their peers born in non-wildfire areas. Wildfire exposure during late pregnancy was also linked with a slight increase in the incidence of preterm births.

### **Conclusion**

Maternal exposure to wildfire during late pregnancy is linked with birth weight reduction and preterm birth. These findings have implications for disaster management programs and perinatal service providers. Further research is needed to elucidate the biological mechanisms through which wildfires impact pregnancy outcomes.

Funded by **This research has been funded by the generous supporters of the Lois Hole Hospital for Women through the Women and Children's Health Research Institute.**

The Power of Partnership





Abstract # 92  
Presenter: Ngwezi, Deliwe  
Supervisor: Hornberger, Deliwe  
Title: **Prenatal features of ductus arteriosus related branch pulmonary stenosis in fetal pulmonary atresia**  
Authors: Deliwe Ngwezi, Marisha Mclean, Angela McBrien, Luke Eckersley, Tim Colen, Jayani Abeysekera, Kim Harberer, Aisling Young, Lisa Hornberger

### **Introduction**

Ductus arteriosus(DA)-related ipsilateral branch pulmonary artery(PA) stenosis (DA-PS) is common in congenital heart disease associated with pulmonary atresia (PAtr) and contributes importantly to the morbidity of affected neonates. We have recently described preoperative echocardiographic features associated with DA-PS in affected neonates, including the inability to examine the branch PAs on the same plane due to the location of ductal insertion and the presence of an obtuse posterior angle of bifurcation ( $>100^\circ$ ). In the present study, we sought to examine whether these same features can be used to identify the at risk fetus prenatally.

### **Methods**

We identified neonates who had been prenatally diagnosed with PAtr and a DA-dependent pulmonary circulation between 2009 and 2018 and who had undergone initial surgical/catheter intervention in our institution. Fetal echocardiograms were reviewed to examine the PA and DA anatomy for features of DA-PS best assessed from axial images with and without color Doppler. Preoperative and postoperative neonatal echocardiograms and clinical records were reviewed to confirm the presence/absence of DA-PS based on need for angioplasty at initial intervention or evolution of discrete PA stenosis postintervention.

### **Results**

In the study period 50 fetuses with PAtr were encountered of whom, 35 had images sufficient for analysis. Of these 35, PAtr was associated with an intact ventricular septum in 13(37%), tetralogy of Fallot (TOF) or TOF-double-outlet right ventricle in 16(46%), and with more complex heart defects in 6(17%). Twenty-one (60%) had evidence of DA-PS postnatally, including 15 who underwent arterioplasty at the time of initial intervention and 6 others who developed DA-PS postintervention. Gestational age at initial fetal echo was 26+6weeks and did not differ between groups. DA-PS was associated with an inability to image the branch PAs on the same plane in 67%, with an obtuse posterior bifurcation angle in 85% or with both features in 52% at a mean gestational age of 30+4weeks. In contrast, in those without DA-PS, the PAs could be imaged on the same plane in all and an obtuse posterior angle was present in only 3 (21%). The sensitivity, specificity and positive predictive value for an inability to image PAs on the same plane was 70%, 100%, 100% and for the finding of an obtuse posterior angle 85%, 79%, 85%.

### **Conclusion**

Features of DA-PS can be identified in fetal PAtr and include an inability to image the PAs on the same plane and an obtuse posterior bifurcation angle. This information is useful for prenatal counseling and planning neonatal intervention.

Funded by WCHRI

The Power of Partnership

Abstract # 93  
Presenter: Misita, Dragana  
Supervisor: Bell, Rhonda  
Title: **Prenatal nutrition care in Alberta: Exploring women's interest in dietetic services during pregnancy and dietitians experiences supporting pregnant women during pregnancy**  
Authors: **Dragana Misita, Sharan Aulakh, Maria Ospina, Rhonda C. Bell**

## Introduction

Evidence from studies focused on the Developmental Origins of Health and Disease have shown that optimal nutrition and weight gain during pregnancy are crucial for the short and long-term health of both mother and child. Access to a Registered Dietitian (RD) could be useful to assist with balancing clinical care with the promotion of a healthy lifestyle in pregnancy. The objectives of our study were to explore women's interest in having access to dietetic services throughout pregnancy and to explore RDs experiences supporting pregnant women during pregnancy in Alberta.

## Methods

A questionnaire was distributed to consecutive pregnant women attending the Maternal Fetal Medicine Clinic at the Royal Alexandra Hospital in Edmonton. The questionnaire assessed women's interest in having access to a RD during pregnancy, the types of nutrition-related questions they had, and the preferred format for potential appointments. Eighty-four women completed the questionnaire. We also conducted five semi-structured phone interviews and one focus group with RDs (n=10) who currently support or have supported pregnant women as part of their practice. We asked RDs about their experiences supporting pregnant women and discussed the resources and tools they currently use to support the nutrition-related needs of this population. Survey results were analysed using descriptive statistics. Qualitative data were transcribed verbatim and analyzed using thematic analysis.

## Results

Survey responses indicated that 94% of women were not seeing a RD while pregnant. Of those, 54% reported that they would like to see a RD during pregnancy and 24% reported that they didn't know if they were interested in seeing a RD. The top-three nutrition related topics of interest identified by women who wanted to see a RD were: meeting nutrition recommendations, physical activity, and weight and weight changes. Our qualitative findings suggest that pregnant women make up a small proportion of RD patient population, unless the RDs role is to support women experiencing a high risk pregnancy. RDs also reported that women had a variety of nutrition related questions during pregnancy, however, they often felt that they were not seeing women early enough and/ or often enough in pregnancy to cover all relevant nutrition topics in a timely manner. RDs identified that resources that were hands on, interactive, picture-based, accessible as both hardcopies and online (and were printable) were preferable and more appropriately helped them support their patients. RDs are using a variety of nutrition resources and tools from an array of credible sources and are creative in their approach to attempt to meet the needs of this population despite the barriers faced.

## Conclusion

Women have nutrition related questions and concerns during pregnancy. Investment must be steered towards optimizing nutrition in pregnancy to improve the health of this generation and others to come. Having early and consistent access to a RD for nutrition counselling during pregnancy could represent one way to achieve this

Funded by **This study was supported by Alberta Innovates. Dr. Ospina is funded by the generous support of the Lois Hole Hospital for Women through the Women and**

The Power of Partnership



Abstract # 94  
Presenter: Matta, Mirna and Mostofi, Emily  
Supervisor: Chaput, Kathleen Helen  
Title: **Recommendations for cannabis use in pregnancy among sources of cannabis sales in Alberta**  
Authors: **Matta M. (1), Mostofi E. (1), Chaput K.H.(2)**

### **Introduction**

Since the legalization of cannabis in Canada, there is increasing awareness in the medical community of the need for high quality evidence of its effects, in particular during pregnancy. Cannabis is the most commonly used drug in pregnancy, with approximately 2.5% of pregnant women in Canada reporting use to their physicians yearly. An increase in cannabis use is anticipated post-legalization. Many pregnant women report using cannabis for morning sickness, despite evidence that it increases risks of preterm birth and maternal pregnancy complications, and may be linked with abnormal infant brain development. Consequently, it is recommended that pregnant women abstain from cannabis use. We sought to explore whether Alberta cannabis dispensaries are sharing the recommendations that pregnant women abstain from use.

### **Methods**

In our preliminary study, we visited 5 dispensaries in Calgary, Alberta and online, including the provincial government website responsible for regulating the sale of cannabis, to measure the proportion that provided warnings and/or information about cannabis use in pregnancy.

### **Results**

60% of the dispensaries, and 15% of the websites visited provided no explicit information or advisory to abstain from use during pregnancy, including the provincial government website. 40% of dispensaries recommended a “start low and go slow” protocol, despite the request for information for a pregnant customer.

### **Conclusion**

Posted warnings advising abstinence from cannabis use during pregnancy in Alberta dispensaries, on websites, and on cannabis products could increase awareness of the maternal and fetal risks associated with cannabis consumption in pregnancy and potentially mitigate negative perinatal health outcomes.

Funded by: Alberta Children's Hospital Research Institute (ACHRI)

The Power of Partnership



Abstract # 95  
Presenter: Marani, Safia  
Supervisor: Ospina, Maria  
Title: Cost evaluation of emergency department use among pregnant and post-partum women in Alberta from 2013-2017  
Authors: Safia Marani, Jesus Serrano-Lomelin, Rhonda J. Rosychuk, Brian H. Rowe, Radha Chari, Susan Crawford, Susan Jelinski, Amy Metcalfe and Maria B. Ospina

### **Introduction**

Pregnant and postpartum women are frequent users of emergency departments (ED). Many of these visits represent pregnancy-related complications and inadequate perinatal care. As part of a larger study describing these visits in Alberta, this cost evaluation describes the characteristics of perinatal women that impact the various costs of visits in EDs in Alberta.

### **Methods**

This study used a population-based, retrospective cohort design of all deliveries (> 20 weeks of gestation) occurring in Alberta between 2011-2017, to identify women who visited the ED in the perinatal period. De-identified administrative data for each of these visits between 2013-2017 were obtained and linked to a comprehensive provincial clinical perinatal registry. The perinatal period of each visit was categorized into pregnancy (divided into trimesters), and post-partum up to one year. Costs per visit were calculated based on the Canadian Institute of Health Information standard resource consumption values, taking into account ED institution, fiscal year, inflation rates, patient's diagnosis, and resource utilization. Further sub-analysis of direct versus indirect costs were also completed. A stepwise multiple linear regression analysis was conducted to assess predictors of cost (\$) of ED use of pregnant and post-partum women.

### **Results**

Overall, 193 965 (51%) women visited the ED in the perinatal period. The mean cost per ED visit was \$364.01. Mean costs between pregnancy and post-partum period (pregnancy \$366.04; post-partum \$361.52), between trimesters (second trimester \$352.50; third trimester \$374.08), and immediately (delivery to 6 weeks) post-partum (\$393.66) were found to be statistically significant; however, these cost differences are small, and likely not clinically or fiscally important. Based on regression analysis, the following factors were found to be predictors of significantly increased ED cost: advanced maternal age, mothers who delivered pre-term, mothers with multiples (vs singleton pregnancies), patients admitted as inpatients, patients with a discharge diagnosis from ICD-10 chapter III, emergent triage scores (1-3), and patients with longer length of stay (>6 hours).

### **Conclusion**

Across Alberta, more than 50% of women visit the ED during the perinatal period, resulting in additional costs to the healthcare system which could be allocated towards optimizing prenatal and postnatal care. These findings demonstrate the various factors impacting cost of ED visits in the peripartum period, including high risk pregnancies and potential gaps in access, quality and equity of prenatal and postnatal care in Alberta that may contribute to at least some of these ED visits. Further research should explore cost analysis of novel programming and strategies to reduce ED visits in the peripartum period.

Funded by Alberta Health Services Health Outcomes Improvement Fund  
Women and Children's Health Research Institute

The Power of Partnership



Abstract # 96  
Presenter: Lau, Stuart  
Supervisor: Kozyrskyj, Anita  
Title: Cesarean section delivery and neurodevelopment: Systematic evidence for variation by birth events and impairment phenotype  
Authors: Stuart Lau, Vidhi Desai, Safia Marani, Omolara Sanni, Liz Dennett, Jens Walter, Maria B. Ospina, Anita Kozyrskyj

## Introduction

Globally, we are dependent on our brains for survival, critical thinking and emotional intelligence. Neurodevelopmental disorders, including intellectual disabilities, communication disorders, autism spectrum disorders (ASD), attention deficit hyperactivity disorder (ADHD), specific learning disorders, motor disorders and tic disorders, impact a child's quality of life. While genetics have been identified as a major causative factor of these disorders, emerging evidence suggests that infants born via cesarean section (CS) have a higher risk of being developmentally vulnerable in cognitive and physical aspects. In view of increasing preference for elective CS among women, we aim to synthesize current evidence on the incidence of neurodevelopmental disorders among children born via CS.

## Methods

A librarian conducted a comprehensive literature search of Medline, Embase, CINAHL, PsycInfo and Web of Science with no language or publication restrictions. Additional studies were identified using key grey literature sources and reference lists of identified articles. Observational studies and experimental studies assessing the prevalence of infant neurodevelopmental delay in those born by CS compared to those born by vaginal delivery were included in this review. Two independent reviewers screened records generated from the searches to identify eligible studies and conducted data extraction. Individual study data was pooled to produce odds ratios (OR) with 95% confidence intervals (CI) under a random effect model and in absence of heterogeneity. Evaluation of risk of bias of cohort studies and case-control using the Newcastle-Ottawa scale, cross-sectional studies using the Quality Assessment for Prevalence and randomized controlled trials appraisal using the Cochrane Risk of Bias tool is on-going.

## Results

The following results are preliminary as the systematic review is ongoing. Of 1905 unique citations (duplicates removed) identified, 131 studies met the inclusion criteria. The included studies consisted of 83 cohort studies, 37 case control studies, 5 cross-sectional and 5 experimental studies. Data analysis was completed for cohort and case-control studies examining the prevalence of ASD and ADHD in children born by CS. In cohort studies, those born by CS have increased odds of ASD (12 studies; OR: 1.22; 95% CI: 1.14-1.30), and ADHD (8 studies; OR: 1.11; 95% CI: 0.98-1.27). In the case-control studies, those born by CS have increased odds of ASD (19 studies; OR: 1.64; 95% CI: 1.33-2.01) and ADHD (4 studies; OR: 1.34; 95% CI: 0.95-1.88).

## Conclusion

Preliminary data analysis suggests that CS delivery may increase the risk of some neurodevelopmental disorders. Future steps include assessment of risk of bias, analysis of other neurodevelopment disorders and subgroup analysis of different types of CS.

Funded by WCHRI Summer Studentship

The Power of Partnership



Abstract # 97  
Presenter: Maki, Claudia  
Supervisor: Ali, Samina  
Title: **Characterizing pain in children with acute gastroenteritis who present to the emergency department**  
Authors: Claudia Maki, Samina Ali, Jianling Xie, Bonita Lee, James Dickinson, Shannon MacDonald, Naveen Poonai, Jennifer Thull-Freedman, Otto Vanderkooi, Manasi Rajagopal, Mithra Sivakumar, Linda Chui, Timothy Graham, Alberto Nettel-Aguirre, Larry Svenson, Stephen Freedman

### **Introduction**

Although acute gastroenteritis is an extremely common childhood illness, there is a paucity of literature describing associated pain and its management. Our primary objective was to assess the pain experienced by children with acute gastroenteritis in the 24-hours prior to emergency department presentation. Secondary objectives included describing pain during the emergency visit, home analgesic use, discharge recommendations, and factors that influenced analgesic use in the emergency department.

### **Methods**

**Design:** Study participants were recruited into this prospective cohort study by the Alberta Provincial Pediatric EnTeric Infection TEam between January 2014 and September 2017.

**Setting:** This study was conducted at two Canadian pediatric hospitals; the Alberta Children's Hospital (Calgary) and the Stollery Children's Hospital (Edmonton).

**Participants:** Eligibility criteria included < 18 years of age, acute gastroenteritis (greater than or equal to 3 episodes of diarrhea or vomiting in the previous 24 hours), and symptom duration less than 7 days at presentation.

**Main Outcomes and Measures:** The primary study outcome, caregiver reported maximum pain in the 24-hours prior to presentation, was assessed using the 11-point Verbal Numerical Rating Scale.

### **Results**

We recruited 2136 patients, median age 20.8 months (IQR 10.4, 47.4) and 45.8% (979/2136) female. In the 24-hours prior to enrollment, caregivers reported that their child experienced moderate (4-6) (28.6% (610/2136, 95% CI 26.7, 30.5)) or severe (7-10) (46.2% (986/2136, CI 44.0, 48.3)) pain. During the emergency visit, caregivers described maximal pain as moderate (31.1% (664/2136, 95% CI 29.1, 33.1)) or severe (26.7% (571/2136, 95% CI 24.9, 28.7)). Analgesia was provided to 21.2% (452/2131) of children. The most common analgesics used in the emergency department and recommended at discharge were acetaminophen and ibuprofen. Factors associated with analgesia use in the emergency department were high pain scores during the index visit, having a primary-care physician, short illness duration, less diarrheal episodes, presence of fever, and hospitalization at index visit.

### **Conclusion**

Caregivers of children presenting to the emergency department with acute gastroenteritis report moderate or severe pain, both prior to and during their visit. Future research should focus on the clinical implication of this pain and the development of effective and safe pain treatment plans.

Funded by Funded in part by The Alberta Provincial Pediatric EnTeric Infection TEam (APPETITE), CRIO, Alberta Children's Hospital Research Institute, and the WCHRI Partnership Award.

The Power of Partnership



Abstract # 98  
Presenter: Knisley, Lisa  
Supervisor: Scott, Shannon  
Title: Improving pediatric emergency care across Canada: The power of networking

Authors: Lisa Knisley<sup>1</sup>, Carly Leggett<sup>2</sup>, Mona Jabbour<sup>3</sup>, David Johnson<sup>4</sup>, Lisa Hartling<sup>5</sup>, Shannon Scott<sup>5</sup>, Terry Klassen<sup>1</sup>  
<sup>1</sup>Children's Hospital Research Institute of Manitoba, <sup>2</sup>George & Fay Yee Centre for Healthcare Innovation, Winnipeg, <sup>3</sup>University of Ottawa, Ottawa, <sup>4</sup>Alberta Children's H

## Introduction

General emergency department (ED) staff are responsible for treating the majority of Canada's acutely ill and injured children. To ensure high quality emergency care for children in Canada, it is critical that two key groups—general ED health professionals and families—have access to up-to-date, evidence-based knowledge. Translating Emergency Knowledge for Kids (TREKK) is a national network of clinicians, researchers and parents/families established in 2011 to ensure the latest research in pediatric emergency care is applied within general EDs. At its inception, TREKK aimed to: (a) determine the knowledge needs and preference of general ED health professionals and the families seeking pediatric care there; (b) assemble existing evidence to create accessible, easy-to-use educational tools for both families and emergency healthcare providers; and (c) build a sustainable KM network in pediatric emergency care.

## Methods

A needs assessment surveyed 1,471 health professionals and 897 parents at 32 general EDs to identify pediatric information needs and preferences. A robust resource development process brings together clinicians, researchers, research librarian, and knowledge broker to create evidence-based tools, contextualized for Canadian EDs. These tools are complemented by on-site teaching sessions to general ED staff. Through consistent engagement of parents, innovative tools are created that merge stories of parents' healthcare experience with the best available synthesized research evidence. Social Network Analyses (SNA) and qualitative interviews were employed over 3 times periods to evaluate network connectivity, impacts, challenges and opportunities.

## Results

TREKK is responding to end-user's information needs by providing accessible, evidence-based pediatric resources and building connections between general and pediatric EDs. Online resources ([trekk.ca](http://trekk.ca)) include Bottom Line Recommendations (summarizing diagnosis and treatment information), treatment algorithms, order sets, transport checklists and parent resources (whiteboard videos, e-books and interactive infographics). Healthcare professionals are using the resources as demonstrated by yearly increases in resource downloads (>30,000 in 2018/19) and feedback from education sessions. The parent videos are played in ED waiting rooms in BC, AB and MB. TREKK has provided >120 education sessions across the country and is now connected with 131 Canadian EDs and nursing stations. Results from the SNAs and qualitative interviews show a reduction in EDs sharing knowledge only within their site, and enhanced network interconnectivity.

## Conclusion

TREKK's activities highlight the power of a network to increase connections between general and pediatric EDs. Its knowledge pipeline facilitates a continuous flow of online, evidence-based knowledge complemented by on-site teaching sessions to those responsible for treating the majority of sick and injured children, and is contributing to the pursuit of equitable emergency care for all children in Canada.

Funded by Networks of Centres of Excellence, Women & Children's Health Research Institute, Children's Hospital Research Institute of MB, Stollery Children's Hospital Foundation

The Power of Partnership

Abstract # 99  
Presenter: Afzalzada-Ahrari, Malema  
Supervisor: Hartling, Lisa  
Title: The use of opioids in children's health and its connection to the opioid epidemic: A systematic review  
Authors: Afzalzada-Ahrari, M., Dyson, M., Hartling, L., DaRosa, D., Dong, K., Drendel, A., Ali, S.

### **Introduction**

Despite an overall decline in opioid prescriptions in Canada, healthcare visits, hospitalizations, and deaths due to opioid-related harms have continued to rise for children. The objective of this study is to synthesize research that examines the association between short-term therapeutic exposure of opioids and opioid use disorder. This review will help clinicians make evidence-informed, personalized decisions regarding opioid use for children.

### **Methods**

A medical librarian conducted a comprehensive search of 10 databases (including 3 grey literature sources) from inception to May 2019. Two authors independently assessed studies for inclusion. Studies were eligible if they reported quantitative primary research in English or French, and study participants had short-term (<14 days) therapeutic exposure to opioids before age 18 years (or non-specific duration of therapeutic exposure). Primary outcome was the development of an opioid use disorder; secondary outcomes included; opioid addiction, dependence, misuse, and abuse. Data extraction involved two independent reviewers utilizing a standardized form. Methodological quality was assessed using the Quality in Prognosis Studies tool. Data was pooled using meta-analysis where possible.

### **Results**

The search identified 4,072 unique citations; 67 were selected for further review, and 15 were included (3 retrospective cohort, 5 prospective cohort, and 7 cross-sectional). All studies took place in the USA. Approximately 45,653 participants were analyzed. Nine studies were administered in schools, 3 studies used administrative data, and 3 were surveys conducted in various settings. Most settings were non-specific, however, 1 study looked at opioid use in the dental setting, 1 in the trauma setting, and 1 based on involvement in organized sports. Three studies demonstrated that short-term therapeutic exposure is associated with opioid misuse; of which, 2 showed an association with opioid-related adverse events (i.e. opioid overdose) and 1 showed an association with opioid abuse. The remaining 12 studies did not specify duration of exposure, and therefore confirming whether the associations between opioid exposure and misuse were due to short or long-term therapeutic exposure was not possible.

### **Conclusion**

This review suggests that there may be an association between short-term opioid use and opioid misuse (final results pending). Careful consideration of the risk and benefits of short-term opioid use should be undertaken prior to prescribing opioids; if prescribed, close follow up for the development of complications is warranted. PROSPERO Registration Number: 122681.

Funded by Alberta Research Centre for Health Evidence Operational Grant, Maternal Newborn Child & Youth Strategic Clinical Network (MNCY SCN), Emergency Strategic Clinical Network (ESCN) Systematic Review Grant

The Power of Partnership





Abstract # 100  
Presenter: Wollin, Bethany  
Supervisor: Richard, Caroline  
Title: Female Wistar rats exhibit a better T-cell response than male rats

Authors: Wollin B, Veida-Silva H, Juarez-Platas M, Azarcoya-Barrera J, McDougall C, Goruk S, Richard C

### Introduction

The prevalence of obesity and the associated health risks are known to differ between females and males. Understanding these differences as well as their underlying mechanisms may improve the prevention and treatment of obesity for both women and men. Chronic systemic inflammation, impaired immune function, and greater risk of infection are common complications of obesity. Consuming a high-fat diet has been shown to decrease T-cell function in male rats, however, the influence of sex on the immune response is less understood. The objective of this study was to evaluate the sex differences in immune function of Wistar rats in response to diet-induced obesity.

### Methods

At 4 weeks of age, male and female Wistar rats were randomized to consume one of two nutritionally complete diets for 9 weeks: 1- low-fat (control 10% fat wt/wt) or 2- high-fat (HF 25% fat wt/wt). Although total fat content differed between diets, the proportion of fatty acids was matched. At 13 weeks of age, rats were terminated and immune cells were isolated from spleens. Ex vivo cytokine production after stimulation with phorbol 12-myristate 13-acetate plus ionomycin (PMA+I), a T cell mitogen, was measured by ELISA to determine immune cell function. Immune cell subsets were determined by flow cytometry.

### Results

Female rats in both diet groups had significantly lower body weights compared to males ( $P < 0.001$ ) and gained less weight on the HF diet compared to males. Splenocytes from female rats in both diet groups tended to produce more IL-2 (a marker of proliferation) than males when stimulated by PMA+I ( $P = 0.078$ ). Both sexes fed the HF diet tended to produce less IL-2 compared to rats fed control diet ( $P = 0.088$ ). Females had a higher proportion of helper T cells ( $CD3+CD4+$ ,  $P = 0.002$ ) and a trend toward higher expression of the IL-2 receptor (total  $CD25+$ ,  $P = 0.067$ ) compared to male rats.

### Conclusion

We demonstrated that a high-fat diet lowers T cell proliferation upon immune challenge in both sexes, however, females have higher production of IL-2 to start with than males, and therefore, greater overall proliferation. The greater IL-2 response in females may be related to the higher proportion of helper T cells and expression of the IL-2 receptor compared to males. While both sexes respond similarly to a high-fat diet, females do not develop diet-induced immune dysfunction to the same extent as males.

Funded by Alberta Innovates and grants from Egg Farmers of Canada and NSERC

The Power of Partnership



Abstract # 101  
Presenter: Chow, Braden  
Supervisor: Menon, Geetha  
Title: Determination of radiobiological parameter values used in cervical cancer brachytherapy through in vitro experimentation  
Authors: Braden Chow (University of Alberta), Brad Warkentin (University of Alberta), Armin Gamper (University of Alberta), Kareena Nanda (University of Alberta), Fleur Huang (University of Alberta), Geetha Menon (University of Alberta)

### Introduction

Brachytherapy (BT) for cervical cancer, delivered either by high-dose rate (HDR) or pulsed-dose rate (PDR) regimens, utilizes radiobiological dose prescription. These doses are calculated using the linear-quadratic model that includes the parameters  $\alpha/\beta$ , a characterization of the sensitivity of the tissue to dose rate and fractionation, and  $T_{1/2}$ , the repair rate of sublethal DNA damage. Literature reported values for these parameters, determined using other treatment schedules, vary significantly from those utilized clinically ( $\alpha/\beta = 10$  Gy and  $T_{1/2} = 1.5$  hrs for tumor). For better tumor control, the current recommendation is to escalate total treatment dose from 80 Gy to 90 Gy, which requires a better understanding of these parameter values to reduce dose uncertainties and improve treatment outcomes. This study was conducted to determine the  $\alpha/\beta$  and  $T_{1/2}$  values through in vitro experiments using cervical cancer cell lines and relevant clinical BT treatment schedules.

### Methods

Three cervical cancer cell lines (C-33A, CaSki, SiHa) were irradiated with different dose rates and fractionation schedules using a Cs-137 irradiator and clinical HDR and PDR Ir-192 afterloaders in single acute fractions (dose range: 0.5-10 Gy, delivered by the Cs-137 irradiator and Ir-192 HDR) and multiple fractions (delivered hourly or bi-hourly, delivered by the Cs-137 irradiator and Ir-192 PDR). Cell colonies were counted to determine the clonogenic survival after irradiation.  $\alpha/\beta$  and  $T_{1/2}$  were estimated for each cell line through minimization of chi-square deviations between the experimental data and fits with the linear-quadratic model.

### Results

The single fraction experiments yielded  $\alpha/\beta$  ratios of  $6.43 \pm 0.90$ ,  $6.62 \pm 2.33$ , and  $4.74 \pm 0.92$  Gy for C-33A, CaSki, and SiHa, respectively. These are significantly smaller than the 10 Gy value used in treatment planning but agrees with the smallest reported literature value of 6 Gy. Fractionated experiments gave a  $T_{1/2}$  of  $1.67 \pm 0.28$ ,  $4.03 \pm 0.73$ , and  $2.14 \pm 0.20$  hours for the same three cell lines, larger than the 1.5 hours used clinically. Analogous experiments using different sources (e.g. - single acute fractions on Cs-137 and Ir-192 HDR) generally yielded similar radiobiological parameters, suggesting that the differences between the sources (e.g. – instantaneous dose rate, radiation energy) did not significantly impact survival.

### Conclusion

There are differences between the clinically used and experimentally determined  $\alpha/\beta$  (about 5 Gy maximum) and  $T_{1/2}$  (about 2.5 hours maximum) values, highlighting possible uncertainties in planned treatment doses. With a treatment aim of 90 Gy, using the values obtained experimentally would suggest differences of up to 6 Gy (>6%) in the delivered dose.

Funded by WCHRI Innovation Grant

The Power of Partnership



Abstract # 102  
Presenter: Ha, Christine  
Supervisor: Phelan, Shanon  
Title: More than just kegels: An alternate lens for maternal pelvic health  
  
Authors: Ha, Christine; Phelan, Shanon

### **Introduction**

It is well-established that pelvic floor dysfunctions (PFDs) are prevalent, affecting 25% of women. These include conditions such as urinary incontinence, which is the unwanted leaking of urine, and pelvic floor prolapse, which is herniation of pelvic organs through the vagina. The prevalence of PFDs increases to 2 out of 3 women after childbirth. These dysfunctions are often stigmatized and many think that conditions such as urinary incontinence are "normal" after childbirth. Therefore PFD symptoms are often under reported and medical interventions are not accessed. When left unattended, these dysfunctions become chronic and worsen with age and menopause. Much of the current literature focuses on the pathophysiology of PFDs, therefore the dominant lens in which the research studies are being conducted is a biomedical one, with the physical body as primary concern. However, there is a paucity of research addressing the larger context in which these problems are embedded.

### **Methods**

Within this theoretical paper the authors argue that while dominant biomedical discourses define PFDs as physical diseases to be treated, this cannot be separated from the sociopolitical and cultural fabric in which women experience symptoms associated with PFDs. In this paper we explore how an alternative theoretical perspective could offer more nuanced ways to consider and understand maternal pelvic health and PFDs. Annemarie Mol, an ethnographic philosopher, proposes a theoretical framework that stems from ethnography and Actor Network Theory, based on the premise "disease is located in a life, not just a body". This framework considers the multiple ways in which disease is constituted and prompts questions about how practices in themselves create realities. In other words, 1) how do current practices performed in postpartum pelvic health (re)create authoritative knowledge? and 2) what are the impacts of these practices on the therapeutic encounter (health professional-patient)? By critically examining the ways in which current practices in this field are enacted, this study will aim to advance understandings about the social, political, cultural, and situational factors that impact maternal pelvic health.

### **Results**

Preliminary results of this theoretical analysis will be discussed. The findings will inform the first author's theoretical perspective for her doctoral work.

### **Conclusion**

PFDs are complex, multifaceted maternal pelvic health issues characterized by long-lasting symptoms that negatively affect quality of life and mental health. More than just kegels, there is a need to consider these dysfunctions in a broader context. Application of a sociocultural-sociopolitical perspective to our understanding of PFDs could be one way to advance or create new approaches to maternal pelvic health.

Funded by Faculty of Rehabilitation Medicine, University of Alberta

The Power of Partnership



Abstract # 103  
Presenter: Bianchi Lemieszek, Marina  
Supervisor: Postovit, Lynne-Marie  
Title: The function of the epithelial splicing regulatory protein 1 (ESRP1) in Luminal A breast cancer cell lines  
Authors: Marina B. Lemieszek, Scott S. Findlay, Krista Vincent, Lynne-Marie Postovit.

### Introduction

Breast cancer is the most common cancer among Canadian women and still has a high rate of metastatic progression after treatment. Breast cancer has different molecular subtypes and Luminal A, which is the most common subtype, shows the most favorable 5-year prognosis; however, its recurrence is responsible for a high increase in mortality after 10 years of diagnosis. Therefore, it is important to identify prognostic markers that promote and predict breast cancer recurrence. The Epithelial Splicing Regulatory Protein 1 (ESRP1) is an RNA binding protein that regulates alternative splicing events associated with epithelial cell types. Importantly, ESRP1 is one of the most up-regulated transcripts in breast cancer when compared to normal breast tissue and high levels of ESRP1 correlate with reduced patient overall and disease-free survival. Thus, ESRP1 may have a pro-metastatic role in breast cancer. This project aims to determine the function of ESRP1 in luminal A breast cancer cell lines. We hypothesize that high ESRP1 levels will prognosticate metastatic disease and that ESRP1 induces a pro-tumorigenic splicing program.

### Methods

Two luminal A breast cancer cell lines, MCF7 and T47D, were edited using CRISPR gene editing to knockout ESRP1 gene. These cells were screened for frameshift mutations with Droplet Digital-PCR (ddPCR) and mutations were confirmed with Sanger Sequencing. The ESRP1 knockout cells and controls will be used to determine in vitro growth rate to determine differences in proliferation and to perform mammosphere formation assay, which quantifies stem cell activity and self-renewal capacity. Expression of Epithelial-to-Mesenchymal transition markers will be analyzed with Real Time-PCR and with Western Blot. Additionally, ESRP1 knockout and controls cells previously developed in the laboratory with MCF7 cell line using CRISPR were used to perform mammosphere formation assay and in vitro growth rate analysis. Finally, breast cancer samples from one hundred patients that had breast cancer recurrence and from one hundred patients that did not recur will be analyzed with ddPCR to determine the copy number of ESRP1 gene.

### Results

Three ESRP1 knockout clones were identified in MCF7 cell line and three wild-type clones were identified in T47D cell line. CRISPR was repeated in T47D cell line and clones were seeded in Matrigel to help in cell attachment. These cells are currently under screening for mutations. Functional assays done with clones previously developed in the laboratory showed no difference in vitro growth rate and mammosphere formation assay between knockout and wild-type clones.

### Conclusion

CRISPR gene editing was performed in two Luminal A breast cancer cell lines and cells were screened for mutations. Functional studies with MCF7 clones previously developed in the laboratory showed no difference between wild-type and knockout clones in proliferation rate and mammosphere formation assay. Breast cancer samples from patients will be analyzed to determine the copy number of ESRP1 gene.

Funded by WCHRI

The Power of Partnership



Abstract # 104  
Presenter: Li, Nicholas  
Supervisor: Kirkham, Amy  
Title: Pulmonary Consequences of Anthracycline and Trastuzumab Treatment for Early-Stage Breast Cancer  
Authors: Nicholas Li, Amy Kirkham, Andrew Brotto, Michael Stickland, Edith Pituskin, D Ian Paterson

### **Introduction**

Anthracycline chemotherapy agents and trastuzumab are some of the most effective treatments for breast cancer, but their use has been limited by negative effects on heart function. However, the long-term impact of anthracyclines and trastuzumab on pulmonary function is not well quantified. Ventilatory drivers of exercise dyspnea are known to lead to early exercise termination, which is a phenomenon observed in anthracycline- and trastuzumab-treated populations. Dynamic hyperinflation, defined as a temporary and variable reduction in inspiratory reserve volume (IRV) with exercise, and low ventilatory efficiency, evaluated by the lowest ratio of ventilation to carbon dioxide output ( $VE/VCO_2$ ), are two such drivers of dyspnea. The purpose of this analysis was to examine the impact of treatment with either anthracyclines or trastuzumab on ventilatory efficiency and the occurrence of dynamic hyperinflation during exercise in women with breast cancer.

### **Methods**

This study was a phase 2, two-arm, randomized controlled trial, that included 80 participants with early stage breast cancer scheduled for anthracycline or trastuzumab adjuvant therapy at the Cross Cancer Institute. Participants were randomly assigned to a multidisciplinary intervention (exercise, diet, pharmacology, smoking cessation) or usual care (UC). Graded maximal exercise testing was performed on a cycle ergometer at 3 timepoints: prior to first or second chemotherapy, 24-week follow up, and 52-week follow up. Spirometry and exercise gas exchange were analyzed using a metabolic measurement system, by which  $VE/VCO_2$  data were obtained. Baseline and peak exercise values were used for analysis. Changes in dynamic hyperinflation were measured by performing inspiratory capacity maneuvers and analyzed by calculated IRV. A generalized linear mixed model was used to assess changes over time and between groups.

### **Results**

The intervention group exhibited a significant increase in peak IRV at 24-weeks relative to pre-chemotherapy ( $p=0.017$ ) but returned to pre-chemotherapy values by the 1-year time point ( $p=0.273$  vs pre-chemotherapy;  $p=0.003$  vs 24-week); whereas peak IRV did not change in the UC group. Both baseline and peak exercise  $VE/VCO_2$  did not change over time or differ between groups.

### **Conclusion**

Overall, changes in dynamic hyperinflation or a reduction in ventilatory efficiency were not observed with anthracycline or trastuzumab treatment. As a lower IRV is indicative of dynamic hyperinflation, the increased peak IRV observed in the multidisciplinary intervention group suggests the intervention reduced dynamic hyperinflation, however the mechanism remains unknown. Future research is needed to more comprehensively assess lung mechanics with breast cancer treatment and the contribution of these changes to cardiorespiratory fitness.

Funded by Supported by an investigator-initiated research grant from the University Hospital Foundation/Mazankowski Alberta Heart institute, Edmonton, Alberta, Canada.

The Power of Partnership



Abstract # 105  
Presenter: Khetarpal, Nitya  
Supervisor: Ross, Sue  
Title: **Exploring effective engagement strategies used to recruit Indigenous participants to community-based research**  
Authors: Nitya Khetarpal, Dr Sue Ross

### **Introduction**

The Sohkitehew (ST) Group received 2019 CIHR funding to design and conduct workshops for women of various ages promoting cultural connectedness in Maskwacis, a rural Indigenous community. The implementation of ST raised questions about best practices for recruiting Indigenous women, specifically on implicit or explicit inducements for participants. We therefore carried out an informal literature review to identify recruitment strategies employed in Indigenous and community-based research and the impact of involving women Elders in the research.

### **Methods**

We identified and collected information from relevant guidelines, such as Tri-Council Policy Statement for ethical conduct in human research, UAlberta Research Ethics Board and Elders Protocol and Guidelines, and OCAP Principles Governing First Nations research. Peer-reviewed publications were searched for discussion about recruitment strategies employed. A clinical ethicist provided advice on our study.

### **Results**

Standard inducements: several guidelines discuss the types of “compensation” researchers ought to provide for Indigenous participants. Recommendations varied according to the specific roles of participants (from attending workshops, to making presentations). In general, compensation should be provided for time given for the research, or recognition of knowledge shared. Compensation could also be considered as inducements for participants to join research. Published research usually provided food and drink at any type of meeting. Participants contributing to interviews or completing questionnaires were usually recognised for giving their time and knowledge (eg monetary gift cards). For women specifically, the availability of child care during events is particularly important.

Influence of Elders: Women Elders are the ‘knowledge keepers and healers’ of a community [Wilson, “Research is Ceremony”] in particular related to children and family: their presence during workshops is a facilitator for recruitment and data collection, because participants trust that the research environment will be safe. However, having (certain) Elders present also influences participants and may affect data validity by contributing to social desirability bias.

### **Conclusion**

Our literature study identified recommendations for good research practice in Indigenous research and specific examples of compensation and inducements specific to women. The findings from this review have led to us to adopt a systematic approach to our practice for ST women's wellness research.

Funded by Nitya Khetarpal's research is funded by the URI. Sue Ross is funded by generous supporters of the Lois Hole Hospital for Women through the WCHRI.

The Power of Partnership



Abstract # 106  
Presenter: Voaklander, Britt  
Supervisor: Ospina, Maria  
Title: Diabetes in pregnancy among Métis women: A retrospective cohort study

Authors: Britt Voaklander, Omolara Sanni, Kelsey Bradburn, Ashton James, Maria Ospina

## Introduction

Métis are a post-contact Indigenous peoples whose beginnings are traced back to unions between European fur traders and First Nations women, and who over time developed their own unique culture and identity. In Alberta, there are 114,375 self-identified Métis. Even though Métis make up a substantial proportion of the Indigenous population in Canada they are underrepresented in health literature. Diabetes in pregnancy among Métis women is an important knowledge gap that has not previously been evaluated. The objective of this study is to assess the prevalence, maternal and perinatal health outcomes of Métis women with diabetes in pregnancy compared to those of non-Métis women.

## Methods

A population-based, retrospective cohort study using data from a validated perinatal clinical registry (the Alberta Health Perinatal Research Program) linked to administrative health databases and the Métis Nation of Alberta Identification Registry. The study population were Métis and non-Métis women who had singleton births in Alberta between 2006 and 2016. The primary study outcome was the prevalence of pre-existing diabetes (PEDM) and gestational diabetes mellitus (GDM). Secondary outcomes included obstetrical (caesarean section, maternal death, preeclampsia, gestational hypertension, obstetric hemorrhage) and perinatal outcomes (stillbirth, neonatal death, congenital anomaly, birth injury, large for gestational age, NICU admission, and preterm birth). Bivariate analyses used t-tests to compare continuous variables, and chi2 test or fishers exact test for categorical variables. Prevalence estimates of GDM and PEDM were calculated and unadjusted logistic and linear regression models were used to compare obstetrical and perinatal outcomes in Métis women with those of non-Métis women as the reference group..

## Results

A total of 483,300 singleton births were included in the study (7,977 births from Métis mothers, and 475,323 were non-Métis births). The prevalence of GDM among Métis women was 4.86% compared to non-Métis women 5.32% (OR=0.90, 95%CI: 0.80, 1.0). Métis women had 22% increased odds of having PEDM compared to non-Métis women (OR=1.22 95%CI: 1.01, 1.47). Métis women with GDM were on average 21 months younger, ( $\beta$ =-1.77 95%CI: -2.29, -1.25), had babies on average 154 g heavier ( $\beta$ =154.44, 95%CI: 94.56, 214.33), have increased odds of having a baby with congenital anomalies (OR=2.31, 95%CI: 1.25, 4.29) and having babies large for gestational age (OR=1.79 95%CI: 1.41, 4.27) compared to non- Métis women. Métis women with PEDM were on average two years younger ( $\beta$ =-2.02, 95%CI: -3.03, -1.00) and have increased odds of having preeclampsia compared to non- Métis women (OR=3.07, 95%CI: 1.62, 5.81).

## Conclusion

This is the first study in Canada to assess diabetes in pregnancy among Métis women and highlights important differences in the outcomes of GDM and PEDM among Métis women compared to their non-Métis counterparts. The information from this study will be used by the Métis Nation of Alberta for developing culturally appropriate prenatal health services for Métis women with diabetes in pregnancy.

Funded by WCHRI Graduate Studentship; Métis Scholars Award and a CIHR Project Grant

The Power of Partnership

Abstract # 107  
Presenter: Cheung, Daphne  
Supervisor: Troster, Sarah  
Title: Addressing educational needs around pregnancy and reproductive health in women with rheumatic disease  
Authors: Daphne Cheung, Maryna Yaskina, Sarah Troster

### **Introduction**

Systemic autoimmune and rheumatic diseases frequently affect women of child bearing age, raising important health considerations and unique educational needs. Although knowledge gaps within this population have been identified, there is limited research that demonstrates if and how these educational needs are being met. This study aims to identify whether patient knowledge gaps around pregnancy and rheumatic disease are being addressed, and how to improve the delivery of patient education and care.

### **Methods**

Questionnaire responses were collected from 43 women patients at the University of Alberta Rheumatology clinic between the ages of 18 to 45 years. Participants were diagnosed with a rheumatic condition before pregnancy and either pregnant within the last 5 years, currently pregnant, or planning pregnancy in the next 2 years. Questionnaire items were generated based on previous published literature, and results analyzed applying descriptive statistics. The questionnaire was distributed and managed using REDCap software.

### **Results**

Among 12 topics previously identified as important educational needs when considering rheumatic disease and pregnancy, 4 topics were discussed most frequently between patients and their rheumatologist: medication safety during pregnancy, medication safety while breastfeeding, managing rheumatic condition during pregnancy, and risks to mother/baby during pregnancy. Most women felt their educational needs were addressed, yet 25.6% (11/43) of patients did not discuss any of these 12 important topics with their provider. 57.1% of participants found additional information on their own, mostly from online resources (63.9%). The majority of participants (90.7%) prefer to receive educational information from their rheumatologist.

### **Conclusion**

There is variation in delivery of patient education around pregnancy and rheumatic disease. Patients indicate they prefer to receive information from their rheumatologist and to use online resources when finding information on their own. Combining these forms of patient education will be important when considering how to improve the delivery of education and care around pregnancy and reproductive health concerns in women with rheumatic disease.

Funded by The Arthritis Society awarded funds

The Power of Partnership





Abstract # 108  
Presenter: Bedi, Iqwak  
Supervisor: Hemmings, Denise G.  
Title: Tumor necrosis factor-alpha (TNF- $\alpha$ ) induces vasoconstriction in uterine arteries during pregnancy when nitric oxide (NO) is reduced  
Authors: Bedi I, Manz J, Hemmings DG

## Introduction

Preeclampsia (PE) is a hypertensive pregnancy disorder that affects 5-7% of pregnant mothers. The hypertensive phenotype, due to increased vascular tone, leads to poor placental perfusion and thus poor oxygen transfer to the fetus. Vascular tone is a balance regulated by dilation and constriction factors. Increased vascular tone can be caused by reduced signalling through NO, a potent vasodilator. Another factor that regulates vascular tone is the bioactive sphingolipid, sphingosine 1-phosphate (S1P) that signals through its receptors (S1PR1-5). When S1P binds to S1PR1 and S1PR3 on the endothelium inside the vessel, it induces dilation through NO. However, signaling through S1PR2 and S1PR3 on vascular smooth muscle cells (VSMCs), the outer layer of the vessel, induces constriction. TNF- $\alpha$  is an inflammatory cytokine that is well known for its constrictive properties but can also lead to S1P production resulting in dilation. We previously showed that TNF- $\alpha$  infused inside pressurized uterine arteries from pregnant mice (P) increased vascular tone but only when NO production was blocked. Lesser effects were seen in arteries from non-pregnant (NP) mice. The direct effects of TNF- $\alpha$  on VSMCs, are not known. And, it is unknown if the dilation effects of TNF- $\alpha$  are due to increased S1P production. Thus, understanding the crosstalk between these pathways may lead us to a mechanism for preeclampsia. We hypothesize that direct addition of TNF- $\alpha$  to the bath when NO production is blocked will elicit stronger constriction than when it is added inside the artery. Moreover, the addition of TNF- $\alpha$  to the bath while blocking sphingosine kinase 1, the enzyme producing S1P, will elicit stronger constriction than when it is added inside the artery.

## Methods

A pressure myograph system was used to assess changes to vascular tone. The uterine arteries from pregnant (n=3; Gestational Day 18.5) and non-pregnant mice (n=13) were dissected out, and then mounted onto glass cannulas. The cannulated arteries were held in a bath of physiological saline solution which was changed as the arteries were gradually pressurized. Drugs infused inside arteries mounted on a pressure myograph system mimic vasoactive factors in circulation; those added to the bath mimic factors in surrounding tissues. TNF- $\alpha$  (10ng/mL) was added in the presence and absence of L-NAME (10mM), a NO synthase inhibitor, or PF-543 (1microM), a SK1 inhibitor.

## Results

TNF- $\alpha$  alone added to the bath did not change vascular tone. L-NAME alone constricted arteries from P (19.7 $\pm$ 3.66%) but not NP mice (0.74 $\pm$ 1.41%). In contrast to our previous findings, addition of TNF- $\alpha$  + L-NAME to the bath led to dilation (7.79 $\pm$ 1.94%) compared to L-NAME alone (P= 0.004). This was not seen in arteries from NP mice. Similar to previous findings, adding TNF- $\alpha$  while blocking SK1, the enzyme producing S1P, had no effect.

## Conclusion

NO is vital for maintaining the vascular tone during pregnancy, especially when TNF- $\alpha$  is increased, as it is in preeclampsia. More replicates are needed to conclude the role of SK1 and S1P production in mediating TNF- $\alpha$ -induced dilation. Our next step is investigating the role of S1PRs in mediating TNF- $\alpha$  regulation of vascular tone

Funded by CIHR and WCHRI

Abstract # 109  
Presenter: Li, Jia Hang  
Supervisor: Bourque, Stephane  
Title: The effects of perinatal iron deficiency on neonatal cardiac development

Authors: Jia Hang Li, Claudia Holody, Ronan Noble, Stephane Bourque

### Introduction

Iron deficiency (ID) is the most common nutritional disorder in the world, affecting 66-80% of the global population. Pregnant women are most susceptible to ID due to maternal blood volume expansion and the nutritional demands of the fetus. ID during pregnancy can alter developmental trajectories and predispose offspring to cardiovascular diseases in adulthood. We have previously shown that ID causes tissue-specific patterns of hypoxia and mitochondrial dysfunction in male but not female offspring. Recently, we found evidence of cardiac dysfunction (i.e. cardiomegaly and reduced ejection fraction), impaired mitochondrial respiration, and increased mitochondrial content in the hearts of neonatal ID rats. Given that the heart is highly metabolically active and undergoing rapid developmental changes in the perinatal period, we hypothesized that the reduced cardiac mitochondrial respiration would stimulate mitochondrial biogenesis and disrupt cardiomyocyte maturation postnatally.

### Methods

Six-week old female Sprague Dawley rats were fed either an iron-restricted or an iron-replete diet before and during pregnancy. At birth, all dams are fed a standard grain based rodent chow. On postnatal (PD)1, 14, and 28, male and female pups were euthanized, and ventricles were collected, stored at -80°C, and subsequently homogenized. Protein levels of mitochondrial biogenesis effectors (PGC-1 $\alpha$ , AMPK : pAMPK ratio, Sirt1, Sirt3) and markers of cardiomyocyte maturation ( $\alpha$ -MHC :  $\beta$ -MHC ratio) and damage (cTnI/T) were assessed by Western Blot;  $\beta$ -actin was used as a loading control.

### Results

Both male and female ID pups had reduced hemoglobin at PD1 and 14 ( $P < 0.0001$  for all outcomes), but all had recovered by PD28. Male and female ID pups were also growth-restricted at all time points compared to control ( $P = 0.001$  males,  $P < 0.0001$  females). PGC-1 $\alpha$  levels increased with age ( $P = 0.004$ ) in both sexes but there was no overall effect of perinatal ID ( $P = 0.60$  males,  $P = 0.69$  females). Analysis of the remaining proteins are ongoing.

### Conclusion

Our preliminary results indicate no upregulation of PGC-1 $\alpha$  due to ID despite increased mitochondrial content in neonatal hearts. Results for the remaining markers will provide additional insights into the mechanisms by which perinatal ID affects cardiac development, which could have important implications for the long-term cardiovascular health of the offspring.

Funded by WCHRI Summer Studentship Award, AIHS Summer Studentship, CIHR, WCHRI.

The Power of Partnership



Abstract # 110  
Presenter: Pasha, Mazhar  
Supervisor: Davidge, Sandra  
Title: The potential role of endoplasmic reticulum stress in vascular dysfunction in a rat model for preeclampsia  
Authors: Mazhar Pasha<sup>1, 2,3</sup>, Raven Kirschenman<sup>2,3</sup>, Floor Spaans<sup>2,3</sup>, Christy Lynn-Cooke<sup>2,3</sup>, Sandra T Davidge<sup>1, 2,3</sup>  
<sup>1</sup>Department of Physiology, <sup>2</sup>Department of Obstetrics and Gynecology, <sup>3</sup>Women and Children's Health Research Institute, University of Alberta, Canada

### Introduction

Preeclampsia (PE) is a unique pregnancy complication characterized by gestational hypertension, proteinuria, edema, and/or signs of damage to other organs (liver and kidneys). Despite PE being one of the leading causes of maternal and perinatal morbidity, the mechanisms responsible for its pathogenesis have yet to be fully elucidated. Further, therapeutic interventions so far remain only experimental and there is no established remedy for the treatment of PE. Although studies have suggested that the maternal symptoms of PE may be the result of endothelial dysfunction with oxidative stress as a key intermediary role, the underlying molecular mechanisms leading to vascular dysfunction have not been elucidated. Interestingly, an emerging body of research underpins a strong interplay between oxidative stress and endoplasmic reticulum (ER) stress leading to endothelial dysfunction. We hypothesize that ER stress is a molecular determinant of oxidative stress that eventually leads to endothelial and vascular dysfunction associated with preeclampsia.

### Methods

The above objective was assessed using a novel selective Reduced Uterine Perfusion Pressure rat model (sRUPP) for preeclampsia that was previously characterized in our lab. Young pregnant Sprague-Dawley rats were randomized into sRUPP (n=5) and Sham control (n=3). On gestational day (GD)14, silver clips of ~100 µm internal planar gap were placed on the ovarian and uterine arteries, to reduce blood flow to the entire fetoplacental unit (sRUPP) or on the abdominal fat (Sham control). On GD19, blood pressure was measured using the CODA tail-cuff system. Rats were euthanized on GD20 (term=GD22) and fetal biometrics were recorded. Mesenteric arteries were isolated to assess ex vivo vascular function using wire myography. Given the potential role of ER stress in modulating endothelial dysfunction, methacholine (Mch)-induced endothelium-dependent relaxation was assessed in the presence and absence of tauroursodeoxycholic acid (TUDCA; an ER stress inhibitor). Vasoconstriction responses to high potassium levels (KPSS) were assessed as a reflection of pregnancy vascular adaptations.

### Results

Preliminary results demonstrated a trend to an increased mean arterial pressure (p=0.078), a decreased litter size (p<0.001) and an increase in the number of resorption sites (p=0.003) in the sRUPP rats compared to controls. No changes were found in placental weight and fetal body weight. MCh-induced endothelium-dependent vasodilation responses were similar in mesenteric arteries from sham control and sRUPP rats. Contrary to our hypothesis, the ER stress inhibitor TUDCA did not alter MCh-induced vasodilation in mesenteric arteries between sRUPP or control rats. KPSS maximal responses tended to be increased in mesenteric arteries from sRUPP rats compared to controls (p=0.078).

### Conclusion

In this pilot study, the sRUPP model was successfully used to mimic aspects of preeclampsia. So far, our preliminary data did not reveal a major role for ER stress. However, further studies will be necessary to increase n-numbers to determine the role of ER stress in vascular dysfunction and increase our understanding of the mechanisms complicated by preeclampsia, for a better therapeutic intervention.

Funded by CIHR and WCHRI

The Power of Partnership



Abstract # 111  
Presenter: Henneberry, Molly  
Supervisor: Steinback, Craig  
Title: Blood pressure control in women with singleton and twin pregnancies

Authors: Henneberry, M., Meah, V., Steinback, C.D., Davenport, M. H.

### **Introduction**

During pregnancy, a woman's heart increases in size and cardiac output. This occurs concurrently with augmented sympathetic nervous activity (SNA), measured in terms of "bursts" of activity/minute. However, there is a large reduction in arterial resistance, resulting in stable or reduced blood pressure. This may be due to the ways in which the sympathetic nervous system (SNS) influences the blood vessels. Cardiovascular adaptations are even more profound in women carrying twins than in those carrying a single baby, including increases in blood volume and cardiac output. Currently, little research exists that compares blood pressure control in women who are pregnant with a single baby vs. twins. This preliminary data explored differences in the cardiovascular characteristics that may be due to changes in the sympathetic nervous system of women who are pregnant with one baby vs. twins; we hypothesized that the cardiovascular changes such as blood pressure and cardiac output would be more pronounced in women with twins, and that SNA in these women would be reduced (fewer bursts/minute) in comparison to women with singleton pregnancies.

### **Methods**

6 women with singleton and 1 woman with a twin pregnancy were tested in the third trimester (range of 29 weeks-30 weeks). Heart rate, systolic and diastolic blood pressure (SBP and DBP), and cardiac output (CO) were collected using multiunit microneurography from 6 women with uncomplicated singleton pregnancies and 1 woman with an uncomplicated twin pregnancy. A tungsten electrode was inserted in the peroneal nerve, and measures were taken in a semirecumbent position following a quiet rest period. These data were collected in LabChart (v8.1.13) and 2 consecutive minutes of rest were analyzed for BP, CO, mean HR, and burst frequency (bursts/min).

### **Results**

Women with twin pregnancies had greater mean CO at rest vs. women with singleton pregnancies (10.23L/min and  $7.06 \pm 1.53$  L/min, respectively). Burst frequency was similar in women carrying one baby compared to the woman pregnant with twins at rest (45 vs 47 bursts/min, respectively). Average heart rate appeared slightly higher in the twin pregnancy at 97 bpm vs  $85 \pm 12$  bpm in those carrying one baby.

### **Conclusion**

These are the first direct comparisons of blood pressure control in women with singleton vs. twin pregnancies. This supports the theory that as blood volume and cardiac output increase along with heart rate during pregnancy, SNA may be altered to maintain normal resting blood pressure. This early analysis suggests that the maintenance of normal blood pressure in pregnant women may be a function of altered sympathetic nervous activity. These are preliminary data from a larger study investigating the role of the sympathetic nervous system in controlling the blood pressure of women who are pregnant with twins. Future directions with these data will explore the firing patterns of individual or small groups of neurons within the overall sympathetic nervous activity, and compare larger cohorts of singleton and twin pregnancies in these measures.

Funded by Summer Studentship

The Power of Partnership

Abstract # 112  
Presenter: Lopes, Nayara A.  
Supervisor: Olson, David  
Title: **Social isolation exposure in rats and the effects of single and multiple hits to inflammatory and stress marker profiles**  
Authors: Lopes NA, Wiley C, Patel V, Matkin A, McCreary K. J., Fang X, Falkenberg E, Metz GAS, Olson DM

### **Introduction**

Maternal stress before and during pregnancy increases the risk of adverse perinatal outcomes, such as preterm labour, leading to metabolic and cardiovascular diseases in the offspring. Social isolation (SI) as a maternal stressor is associated with altered brain development and behaviour in rodents. We hypothesize that SI before conception and during pregnancy predisposes a rat to adverse pregnancy outcomes and to an altered profile of inflammatory and stress markers.

### **Methods**

Female rats of the F0 parental and F1-F3 generations were assigned to SI or control groups. SI involved housing dams alone for two weeks before breeding and during pregnancy. This gave rise to three groups of F1-F3 dams: control, single generation SI (SG) and multigenerational SI (MG). Uterine tissues were collected at weaning of offspring. RT-qPCR for mRNA abundance analysis was performed to assess uterine inflammatory and stress markers such as Il1b, Il1ra, corticotropin-releasing hormone and receptors (Crh, Crhr1/2) and 11 $\beta$ -hydroxysteroid dehydrogenase type 2 (Hsd11b2). Data were analyzed using t-test (gestational length) and independent-samples median test,  $p < 0.05$  with  $0.05 < p \leq 0.1$  will be discussed as trends.

### **Results**

SI decreased gestational length of F0 pregnancies by 3 hours ( $p = 0.085$ ). In F1 uterus, Hsd11b2 mRNA levels were significantly increased 2.4 fold in the SG stress group ( $p < 0.005$ ). Il1a had a trend to increase (1.9 fold) in F1 animals, however, no other changes were detected in other pro-inflammatory mediators. Conversely, mRNA expression levels from Il1r1, Il6, Crh, and Il1a showed a trend to increase in the F3 generation when animals were stressed multi-generationally. Protein levels of Il1a, Il1b, Il6 in uterine tissues were not changed between controls and stress animals.  $n = 8-10$  animals.

### **Conclusion**

SI in pregnancy differentially affects gene expression related to inflammatory/stress markers in F0-F3 generations postpartum uteri. SG stress increased Hsd11b2 expression in F1 animals only, which encodes the enzyme that inactivates corticosterone, potentially altering local corticosterone levels. Conversely, in all generations, SI exposure altered expression of markers in the F3 generation only, but not significantly. Altered programming is a consequence of stress and can change the offspring's ability to adapt to stress later in life.

Funded by CIHR

The Power of Partnership



Abstract # 113  
Presenter: Amodu, Oluwakemi  
Supervisor: Salami, Bukola; Richter, Solina  
Title: **Access to Reproductive healthcare for Internally Displaced Women in Nigeria: A Critical Ethnography Study**  
Authors: **Oluwakemi Amodu, MN**

### **Introduction**

My doctoral research explores access to reproductive healthcare for women displaced by the Islamic terrorist groups, Boko Haram and Fulani herdsmen in northern Nigeria. My aim is to understand how women negotiate healthcare needs pertaining to reproductive and maternal health in long term displacement settlements including socio-structural factors shaping their care experiences. With an intersectional analysis as proposed by Kimberly Crenshaw, interlocking variables shaping health care access for internally displaced women is examined through a critical ethnography.

### **Methods**

In-depth interviews of 40 participants were conducted, which include internally displaced women living in a displacement camp, health service providers, and policy makers. Using a semi-structured interview guide, inquiries were made on issues related to health before displacement, healthcare access following displacement, four aspects of reproductive health access including: family-planning information and services; education and services for prenatal care, safe delivery and postnatal care; the management of abortion; treatment of reproductive tract infections. The sub-steps in data analysis include an intersectional analysis of descriptive data, the analysis of wider policy context of reproductive health in Nigeria and integration of the stakeholder perspectives and, critical aspects of the observational findings.

### **Results**

My preliminary findings show that displacement changes the experience of health for women. Women experience financial barriers to healthcare access due to the lack of reliable livelihood. Most child births are attended in the home by local caregivers. Major reproductive and maternal health concerns include vaginal infections and high birth rates. Family planning access is a discrete practice often completely precluded by cultural and familial values against its use. Structural limitations against access to reproductive health include shortage of health human resources and poor clinic staff remuneration. Women generally stated that healthcare access was better in their source villages compared with the present experience.

### **Conclusion**

There is an urgent need for reproductive health interventions for displaced women. Empowerment opportunities and health awareness campaigns will help improve women's socioeconomic status and knowledge about their reproductive and maternal health.

Funded by **Women's and Children's Health Research Institute through the Royal Alexandra Hospital Foundation**

The Power of Partnership



Abstract # 114  
Presenter: Sanni, Omolara  
Supervisor: Ospina, Maria  
Title: Obstetric outcomes among the Métis in Alberta

Authors: Sanni OB, Serrano-Lomelin J, James A, Bradburn K, Crawford S, Bakal J, Ospina MB on behalf of the Ehawawisit team.

### Introduction

The Métis are post-contact Indigenous peoples with a unique combination of identity, values, language, and cultural traditions. Métis are largely underrepresented in Indigenous health literature. The knowledge gap is particularly wide regarding Métis-specific information on maternal and perinatal health. This study evaluates maternal characteristics and obstetric outcomes of Métis women compared to their non-Métis counterparts in Alberta, Canada.

### Methods

Population-based retrospective cohort study of singleton livebirths born at 22 or more weeks' gestation in Alberta between 2006-2016. We obtained information on maternal characteristics from a validated clinical perinatal registry. A Métis cohort was identified through probabilistic linkage with the Métis Nation of Alberta Identification Registry. Odds ratios (OR) and 95% confidence intervals (CI) were calculated to compare sociodemographic, antenatal characteristics and obstetric outcomes relative to a non-Métis cohort.

### Results

A total of 479,432 singleton live births were included in this analysis (7,910 births from Métis mothers and 471,522 from non-Métis mothers). Compared with non-Métis mothers, Métis mothers were younger at delivery (27.2 versus 29.7 years) and were more likely to be materially deprived (OR 1.34; 95%CI 1.19-1.50). Métis mothers were more likely to have a high antepartum risk score (7 points or more) (OR 1.27; 95%CI 1.16-1.39) consume alcohol (OR 2.76; 95%CI 2.25-3.40) or smoke during pregnancy (OR 2.64; 95%CI 2.51-2.78 respectively). After adjusting for covariates, Métis mothers were more likely to receive intensive prenatal care, have a vaginal delivery and breast feed at discharge (OR 1.22; 95%CI 1.03-1.45, 1.70; 95%CI 1.54-1.88 and 1.80; 95%CI 1.55-2.09 respectively). There was no significant difference between Métis and non-Métis mothers in type of labour or the occurrence of adverse obstetric outcomes at delivery (obstetric hemorrhage, abruptio placentae, placenta previa, or preeclampsia).

### Conclusion

We identified important differences in adequacy of prenatal care, method of delivery, as well as breastfeeding at discharge between Métis mothers compared with their non-Métis counterparts in Alberta. These preliminary results will be used to explore relationships with proximal, intermediate and social determinants of health.

Funded by Canadian Institutes of Health Research

The Power of Partnership



Abstract # 115  
Presenter: Mah, Richard  
Supervisor: Bourque, Stephane  
Title: **Assessment of apoptosis, autophagy, and cellular senescence in developing kidneys exposed to perinatal iron deficiency**  
Authors: Richard Mah, Andrew Woodman, Ronan Noble, Stephane Bourque

### **Introduction**

Iron Deficiency (ID) is the most common nutritional deficiency worldwide with pregnant women most at risk. ID during gestation can alter offspring developmental trajectories, making them more susceptible to cardiovascular dysfunction later in life. We have shown that perinatal ID causes oxidative stress in the developing kidney of male, but not female offspring; however, it is unclear how these mechanisms impact cellular health and survival. We hypothesized that ID increases cellular senescence, autophagy, and apoptosis in developing kidneys.

### **Methods**

Sprague Dawley dams were fed an iron-restricted or iron-replete diet two weeks prior to and throughout gestation. Offspring kidneys were collected on postnatal day (PD)1 and PD28 and were either flash frozen or cryopreserved and sectioned. Apoptosis was assessed by TUNEL staining, and Caspase 3 and 9 activity assays. Autophagy was assessed by Western blot for microtubule-associated protein 1 light chain 3B (LC3). Cellular senescence was assessed via senescence-associated  $\beta$ -galactosidase (SA- $\beta$ Gal) activity.

### **Results**

ID resulted in neonatal anemia and decreased birth weight ( $P < 0.0001$ ). On PD1, TUNEL staining and caspase 3, but not caspase 9, activity was increased in only male ( $P = 0.01$ ) perinatal ID offspring. The ratio of LC3-II to LC3-I was increased in male ( $P = 0.05$ ), but not female perinatal ID offspring on PD1. Perinatal ID offspring, irrespective of sex, exhibited reduced SA- $\beta$ Gal activity on PD1 ( $P = 0.02$ ), however on PD28 ID offspring exhibited increased activity ( $P = 0.02$ ). On PD28, no differences were observed in apoptosis or autophagy measurements in male or female offspring.

### **Conclusion**

These results suggest perinatal ID causes alterations in cellular health and survival in the developing kidney, particularly in males, which may play a role in altering long-term renal function. These findings may be important for development of interventions to mitigate the effects of prenatal ID in the offspring. In addition, understanding how perinatal ID affects males and females differently may be important in devising personalized therapies. Future directions to improve outcomes in perinatal ID offspring includes using prenatal therapeutics to target cell senescence and apoptosis.

Funded by Alberta Innovates Summer Studentship, Canadian Institutes of Health Research, Women and Children's Health Research Institute.

The Power of Partnership





Abstract # 116

Presenter: Saadat, Saba

Supervisor: Riddell, Meghan

Title: **Optimization of first trimester trophoblast isolation for the development of physiologically oriented placental organoids**

Authors: Saba Saadat, Jasmine Ngyuen, Colette Watkins, Meghan Riddell

### **Introduction**

The placenta is a transient fetally derived organ that is responsible for nutrient, gas, and waste exchange between the mother and the fetus. Trophoblasts (TB) are placental specific epithelial cells. Progenitor cytotrophoblasts (CT) fuse to form the multinucleated syncytiotrophoblast (ST), which serves as the interface between the mother and fetus. Currently, there are no available models that allow for TB proliferation *in vitro*. Two recent papers have developed methods to grow self-renewing 3D placental organoids, but the ST forms in the opposite orientation than *in vivo*. Thus, they are not suitable for modelling the maternal/fetal interface. Our goal is to develop physiologically oriented self-renewing placental organoids using isolated human trophoblasts

### **Methods**

CT were isolated from first trimester placenta by trypsinization and immuno-elimination with MHC-class I/II and CD9 antibodies. We characterized the isolated cell population and tissue with known TB and common contaminating cell markers and validated ST apical membrane markers in tissue sections by immunofluorescence.

### **Results**

Isolated cells were positive for the trophoblastic markers GATA-3 and p63. In addition, a high proportion of the cells were positive for E-cadherin (CT marker), and negative for HLA-G and Vimentin (contaminating cell markers). Anti-ezrin and anti-EGFR antibodies were validated to be expressed at the ST microvillus membrane for future characterization of organoid orientation.

### **Conclusion**

We have successfully optimized the isolation procedure to obtain highly pure populations of CT from first trimester placentas. This method will serve as the basis for the development of physiologically oriented self-renewing placental organoids.

Funded by: **WCHRI**

The Power of Partnership



Abstract # 117  
Presenter: Desai, Vidhi  
Supervisor: Ospina, Maria  
Title: **Effectiveness of prebiotic, probiotic, and synbiotic supplementation in pregnancy to reduce risk of maternal mental health disorders in the perinatal period: A systematic review**  
Authors: **Vidhi Desai, Stuart Lau, Omolara Sanni, Anita Kozyrskyj, Liz Dennett, Jens Walter, Maria B. Ospina**

### **Introduction**

Mental health disorders (ie. depression, anxiety, posttraumatic stress disorder) that affect women during the perinatal period can have long-lasting negative effects on both the mother and child. Gut microbiota dysbiosis has already been linked with the development of many mental health disorders. Supplementation with prebiotics, probiotics and their combination (synbiotics) has been proposed as an effective mean to rebuild the gut microbiota composition and reduce depressive symptoms in the general population. However, the evidence in the scientific literature about the administration of these supplements during pregnancy has not been systematically evaluated. This systematic review evaluates the evidence on the effectiveness of prebiotics, probiotics, and synbiotics taken during pregnancy to reduce the risk of developing maternal mental health disorders in the perinatal period.

### **Methods**

The systematic review protocol was registered in the International prospective register of systematic reviews (PROSPERO) database (CRD42019137158). A librarian conducted comprehensive literature searches of seven electronic databases from database inception to April 2019; there were no language or publication restrictions. Two independent reviewers conducted study screening/selection, data extraction, and risk of bias assessment.

### **Results**

From 1,639 studies identified through the search strategy, two studies met the inclusion criteria for the review. Three ongoing trials were also identified; however, the authors were unable to provide data that could be included in this review. A meta-analysis was not conducted because of study heterogeneity. Both studies had an overall low risk of bias. The first study was a randomized controlled trial (RCT) conducted in Iran assessing the mental health scores of pregnant women that were given probiotic yogurt compared to conventional yogurt. Pregnant women given probiotic yogurt did not have significantly different mental health scores than women given conventional yogurt. The second RCT conducted in New Zealand assessed depression and anxiety scores of pregnant women given probiotic capsules compared to placebo capsules. Women given probiotic capsules had significantly lower depression and anxiety scores postpartum. There were no RCTs identified that assessed the effect of prebiotics and synbiotics on perinatal depression or other perinatal mental health disorders.

### **Conclusion**

This systematic review summarized the limited and inconclusive evidence about the effectiveness of probiotics administered during pregnancy to reduce the risk of maternal mental health disorders in the perinatal period and highlights the lack of evidence on prebiotics and synbiotics supplementation to inform their use for similar purposes. There is a huge knowledge gap and more research is needed to assess the effect of prebiotics, probiotics, and synbiotics on maternal mental health in the perinatal period.

Funded by **WCHRI Summer Studentship**

The Power of Partnership



Abstract # 118  
Presenter: Fakhr, Yuliya  
Supervisor: Hemmings, DG  
Title: Investigating sphingosine 1-phosphate kinase 1 (SphK1) as a mediator of tumour necrosis factor alpha (TNF- $\alpha$ ) effects on placental barrier formation  
Authors: Fakhr Y, Saadat S , Guo J, Huntley K, Mackova M, Hemmings DG

### Introduction

The etiology of preeclampsia (PE), a hypertensive pregnancy disorder remains unknown. However, abnormal placental development plays a pivotal role. Nutrient and oxygen exchange are compromised due to hindered fusion/differentiation of cytotrophoblasts to form the placental layer that performs these functions, the syncytiotrophoblast. TNF- $\alpha$ , a pro-inflammatory cytokine elevated in serum from mothers with PE, decreases trophoblast fusion/differentiation. However, inhibition of TNF- $\alpha$  is contraindicated in pregnancy due to its role in fetal development. Thus, it is necessary to identify a signalling pathway downstream of TNF- $\alpha$  that causes negative effects and can be targeted independently of the positive effects of TNF- $\alpha$ . Sphingosine-1-Phosphate (S1P), a bioactive sphingolipid hinders trophoblast syncytialization and mediates TNF- $\alpha$  signaling in non-placental endothelial cells. S1P is mainly formed by SphK1. By targeting SphK1, we aim to reduce S1P levels produced by TNF- $\alpha$  to reduce the harmful effects of TNF- $\alpha$  on placental development. We hypothesize that blocking SphK1 will block the negative effects on trophoblast syncytialization induced by TNF- $\alpha$ .

### Methods

SphK1 levels and localization in placental tissues from women with normal pregnancies or PE was assessed using immunohistochemistry staining.

Primary trophoblasts isolated from normal placentas delivered at term will be treated with 100microM cAMP to induce syncytialization. Cultures will be treated with and without 25microM of PF-543 (SphK1 inhibitor) with and without 1ng/ml of TNF- $\alpha$ . Syncytialization will be assessed by measuring beta-human chorionic gonadotropin ( $\beta$ -hCG) by ELISA, since only syncytiotrophoblast releases  $\beta$ -hCG. Trophoblast fusion will be assessed by E-cadherin staining and analyzed using Image J.

### Results

SphK1 protein expression did not differ in whole placental biopsies from mothers with PE (n=7) and mothers with normal pregnancies (n=6). TNF- $\alpha$  did not affect SphK1 protein expression in cultured primary trophoblasts at 24 hrs (n=3). TNF- $\alpha$  may increase mononucleated cells at 1ng/mL after 72 hrs. SphK1 inhibition appears to reduce mononucleated cells back to control levels. SphK1 inhibition alone had no effect.

### Conclusion

SphK1 signaling appears to mediate TNF- $\alpha$ -induced hindered syncytialization. However, TNF- $\alpha$  does not increase SphK1 levels. We will investigate whether TNF- $\alpha$  increases the activation of SphK1 by measuring the phosphorylation of SphK1 using radioactive phosphate as well as measuring S1P levels by mass spectrometry.

Funded by CIHR and WCHRI

The Power of Partnership

Abstract # 119  
Presenter: Babolmorad, Ghazal  
Supervisor: Bhavsar, Amit  
Title: TLR4 inhibition mitigates cisplatin-induced ototoxicity.

Authors: **Ghazal Babolmorad, Ivan Kristell Domingo, Cole Delyea and Amit P. Bhavsar**

### **Introduction**

Cisplatin is a chemotherapeutic used in childhood cancer patients to treat solid tumors. However, cisplatin usage is limited due to possible irreversible adverse drug reactions, including ototoxicity. A preliminary pharmacogenomic study identified associations of cisplatin ototoxicity with genetic variations in the TLR4 receptor. We were trying to understand the role of TLR4 in cisplatin ototoxicity in a murine Organ of Corti cell-based model (HEI-OC1). Main objectives of this study are: 1) Create a Tlr4 deletion in an in vitro hair cell model (HEI-OC1). 2) Confirm the loss of Tlr4 through genetic, and functional analyses. 3) Examine the impact of Tlr4 deletion on cisplatin induced-ototoxicity (CIO) in vitro. 4) Design and examine TLR4 syntagonists that prevent CIO in vitro.

### **Methods**

To meet objective 1, CRISPR/Cas9 genome-editing was used to disrupt the Tlr4 gene in HEI-OC1 cells. To meet objective 2, CRISPR-targeted clones were sequenced at the Tlr4 locus and tested for ligand (LPS) binding/internalization and LPS-induced Tlr4 activation with and without a complementing copy of Tlr4. To meet objective 3, cisplatin ototoxic responses were compared between Tlr4-deleted or control cells. Finally, to meet objective 4, cisplatin ototoxic responses were studied after syntagonists pre-treatment.

### **Results**

Sequencing results confirmed frame-shift mutations in Tlr4. CRISPR-targeted cells internalized less LPS and released less IL-6 after LPS stimulation. IL-6 secretion was restored upon expression of a complementing copy of Tlr4. Similar results were observed for reactive oxygen species generation and IL-6 secretion after cisplatin stimulation. Syntagonists mitigated CIO while preserved LPS/TLR4 signaling pathway.

### **Conclusion**

This work identifies a new innate immune pathway that contributes to the development of cisplatin ototoxicity and has implications for mitigating this adverse outcome of childhood cancer treatment.

Funded by WCHRI Hair Massacure Grant, WCHRI Graduate Studentship, FoMD Graduate Student Recruitment Studentship

The Power of Partnership



Abstract # 120  
Presenter: Bennett, Jessica  
Supervisor: Godbout, Roseline  
Title: **Understanding the role of DDX1 expression in the resistance of neuroblastoma cell lines to treatment**  
Authors: **Bennett, Jessica; Li, Lei; Wang, Yixiong; and Godbout, Roseline**

### **Introduction**

Neuroblastoma is a cancer originating from developing nerve tissue, and is responsible for about 15% of all childhood cancer deaths. Over 60% of neuroblastoma patients classified as "high-risk" pass away within 5 years after diagnosis. Classification of "high-risk" neuroblastoma is often associated with amplification of the MYCN oncogene. DEAD box proteins are involved in modification of RNA secondary structure, and hence play significant roles in cell survival. Previous research undertaken by the Godbout lab indicates that the DEAD Box 1 (DDX1) gene is co-amplified and overexpressed with MYCN in 25-50% of high-risk neuroblastoma tumours.

### **Methods**

The goal of this research project is to determine the relationship between the level of DDX1 and the resistance of neuroblastoma cell lines to drug treatment. To achieve this, a soft agar colony formation assay was performed both pre- and post-treatment using the chemotherapy drugs doxorubicin and vincristine. For these experiments, we used DDX1/MYCN co-amplified, MYCN-amplified, and non-amplified neuroblastoma cell lines, as well as DDX1-knockdown cell lines. Cell survival was determined using colony counts following a 2-3 week growth period. In addition, because in DDX1/MYCN co-amplified cells, DDX1 levels are elevated in both nucleus and cytoplasm, we used protein co-immunoprecipitation to investigate proteins that interact with cytoplasmic and nuclear DDX1 to deduce a possible mechanism of action.

### **Results**

To date, we have optimized the conditions for successful growth of one DDX1/MYCN co-amplified cell line, and one MYCN-amplified cell line in soft agar. We have also generated stable DDX1 knockdown in the DDX1/MYCN co-amplified and MYCN-amplified cell lines. Since all cell lines require a prolonged growth period, the relative effects of chemotherapy drugs and DDX1 depletion on neuroblastoma cell survival are still under investigation. Preliminary data suggest that both DDX1/MYCN co-amplified and MYCN-amplified neuroblastoma cell survival is reduced when treated with vincristine. In addition, we have also optimized the conditions to generate cytoplasmic and nuclear extracts from DDX1/MYCN co-amplified cell lines. We are now in the process of developing an antibody crosslinking method that will allow detection of DDX1-interacting proteins with high sensitivity using mass spectrometry.

### **Conclusion**

Our results indicate that neuroblastoma cell lines form robust colonies using an anchorage independent assay. The relative effects of DDX1 depletion and of chemotherapy drugs on neuroblastoma cell survival in DDX1/MYCN co-amplified, MYCN-amplified, and non-amplified cell lines are still under investigation. Identification of novel DDX1-interacting partners is expected through improved cellular fractionation and antibody crosslinking methods as well as high sensitivity mass spectrometry.

Funded by **Stollery Children's Foundation, Alberta Cancer Foundation, and Cancer Research Institute of Northern Alberta**

The Power of Partnership



Abstract # 121  
Presenter: Landry, Takaaki  
Supervisor: Persad, Sujata  
Title: **Validation of a role for active beta-catenin (ABC) in promoting metastatic phenotype in osteosarcoma**  
Authors: Takaaki Landry, Noureen Ali, Elizabeth Garcia, Jonathan Bush, Danielle Cohen, Rebecca Deyell, Mary Hitt, David D. Eisenstat, Sujata Persad

### Introduction

Osteosarcoma is an aggressive primary bone malignancy with peak incidence in children/young adults <25 years of age. The 5-year event-free-survival for patients with localized disease is ~65% and ~25% for patients with metastatic disease. Despite intensive chemotherapy, metastasis of osteosarcoma occurs in 15-20% of cases. This goes to show that there is an urgent need for identifying prognostic markers to facilitate risk stratification. The Wnt/ $\beta$ -cat pathway plays a crucial role in skeletal development and is dysregulated in osteosarcoma. However, its role in osteosarcoma, especially in osteosarcoma progression, remains unknown. We investigated the role of the Wnt/ $\beta$ -catenin ( $\beta$ -cat) pathway, specifically the transcriptionally active form of  $\beta$ -cat, Active Beta Catenin (ABC), in osteosarcoma progression. ABC constitutes a unique pool of  $\beta$ -cat that is dephosphorylated at Serine 37 and Threonine 41 at the N-terminal domain. The focus of our study was to determine ABC as a prognostic biomarker that correlates with metastatic dissemination at disease progression

### Methods

Two sets of paired cell lines, SaOS2/SaOS2-LM7 and HOS/HOS-143B were utilized for this study. SaOS2-LM7 and HOS-143B are metastatic lines derived from the parental SaOS2 and HOS cells, respectively. Using a pEGFP- $\beta$ -cat fusion construct plasmid, we carried out site directed mutagenesis to the N-terminal S33, S37, T41 and S45 in order to mimic endogenous ABC [GeneArt, Invitrogen]. The pEGFP-ABC and pEGFP- $\beta$ -cat constructs were then transfected into SaOS2 cells and subject to Western Blot analysis and immunofluorescence. We also carried out immunohistochemical analysis on 30 OS patients samples to determine whether nuclear ABC levels were correlated to “aggressive” disease.

### Results

Initial observations from testing both the paired cell lines indicated that endogenous nuclear ABC levels, but not  $\beta$ -cat, increase with osteosarcoma progression. Our new pEGFP-ABC and pEGFP- $\beta$ -cat plasmid constructs were shown to have similar activity to that of the endogenous ABC and  $\beta$ -cat: endogenous and pEGFP ABC were both seen to translocate to the nucleus while both the endogenous and pEGFP- $\beta$ -cat remained cytosolic or membrane bound. The transfected SaOS2 cells were visualized with immunofluorescence and both the plasmids pEGFP-ABC and pEGFP- $\beta$ -cat and endogenous ABC and  $\beta$ -cat levels were measured with Western Blot analysis. We analyzed whether nuclear ABC levels were correlated to “aggressive” disease, as determined by metastasis at diagnosis or resection (30 patients). We observed that a significantly greater number of patients with metastatic disease at diagnosis ( $p=0.029$ , two tailed) or at the time of resection ( $p=0.007$ , two tailed) showed high nuclear levels of ABC (>25% nuclear positivity).

### Conclusion

This strong correlation between high nuclear ABC levels and metastatic disease supports the hypothesis that ABC may be a marker of “aggressiveness” as defined by metastatic potential.

Funded by Women and Children’s Health Research Institute/Hair Massacure grant to Sujata Persad.

The Power of Partnership



Abstract # 122  
Presenter: Cao, Amanda  
Supervisor: Hornberger, Lisa  
Title: Impact of adverse early life exposures (AELEs) on surgical outcomes for congenital heart disease (CHD)  
Authors: Amanda Cao, Deliwe Ngwezi, Jimmy Kang, Daniel Garros, Dominic Cave, Luke Eckersley, Lisa K. Hornberger

### **Introduction**

Infants with congenital heart disease (CHD) and adverse early life exposures (AELEs) have worse surgical outcomes, the cause of which remains uncertain. Animal studies have suggested exposure to AELEs may predispose the myocardium to ischemic reperfusion injury. We sought to determine whether infants with AELEs undergoing cardiopulmonary bypass surgery at <1 year for CHD have evidence of worse ischemic reperfusion injury compared to those without AELE.

### **Methods**

We identified all Albertan infants who required surgery for CHD from 2007-2018 in our institution. We identified those born of diabetic mothers (IDMs) and/or born preterm (<37 weeks) and infants without AELEs age-matched and matched for surgical intervention. We reviewed their medical records for CHD diagnosis, prenatal and birth history, and surgical outcomes. We also recorded postoperative variables including the Pediatric Risk of Mortality score (PRISM), a collective 20 point measure of hemodynamic instability in the first 24 hours of surgery (high=worse status), a time when ischemic reperfusion injury is often most evident.

### **Results**

We identified 524 infants with available perinatal histories who underwent surgery for CHD. Two of the largest subgroups included those with repair of ventricular septal defect (VSD, n=114) and tetralogy of Fallot (TOF, n=123). Infants with AELE and TOF or VSD repair demonstrated a significantly higher PRISM score at 24 hours for those without AELE's (all AELE 7.5±4.5 vs no AELE 4.8±4.6, p=0.0008).

### **Conclusion**

AELEs may contribute to increased ischemic reperfusion injury associated with VSD and TOF repair. In the coming months, further analysis will be done examining infants with other CHD types as well as other early postoperative hemodynamic variables, length of ICU and hospital stay and survival rates, and examining impact of biological sex.

Funded by Women and Children's Health Research Institute (WCHRI) Summer Studentship

The Power of Partnership



Abstract # 123  
Presenter: Han, Angela  
Supervisor: Mackie, Andrew  
Title: **Just TRAC It! Transitioning responsibly to adult care using smart phone technology**

Authors: **Angela Han, Jody Gingrich, Kathryn Rankin, Andrew Mackie**

### **Introduction**

Many adolescents living with heart disease face challenges when transitioning from pediatric to adult care. There is little evidence on how smartphone technology can be used to help during transition. We aimed to investigate if smartphone technology (Just Trac It!) can improve self-management skills and transition readiness in this population.

### **Methods**

We conducted a randomized clinical trial of 16-18 year olds with congenital heart disease (CHD) or acquired heart disease requiring surgery. Participants were randomly allocated 1:1 to either usual care (control; 1hour education session) or the smartphone intervention (1hour education session including Just TRAC It!) with a planned enrolment of 60. The primary outcome was change in TRANSITION-Q score between baseline, 3 and 6 months. Secondary outcomes were frequency of use and perceived usefulness of Just TRAC It! at 3 and 6 months post intervention. Analysis was intention to treat.

### **Results**

Forty-seven patients (43% female) have been enrolled to date; 33% have simple CHD, 54% moderate CHD, 9% complex CHD, and 4% have acquired heart disease. Twenty-four (51%) of patients were enrolled in the intervention group. Sixty-one percent of patients enrolled have completed the 3 month follow up survey and 33% of patients have completed the 6 month survey thus far. No interim analysis of the primary outcome is planned. All respondents in the intervention group answered that they would recommend Just TRAC It! to others.

### **Conclusion**

Preliminary data analysis shows that youth have a positive reception to Just TRAC It! and find it an easily accessible and reliable way to stay organized in managing their health. The results of this study will inform pediatric cardiology programs, patients and policy makers in judging whether a smartphone-based transition intervention provides clinically meaningful outcomes for adolescents living with CHD.

Funded by **WCHRI**

The Power of Partnership





Abstract # 124  
Presenter: Wewala, Gayathri  
Supervisor: Hornberger, Lisa K.  
Title: **Evidence of early cardiovascular programming in 9-16 year old children of Type 1 diabetic mothers**  
Authors: Gayathri Wewala, Victor Do, Lily Lin, Edmond Ryan, Luke Eckersley, Michael Stickland, Sandra Davidge, Lisa K Hornberger

### **Introduction**

Children of diabetic mothers (CDM) are at an increased risk for adult cardiovascular disease (CVD). We have previously demonstrated that CDMs have persistent left ventricular (LV) thickness and aortic stiffness from late infancy to early childhood. These findings led us to study the cardiovascular health of an independent cohort of preteens/early teens of diabetic mothers. We hypothesized that CDMs aged 9-16 years will have increased LV thickness and aortic stiffness in comparison to aged-matched controls.

### **Methods**

We prospectively recruited 9-16 year old CDM of mothers with a history of pre-gestational (type 1) diabetes and age matched healthy children of healthy mothers to participate. Their height, weight, and blood pressure (average of 3 measures) were recorded. A full structural and functional echocardiogram was performed to assess measures of LV wall thickness and systolic, diastolic and global function. Blood vessel reactivity was assessed non-invasively using the VENDYS system and aortic and peripheral arterial stiffness (pulse wave velocity, PWV) were measured by Doppler at echocardiography. Participants completed a 3-day diet log, HAES physical activity questionnaire, survey of family history, and wore an activity monitor for 1 week. Offline analysis of the echocardiograms was completed with a focus on LV thickness, diastolic function and PWV.

### **Results**

To date, 14 CDMs and 16 children from healthy pregnancies completed assessments. There was no difference in mean age, body surface area, and blood pressure between groups. Preliminary analysis showed no difference in LV thickness and blood vessel reactivity. Compared to controls, CDMs had evidence of increased aortic (PWV  $3.3\pm 0.4$  m/s versus  $2.6\pm 0.4$  m/s,  $p=0.0003$ ) and peripheral arterial stiffness (PWV  $7.0\pm 0.8$  m/s versus  $6.5\pm 0.6$  m/s,  $p=0.03$ ). Although LV free wall and septal wall thickness and measures of systolic and diastolic function did not differ, compared to controls, CDMs had increased isovolumic contraction time ( $69\pm 8$  ms versus  $63\pm 4$  ms,  $p=0.02$ ) and LV Tei index, a measure of global function, ( $0.4\pm 0.05$  versus  $0.3\pm 0.02$ , respectively,  $p=0.04$ ). There were no correlations between maternal HbA1C levels in the first, second and third trimester, and aortic PWV and peripheral PWV. The contributions of diet and physical activity level to these findings are currently being explored in a larger cohort.

### **Conclusion**

Preteens/early teens of type 1 diabetic mothers have increased aortic and peripheral vascular stiffness and show a difference in global left ventricular function which may be driven by longer isovolumic contraction time, findings that may contribute long-term to adult cardiovascular disease.

Funded by WCHRI Summer Studentship 2018, AIHS Summer Studentship 2018, FOMD Summer Studentship Award 2019

The Power of Partnership



Abstract # 125  
Presenter: Beigh, Mirza Vamiq  
Supervisor: Eckersely , Luke  
Title: A novel measure of dyssynchrony outperforms traditional measures during RV pacing in pediatric patients  
Authors: Mirza Beigh , Ganesh Gnanappa, Nee Khoo , Joseph Atallah, Michal Kantoch, Carolina Escudero, Luke Eckersley

### **Introduction**

Electromechanical dyssynchrony is common in patients with cardiomyopathies and congenital heart disease and is associated with reduced cardiac output.

Assessment of dyssynchrony in pediatric patients guides potential for response to resynchronization therapy, however current echocardiography measures are laborious, angle-dependent and poorly predict response to resynchronization.

In this study, we aimed to compare a novel deformation-based measure to standard approaches.

### **Methods**

We prospectively recruited patients with normal cardiac anatomy undergoing electrophysiological study under general anesthetic for ablation of supraventricular tachycardia.

Following successful ablation, a baseline echocardiogram was performed.

The right ventricular apex was then paced at 10 bpm above baseline to create dyssynchrony, and the echocardiogram was repeated.

Offline analysis included:

Global measures of cardiac function (LV output by Doppler continuity equation, Simpson's biplane ejection fraction, global longitudinal and circumferential strain (LS, CircS)

Measures of dyssynchrony (long and short axis (papillary muscle level) septal-posterior wall motion delay (SPWMD), time to peak longitudinal and circumferential strain standard deviation (T2PSD), novel DI

Patient ages ranged from 6.9 to 15.7 years.

### **Results**

Results:

Baseline QRS duration was  $88\pm 9$ , and paced QRS duration was  $133\pm 21$ ms,  $p < 0.001$ .

Pacing resulted in impaired global function, with reduced peak global LS, CircS, ejection fraction and stroke volume.

Longitudinal and Circumferential DI increased with pacing. LS T2PSD was also increased. Other measures of dyssynchrony were not significantly different

### **Conclusion**

Conclusion:

Right ventricular pacing minimally above baseline heart-rate resulted in impaired measures of LV global function. A novel dyssynchrony index was more sensitive than standard measures in detection of pacing related dyssynchrony.

Funded by WCHRI

The Power of Partnership



Abstract # 126  
Presenter: Shigemitsu, Sachie  
Supervisor: Colen, Timothy  
Title: Tricuspid valve prolapse in children with hypoplastic left heart syndrome patients requiring tricuspid valve repair is due to leaflet mal-adaptation, not sub-valve changes  
Authors: Sachie Shigemitsu, Kandice Mah, Richard Thompson, Justin Grenier, Lily Lin, Amal Silmi, Mirza Beigh, Nee Khoo, Timothy Colen

### Introduction

Tricuspid valve regurgitation (TR) is associated with morbidity and mortality in hypoplastic left heart syndrome (HLHS). Over 25% of HLHS patients require tricuspid valve (TV) repair within 10 years, while the mechanism of TR remains poorly understood. This study explores TV remodeling in HLHS requiring surgical repair, using novel quantitative three-dimensional echocardiography (3DE) to further understand the mechanisms of TV failure in HLHS.

### Methods

This case-control study with prospectively acquired 3DE in 72 children with HLHS, 36 children prior to TV repair (group 1) and 36 age- and stage-matched controls with no TV repair and mild or less TR (group 2). All 3DE were analyzed using a specific custom TV software (MATLAB) to quantitate TV annulus and leaflet area (Figure), prolapse and tethering volumes, and bending angle. TV leaflets were segmented into the anterior (AL), septal (SL) and posterior (PL) to measure regional areas and volumes. We also measured position of papillary muscle (PM) and chord length. Variables were indexed by body surface area (BSA), and comparison was performed using t-test with significance at  $p < 0.05$ .

### Results

Group 1 and 2 had similar age and BSA (mean: 2.3 years; 0.47 m<sup>2</sup>) at assessment. Group 1 had larger total annulus (11.1 vs 8.4 cm<sup>2</sup>/m<sup>2</sup>,  $P < 0.001$ ) and leaflet (13.4 vs 9.9 cm<sup>2</sup>/m<sup>2</sup>,  $P < 0.001$ ) area. AL and SL area (5.72 vs 4.24 cm<sup>2</sup>/m<sup>2</sup>,  $P < 0.001$ ; 3.08 vs. 2.23 cm<sup>2</sup>/m<sup>2</sup>,  $p = 0.036$ ) was larger. Group 1 had larger total prolapse volume and AL leaflets (Total leaflet 126 vs 5.8  $\mu$ l/m<sup>2</sup>,  $P < 0.001$ ; AL: 39.4 vs 2.2  $\mu$ l/m<sup>2</sup>,  $p = 0.001$ ). No difference in tethering volume for total or each leaflet. Group 1 had greater bending angle (156.4 vs 151.8 degree,  $p = 0.035$ ), hence a flatter annulus. No difference in PM angle and length, nor chord length between the groups.

### Conclusion

Failing TV in children with HLHS had larger annulus and leaflet size, specifically in SL and AL, and greater prolapse of all the AL leaflets compared to HLHS with competent TV. Despite increased leaflet prolapse, there is no difference in chord or PM length, suggesting that failing TV prolapse is due to leaflet mal-adaptation, rather than chord or PM changes. This novel insight suggests future research into TV leaflet mal/adaptation in HLHS maybe important.

Funded by WCHRI

The Power of Partnership



Abstract # 127  
Presenter: Pherwani, Simran  
Supervisor: Lopaschuk, Gary  
Title: **Maturation of fatty acid oxidation in the newborn heart**

Authors: **Simran Pherwani, Sonia Rawat, Arata Fukushima, Cory S. Wagg, Liyan Zhang, and Gary D. Lopaschuk**

### **Introduction**

Immediately post-birth, newborns normally undergo a major maturational increase in cardiac fatty acid oxidation (FAO), providing a major fuel for the heart to make energy in the form of ATP to power cellular processes. Newborns may be affected by congenital heart defects (CHDs), leading to improper heart function and the development of cardiac hypertrophy, where the heart muscle thickens and impedes blood flow. Stress from reparative surgery can cause additional hypertrophy. Post-translational modifications, such as acetylation, can regulate metabolic enzymes of cardiac FAO (which increases FAO), with hypertrophy delaying this acetylation. My project investigated how acetylation is mediated in the newborn heart and the impact of cardiac hypertrophy on this alteration, as well as the mechanisms involved in newborn cardiac energy metabolism during maturation.

### **Methods**

Infant surgical heart tissue was analyzed through immunoblotting and immunoprecipitation techniques, where the expression of FAO enzymes in the myocardium were measured. Additionally, acetylase and deacetylase enzyme levels were also measured to assess the amount of FAO acetylation.

### **Results**

We saw a maturational increase in total protein acetylation in non-hypertrophied hearts, which was blunted with hypertrophy. Protein expression of the acetyltransferase, GCN5L1, was decreased in hypertrophied hearts, and expression of the mitochondrial deacetylase, SIRT5, showed no change between groups. Both the acetylation and activity of FAO enzymes, long-chain acyl CoA dehydrogenase (LCAD) and B-hydroxyacyl CoA dehydrogenase (BHAD) increased in non-hypertrophied hearts compared to hypertrophied hearts. Therefore, hypertrophy prevented the increase in both myocardial acetylation and activity of FAO.

### **Conclusion**

This research is integral to gain a better understanding of newborn cardiac energy metabolism and how changes in this can influence heart disease. Research findings will help develop novel strategies to protect newborn hearts from surgical stress and improve patient care of these newborns with CHDs.

Funded by **WCHRI Summer Studentship, Project Funded by the Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute**

The Power of Partnership



Abstract # 128  
Presenter: Trakulmungkichkarn, Thotsapon  
Supervisor: McBrien, Angela  
Title: Clinical presentation, genetic etiologies and outcomes associated with fetal cardiomyopathies  
Authors: Thotsapon Trakulmungkichkarn MD, Lisa Hornberger MD, Simon Urschel MD, Luke Eckersley MD, Oana Caluseriu MD, Karen Y. Niederhoffer MD, Gayathri Wewala BSc, Jennifer Conway MD, and Angela McBrien MB BCh MD

### Introduction

Cardiomyopathy (CM) refers to a broad range of heart muscle pathologies. Prenatally-detected CM has been associated with poor survival. We sought to review our experience of fetal CM including genetic etiologies and outcomes in a contemporary series.

### Methods

Retrospective, descriptive cohort study over a 15-year period (2005-2019). Cases were identified from our institutional database and echo reports and charts were reviewed.

### Results

Twenty cases were diagnosed at a median gestational age (GA) of 23 weeks(13-35 weeks). Subtypes were: 35%(7/20) non-compaction, 15%(3/20) hypertrophic, 30%(6/20) mixed, 10%(2/20) dilated, 10%(2/20) restrictive CM. At diagnosis 35%(7/20) had hydrops and another 20%(4/20) developed hydrops later. There were 55%(11/20) terminations, 5%(1/20) intra-uterine deaths and 40%(8/20) livebirths at a median GA of 36 weeks(30-39 weeks). Of the livebirths, 50%(4/8) remain alive at a mean of 16+/-15.6 months (1 post-heart transplant). Of the whole cohort, 55%(11/20) had associated congenital heart defects and 25%(5/20) had arrhythmias. 55%(11/20) had a likely or known genetic cause: 2 had suspected mitochondrial lesions; 2 cousins had an MYH7 mutation; 2 fetuses of the same couple had restrictive CM with an SCN5A and additional channelopathy gene mutation; 1 had an unbalanced 3;18 translocation; 1 had a NONO gene mutation; 1 had Noonan syndrome; 1 had Costello syndrome; 1 with two affected siblings was from a Hutterite family still undergoing genetic investigation.

### Conclusion

In our experience, ventricular non-compaction constitutes the most common fetal CM phenotype. Outcomes remain poor and associated structural heart defects and genetic etiologies are common. Further exploration of fetal CM in the context of advanced genetic testing is critical to improve counselling and develop strategies to improve outcomes.

Funded by Unfunded, Dr Trakulmungkichkarn is supported by funding from Phramongkutklao Hospital, Thailand

The Power of Partnership



Abstract # 129  
Presenter: Yozo Teramachi  
Supervisor: Lisa Hornberger  
Title: **Left ventricular dysfunction in neonatal Ebstein's anomaly and tricuspid valve dysplasia**  
Authors: **Yozo Teramachi, Lisa K Hornberger, Lisa Howley, Mary E van der Velde, Luke G Eckersley**

### **Introduction**

Neonates with severe Ebstein's anomaly and tricuspid valve dysplasia (EA/TVD) are often hemodynamically unstable with low systemic perfusion and hypoxia; whereas, this is uncommon in another critical right heart lesion, pulmonary atresia with intact ventricular septum (PAIVS). We have recently demonstrated left ventricular (LV) dysfunction and dyssynchrony to be common in fetal EA/TVD but not PAIVS. In the current study we sought to explore LV function and mechanics in neonatal EA/TVD with comparison to PAIVS in the early neonatal period.

### **Methods**

This was a retrospective case-control study including cases of EA/TVD, PAIVS and healthy term controls from healthy pregnancies encountered in 3 pediatric cardiology programs from 2004 to 2018. LV global function and six segment myocardial mechanics were assessed using Vector Velocity Imaging with analysis of LV 4- chamber and short axis images acquired at echocardiography in the first 48 hours after birth. Global longitudinal strain (GLS), global circumferential strain (GCS) and average segmental strain were measured. LV dyssynchrony was assessed by standard deviation of time-to-peak (T2PSD) and using a novel global dyssynchrony index (DI).

### **Results**

Analyses were performed for 34 EA/TVD, 17 PAIVS and 15 healthy control neonates. LV ejection fraction and LV FAC was reduced compared to controls, While there was no observed difference in global longitudinal LV strain, EA/TVD neonates had significantly reduced global circumferential strain compared to both healthy newborns and neonates with PAIVS. Significant dyssynchrony was also observed in the EA/TVD neonates by DI index and T2PSD in circumferential strain.

### **Conclusion**

LV circumferential deformation is impaired in neonatal EA/TVD, and there is increased dyssynchrony compared to neonates with PAIVS and healthy newborns. Further work will examine the impact of LV mechanics on clinical outcomes and the impact of medical and surgical interventions.

Funded by **WCHRI**

The Power of Partnership



Abstract # 130  
Presenter: Luong, Deandra  
Supervisor: Schmolzer, Georg  
Title: **Analysis of healthcare providers' visual attention during neonatal resuscitation using eye tracking**  
Authors: Deandra Luong, Sylvia van Os RRT, Caroline Fray RN, Georg Schmolzer MD PhD, Brenda Law MD

### **Introduction**

Success neonatal resuscitation depends on clinical assessments, vital signs monitoring, teamwork, quick decisions, and effective interventions. Healthcare providers' (HCPs) attention is divided between these tasks. What HCPs focus on during neonatal resuscitation may affect their performance. Previously, a pilot study tested the feasibility of using eye-tracking to study HCPs' visual attention (VA) during neonatal resuscitation.

### **Methods**

In this prospective observational study, 24 recordings were obtained using eye-tracking glasses (Tobii Pro, Tobii Technology, Inc., Falls Church, VA) worn by HCPs in the first 10 minutes of neonatal resuscitation. Videos were analyzed to obtain i) areas of visual interest, ii) duration spent on each area and iii) frequency of saccades (shifts in visual focus). Surveys asked if the glasses were comfortable and if they interfered with clinical work.

### **Results**

All 24 videos were analyzed. Infants had a median(IQR) gestation of 30.5(29-34) weeks and birth weight of 1650g(1026-2425g). Fifteen infants received mask ventilation and 3 were intubated. Half of VA was directed at the infant (55.7%, IQR 44-60%), with 17.9% (10.6-23.1%) focused on displays and gauges. There were 49(40-53) saccades/min. There were no differences in VA in resuscitations of infants who received mask ventilation vs. those who did not. HCPs looked at the vital signs monitor 4.8 times/minute (IQR 2.7-7.2). Only 3 HCP (12.5%) reported that the glasses were uncomfortable, and only 1 (0.5%) felt that the glasses interfered with clinical work.

### **Conclusion**

Healthcare providers' visual attention during neonatal resuscitation varies and is not affected by the need for mask ventilation. Half of VA is focused on the infant. Eye-tracking glasses were acceptable to HCPs.

Funded by The Heart and Stroke Foundation, Women and Children's Health Research Institute (WCHRI)

The Power of Partnership



Abstract # 131  
Presenter: Zehnder, Emily  
Supervisor: Schmolzer, Georg  
Title: Subjective workload assessment of health care providers during neonatal resuscitation

Authors: Zehnder E., Law B. van Os S., Schmolzer G.

### **Introduction**

10% of babies will require assistance with their breathing at birth called neonatal resuscitation. The health care team who provides this assistance must analyze data, make decisions, and communicate effectively to coordinate appropriate and timely interventions. Given these demands it is not surprising that the prevalence of human errors and protocol deviations during neonatal resuscitation is high. Health care providers (HCPs) experience of workload results from the objective demands of their role-specific task, as well as situational (e.g. number of individuals observing, resources available) and personal factors (e.g. energy levels, stress). Our aim is to characterise HCP experience of workload and determine how various factors are associated with perceived workload of HCPs during neonatal resuscitation.

### **Methods**

Perceived workload was measured using the National Aeronautics and Space Administration Task Load Index (NASA TLX) survey. NASA TLX is a multi-dimensional retrospective survey which has been validated in the measurement of HCP workload. Six workload dimensions are considered in this measure mental demand, physical demand, temporal demand, performance, effort and frustration, with each rated independently by participants on a scale of 0 to 20 (0 being lowest or best and 20 being highest or worse depending on the dimension). Overall workload is the sum of the six dimensions (0 to 120). HCPs at the Royal Alexandra Hospital, Edmonton, AB were asked to complete a paper and pencil survey following their participation in a neonatal resuscitation in the delivery room. The survey consisted of the NASA TLX along with questions about professional, procedural and patient characteristics

### **Results**

201 surveys were completed. The mean (SD) overall workload score for all respondents was 42 (22.8). This value was the sum of mental demand 9.6 (5.6), temporal demand 8.9 (6.1), effort 8.6 (5.1), frustration 6.0(5.5), physical demand 5.1(4.3) and performance 4.6 (3.7). Overall workload scores varied within and between HCP roles during resuscitation. Respiratory therapists reported the highest overall workload score of 58.3 (15.0), followed by recorders 51.2 (13.0), registered nurses 42.8 (23.8), airway managers 42.3 (21.6), team leads 37.0 (23.6) and observers 27.7 (19.1). Resuscitations which required positive pressure ventilation had a mean overall workload of 54.0 (19.5), compared to those which did not require positive pressure ventilation 31.1 (20.1).

### **Conclusion**

Perceived workload during neonatal resuscitations was highly variable and differed by provider role, and interventions required.

Funded by Maternal and Child Health Scholarship Program

The Power of Partnership





Abstract # 132  
Presenter: Deschenes, Sadie  
Supervisor: Scott, Shannon and Kunyk, Diane  
Title: Developing an educational intervention on moral distress for PICU nurses  
  
Authors: Sadie Deschenes, Shannon Scott, Diane Kunyk

### **Introduction**

Pediatric intensive care units are highly specialized, fast paced, and high-pressure environments with many different healthcare professionals providing numerous forms of advanced life sustaining care to critically ill children. Without the acute management offered in the PICU, many children would not have survived. With major medical and technological advances, there are more unrealistic expectations placed on the healthcare team. These environments are ripe settings for moral distress in healthcare professionals, particularly nurses given the nature and scope of their practice. Moral distress occurs when an individual is unable to act according to his/her moral judgement due to external constraints (e.g., environmental demands, pace of work, available resources, etc.) or personal factors (e.g., professional role, work responsibilities, etc.). Moral distress can result in emotional, psychological and physical symptoms, leading to reduced job satisfaction, burnout and poor patient outcomes. While moral distress has been found in all intensive care unit studied, it has been shown that there is an increase rate of moral distress within the PICU (as compared to adult ICUs, neonatal ICUs and pediatric wards). In a systematic conducted within PICUs and NICUs, it has been demonstrated that moral distress affects neonatal and pediatric care. Moral distress has also been demonstrated to affect retention of nurses. The purpose of this study is to develop an educational intervention for PICU nurses to manage morally distressing situations.

### **Methods**

Interpretive description will be used to explore key elements of moral distress and preferences for delivery of the educational intervention. Nurses who have experienced moral distress in the PICU will be invited to participate in semi-structured interviews. Data collection and analysis will be done concurrently. A three-phase process will guide analysis. Participant perspectives will inform the content and method of delivering the educational intervention (e.g., digital tool, didactic presentation in orientation, annual competency requirements, etc.).

### **Results**

The intervention developed has the potential to better prepare nurses for complex ethical issues in their work that may result in increased nurse job satisfaction, increased retention/recruitment rates, and improved patient outcomes.

### **Conclusion**

Moral distress is common in the PICU given the nature of the unit. This phenomenon impacts many aspects of nurses' work, including the care they provide to the smallest and most vulnerable patients in the hospital. The findings of this study may be used to inform and improve how nurses are prepared for morally distressing situations.

Funded by N/A

The Power of Partnership

Abstract # 133  
Presenter: Patel, Siddhi  
Supervisor: Schmölzer, Georg  
Title: Chest compression with sustained inflation versus with asynchronous ventilation during cardiopulmonary resuscitation in asphyxiated pediatric piglets – a randomized animal trial  
Authors: Siddhi D. Patel, Po-Yin Cheung, Tze-Fun Lee, Megan O'Reilly, Georg M. Schmölzer

### Introduction

The incidence of pediatric cardiopulmonary resuscitation (CPR) is low (8-20/100 000 children/year). However, only ~40% of these children survive to discharge, and survival with good neurologic outcome is rare. Currently, during pediatric resuscitation, chest compressions (CC) are continuously delivered with asynchronous ventilation (CCaV) at a rate of ~30/min. Our group has previously shown that CC superimposed by a sustained inflation (CC+SI) significantly decreases time to return of spontaneous circulation (ROSC) and improves survival when compared to CCaV in asphyxiated newborn infants. We aimed to compare CC+SI and CCaV and their effect on ROSC and survival during CPR of pediatric piglets. We hypothesized that in asphyxiated pediatric piglets, CPR with CC+SI compared to CCaV will reduce time to ROSC and improve survival.

### Methods

Eleven pediatric piglets (20-23 days) were anesthetized, intubated, instrumented, and exposed to asphyxia by clamping the endotracheal tube. Piglets were randomized into three groups: CC+SI (n=5), CCaV (n=4), and sham group (n=2) that did not undergo asphyxiation or CPR. During CC+SI, piglets received continuous CC with a sustained inflation with a peak inflation pressure of 20cmH<sub>2</sub>O. During CCaV, piglets received continuous CC with asynchronous ventilation at a rate of 30/min.

### Results

The mean(SD) age and weight was 21(1)days and 7.5(1)kg. Mean(SD) asphyxia time was similar in the CC+SI and CCaV groups with 313(69) and 302(46)sec (p=0.7844). 5/5 (100%) of CC+SI piglets achieved ROSC compared to 2/4 (50%) in the CCaV group (p=0.073). The median (IQR) time to ROSC was lower in the CC+SI group compared to the CCaV group with 225(45-302) and 420(90-720)sec, p=0.3252, respectively.

### Conclusion

CC+SI decreased mortality and had faster time to ROSC compared to CCaV. This warrants further studies examining CC+SI.

Funded by Heart & Stroke Foundation

The Power of Partnership



Abstract # 134  
Presenter: Baqays, Abdulsalam  
Supervisor: El-Hakim, Hamdy  
Title: A novel parent-reported outcome tool to assess swallowing dysfunction in otherwise healthy infants and toddlers  
Authors: Abdulsalam Baqays, Wendy Johannsen, Maraghalara Rashid, Hadi Seikaly, Hamdy El-Hakim.

### **Introduction**

There is limited epidemiological information on swallowing dysfunction (SwD) in otherwise healthy infants and toddlers (OHIT). Cost, invasiveness, expertise and resource related limitations constrain the repeatability and utility for screening of instrumental diagnostic tests. Patient-reported outcomes (PRO) tools have the potential to mitigate these disadvantages. Hence, we set to develop and validate a novel PRO tool to assess SwD in OHIT.

### **Methods**

A prospective mixed method study was designed. We recruited parents of OHIT with SwD and excluded those with a confounding diagnosis (syndromes or related neurological impairments). In-person interviews were conducted and thematically analyzed to extract the relevant domains and items. Similar procedure was performed on the related reports generated from a systematic literature review. The emerging domains and items were examined over expert focus group meetings. A different expert group assessed and established the content validity using a modified Delphi exercise. A separate parents' group meeting examined the wording and relevance.

### **Results**

We achieved saturation of information after interviewing ten parents and generated seven domains with 72 items. They were reduced to five domains and 62 items by the focus group. These five essential domains inquired about swallowing, breathing, sickness time, level of activity, sleep, and impact on the family. Following the modified Delphi meetings, nineteen items passed a content validity ratio threshold of 0.622.

### **Conclusion**

We extracted the primary domains and validated the content of a new PRO instrument to assess SwD in OHIT. This tool has the potential to screen and assess management outcomes specifically for this population.

Funded by Saudi Cultural Bureau

The Power of Partnership



Abstract # 135  
Presenter: Mason, Alleson  
Supervisor: Salami, Bukola  
Title: **Barriers and facilitators to immigrant families' access to healthcare for their children in Edmonton, Alberta**  
Authors: Alleson Mason, B.Ed, M.Ed Bukola Salami, RN, MN, PhD,

## **Introduction**

Immigrants' health declines after immigration to Canada (Gushulak, Pottie, Roberts, Torres & DesMeules, 2011). This is due to barriers to healthcare access such as cultural differences, lack of social contacts, socioeconomic status, health system structure, lack of universal healthcare coverage upon initial arrival in Canada, language barriers, limited knowledge of health services, treatment preferences, and geographic distance Canada. Conversely, several factors facilitate access to healthcare by immigrant families such as universal healthcare and having access to persons who can explain how the health system works and how to navigate it. Studies on access to healthcare for immigrants are largely focused on immigrant adults. We seek to fill the gap on access to healthcare for immigrant children in Alberta. The purpose of this study was to investigate how immigrants, of various immigrant categories, access health services for their children in Alberta. We were guided by the following research questions:

1. What are the experiences of immigrant parents in accessing health services for their children in Alberta?
2. How do the facilitators of and barriers to access to healthcare for immigrant children compare across immigrant groups, including children of temporary foreign workers, skilled immigrants, international students, refugees, and undocumented migrants?

## **Methods**

Semi-structured individual interviews were conducted with 50 participants between April and October 2019. We used purposive sampling to select participants. We received assistance from immigrant settlement agencies to identify participants, as well as snowballing, face to face recruitment at a clinic, and drawing in the personal network of the researchers. The data was analyzed thematically using NVivo 11. Data collection and analysis were done simultaneously. The interview transcripts were read and codes applied to sections of the data that provided answers to the research questions. The codes that spoke to similar ideas were then coalesced into themes.

## **Results**

We found that participants faced the following barriers: long wait times, lack of interpreters, financial barriers to care, the location of services. Other barriers identified were inflexible opening hours, balancing of responsibilities, cultural expectations regarding doctor-patient relationship and treatment of illnesses, and lack of knowledge about the health care system and how to access services. Facilitators to healthcare include compassionate healthcare providers, free healthcare, easy access to doctors, and having access to healthcare workers from a similar cultural background.

## **Conclusion**

Considering these findings, there is a need for government to increase public education programs to inform immigrants and refugees about their health coverage. There is also a need to expand the range of services covered by the provincial healthcare insurance to include counselling and medication as finances pose a challenge to some persons accessing health services that are not covered.

Funded by Killam Cornerstone Grant, University of Alberta, Office of the Vice-President (Research)

Abstract # 136  
Presenter: Mella, Allison  
Supervisor: Richer, Lawrence  
Title: **Mobile app for symptom management in postural orthostatic tachycardia syndrome (POTS): Benefits and limitations**  
Authors: Allison Mella, Meghan Linsdell, Eric Mathieu, Lawrence Richer

### **Introduction**

Postural orthostatic tachycardia syndrome (POTS) is defined in children or adolescents as an increased heart rate of 40 bpm in the first 10 minutes of standing. Main symptoms reflect a reduction in cerebral perfusion and include lightheadedness, dizziness, pre-syncope and other dysautonomia symptoms. Symptom management is personalized and benefits from symptom tracking tools so a mobile symptom tracking solution was developed. The objectives of this study were to test the feasibility, acceptability, and usability of the mobile app in pediatric patients with POTS.

### **Methods**

This app was developed using the REDCap electronic data capture system and associated app (MyCap). The tracked symptoms were selected by previous studies and the most requested symptoms included were: brain fog, dizziness, fatigue, and headache/migraine. Also, the app tracked heart rate (BPM), exercise, and treatments. Enrollment was limited to those with an iOS device as the Android app was not functional. Participants were recruited from a tertiary POTS clinic (LR) at the Stollery Children's Hospital and asked to use the app daily for one month.

### **Results**

Four participants ages 11 to 16 were recruited (3 female, 1 male). Participants missed 18, 6, 4 and 14 days respectively. Two participants only tracked dizziness, brain fog and fatigue, whilst the other two tracked all the listed symptoms. The three participants that tracked heart rate had an average supine heart rate of 78bpm ( $\pm 8.1$ ) and upright of 124bpm ( $\pm 15.1$ ).

### **Conclusion**

Overall all participants found the app useful in symptom tracking but three participants found the functionality was otherwise limited. The app is feasible and a desirable way for symptom management, but numerous adjustments are required to increase acceptability. The results gained will be used for a new wrist based ECG app that would include more features to overcome the current app limitations.

Funded by Northern Alberta Clinical Trials and Research Centre (NACTRC)

The Power of Partnership



Abstract # 137  
Presenter: Pajkic, Andrea  
Supervisor: Whittaker, Jackie  
Title: Sport participation and physical activity following a youth sport-related knee injury

Authors: Andrea Pajkic, Christina Y. Le, Joshua B. Kennedy, Jackie L. Whittaker

## Introduction

Sport and recreation are leading causes of musculoskeletal injury in school-aged children and adolescents. Youth who suffer a sport-related knee injury have a higher risk of physical inactivity 3-10 years after injury compared to uninjured youth. Currently, little is known about the physical activity patterns of adolescents in the months following a sport-related knee injury. This study will describe and compare the type, level, and amount of sport and physical activity participation over the first 11-months following a youth sport-related knee injury compared to uninjured youth disaggregated by sex.

## Methods

Participants included 90 youth (11-19 years) who suffered a recent sport-related knee injury and 53 uninjured youth. Outcomes were collected at baseline (within 3 months of injury) and follow-up (6-11 months later) and included: self-reported pre-injury sport level (e.g., recreational, club, school), sport type (i.e., team, cutting, multi-sport), amount of sport (weekly minutes per year) and current physical activity (average daily minutes of sedentary, light, moderate, and vigorous physical activity; accelerometer). Descriptive statistics [median (range), proportion or mean (95%CI)] were calculated for participant characteristics, outcomes, and change in outcome between timepoints by study group and sex. Multivariable logistic regression (OR [95% CI];  $p < 0.05$ ) was used to assess the odds of meeting age-appropriate guidelines for moderate-to-vigorous (MVPA) activity at both timepoints.

## Results

Participant median age was 17 years (11-20), and 68% were female. The median time between injury and baseline and between injury and follow-up was 1.3 months (0.3-4.5) and 7.7 months (5.6-10.8) respectively. While the injured group had 0.3 (95%CI 0.12, 0.58;  $p = 0.001$ ) times the odds of meeting MVPA guidelines than the uninjured group at baseline, no difference was found at follow-up. Boys had 3.9 (95%CI 1.71, 9.08;  $p = 0.001$ ) and 4.5 (95%CI 1.44, 14.16;  $p = 0.010$ ) times the odds of meeting MVPA guidelines than girls at baseline and follow-up, respectively. Injured girls accumulated less total physical activity (238 min/day) than uninjured girls (255 min/day;  $p = 0.049$ ), spent greater time sedentary (1146 min/day) than injured boys (1072 min/day;  $p = 0.033$ ) and had less MVPA (32 min/day) time than uninjured girls (41 min/day;  $p = 0.001$ ) at baseline. At follow-up, injured girls demonstrated less MVPA (27 min/day) than uninjured girls (41 min/day;  $p = 0.017$ ) and injured boys (46 min/day;  $p = 0.005$ ). Fifty-three percent fewer injured girls participated in club-level sport at follow-up compared to pre-injury. We found no evidence of other differences in pre-injury sport type or amount of participation, or physical activity levels between study groups or sex.

## Conclusion

Our findings suggest that youth (in particular girls) that suffer a sport-related knee injury are unlikely to meet recommended levels of MVPA at 3-months. Furthermore, sport and physical activity participation outcomes following injury are sex/gender specific, with injured girls demonstrating the least participation. This study highlights the need to consider sex/gender differences when addressing physical inactivity following a sport-related knee injury.

Funded by Undergraduate Research Initiative Stipend

The Power of Partnership

Abstract # 138  
Presenter: Afsharipour, Babak  
Supervisor: Gorassini, Monica  
Title: Using grid electrodes to isolate motoneuron activity in children with Cerebral Palsy  
  
Authors: Babak Afsharipour, Jennifer Duchcherer, Monica Gorassini

### Introduction

Cerebral palsy (CP) is a brain injury occurring in the developing fetal or infant brain (2.1-per-1000-live-births), causing permanent disorders in movement and posture. Although changes to the brain are well studied in CP, less is known about the spinal cord. One possible source of abnormal muscle tone and reflexes in CP is excessive activation of intrinsic calcium currents in spinal motoneurons. We aim to measure the activation of calcium currents in motoneurons using a non-invasive method called High Density surface ElectroMyoGraphy (HDsEMG), where 64 recording sites are placed over the muscle to isolate the activity of several single motor units (motoneurons), avoiding the traditional use of invasive intramuscular needle electrodes. HDsEMG is reliable in adults but has not been tested in children.

### Methods

In seven typically developing children, aged 7 to 13, a grid electrode (13x5) with 10mm inter-electrode distance was placed over the tibialis anterior muscle while children performed a triangular dorsiflexion (10s up+10s down) with peak force at 10, 20, 30, and 40% of maximum voluntary contraction (MVC). The HDsEMG was decomposed to motor unit action potentials (MUAPs) using a blind source separation algorithm and the firing frequency profile of the decomposed units were obtained.

### Results

In general, the decomposition results were promising for the lower contraction levels [data are described as mean (standard deviation)]. For the 10% MVC contractions, an average of 5.3(3.9) units [n=4 participants] were isolated, 2.7(2.9) for 20%MVC [n=6], 1.75(1.93) for 30%MVC [n=7] and 0.75(0.98) for 40%MVC [n=3]. A lower number of units were decomposed at the higher contractions, likely because the separation of overlapped MUAPs by the available algorithms was difficult. For similar contraction levels, a lower number of motor units were decomposed in children (2-10) compared to adults (8-30). Further development of electrode placement and/or algorithm code is required to decompose more motor units in children. None-the-less, there were enough decomposed units to estimate the activation of intrinsic calcium currents in the motoneuron using the firing rate profiles of 2 or more decomposed units as per published protocols (Gorassini et al. Brain 127:2247,2004), which was similar in children compared to adults. This data will be used to compare to children with CP.

### Conclusion

Decomposing HDsEMG from children yields a higher number of motor units compared to needle EMG. Low contraction levels (10-20%MVC) produce higher numbers of decomposed motor units which will be useful to measure intrinsic calcium currents in motoneurons of children with CP.

Funded by WCHRI Postdoctoral Fellowship

The Power of Partnership



Abstract # 139  
Presenter: Simin, Irina  
Supervisor: Andrews, Debra  
Title: **Developing skills for developmental disabilities: How does clinical experience as an adjunct to current preclinical curriculum improve student confidence**  
Authors: **Simin, I., Thornton, S., Fong-Leboeuf, A., Andrews, D.**

### **Introduction**

There is an increasing recognition for medical students to receive more training in caring for persons with developmental disabilities (PWDD). Studies have found that providing training and encounter opportunities with PWDD for medical students improves their attitudes, comfort level, and knowledge of PWDD. However, description of such training in the pediatric population is rare. Our preclinical 12-hour elective, "Developing Skills with Developmental Disabilities" (DSDD), has a primary learning objective of improving students' knowledge of and attitudes toward PWDD in children. The current study's objective was to assess improvement in students' perceived confidence in interacting with and assessing children presenting with a developmental delay or disability.

### **Methods**

Students participated in a preclinical elective, Developing Skills for Developmental Disabilities, in addition to the regular curriculum. The developmental week in the mandatory pre-clinical Neurosciences block is comprised of didactic lectures on developmental disabilities, a problem-based learning case on developmental delay, and small-group clinical skills sessions with typically developing children and their parents. DSDD elective students also received 6 hours of content-specific didactic teachings and discussion from a team of developmental pediatricians and psychiatrists, including sessions on estimating developmental age, assistive technologies, and giving the news of a developmental diagnosis. Students were also scheduled for 6 clinical hours at a rehabilitation hospital, where they attended a medical intake session, conducted a brief interview with the child's family, observed school-aged PWDD in a modified classroom, and interacted with the interdisciplinary team. Participating DSDD students were given pre- and post-elective self-assessment surveys administered on a 5-point Likert scale. Questions pertained to students' self-perceived comfort and knowledge regarding PWDD. Scores pre- and post-elective were used to calculate statistically significant improvement of elective participants.

### **Results**

Data was collected from 5 consecutive years, including 94 students total who completed DSDD. Statistically significant ( $p < 0.05$ ) relative improvements were present in 9 of 10 self-reported scores for 1 of the 5 years and all 10 in the other 4 years. The statistically significant scores involved increases in confidence interacting with PWDD, taking histories, recommending appropriate resources to families, and estimating developmental age.

### **Conclusion**

Participants reported improvements in interacting with and assessing PWDD in the pediatric population. This is important as improvement in confidence is a first step in implementing a new skill or changing a behaviour. As a high proportion of participants have previous work and/or personal experiences with people who have disabilities, the focus of future work will look at identifying how this impacts outcomes of student confidence and perceived ability.

Funded by **Medical Students Association**

The Power of Partnership





Abstract # 140  
Presenter: Kennedy, Joshua  
Supervisor: Whittaker, Jackie  
Title: **Scared to move: The influence of kinesiophobia on physical activity after a youth sport-related knee injury**  
Authors: Joshua B Kennedy, Christina Y Le PT, Amber D Mosewich PhD, Jackie L Whittaker PT PhD

### Introduction

Kinesiophobia (fear-of-movement) is the most common reason for discontinuing sports participation following a serious knee injury. Currently, little is known about the relationship between kinesiophobia and physical activity levels in youth within the first months following injury. This research assessed the relationship between self-reported kinesiophobia and average daily moderate-to-vigorous physical activity (MVPA) or sedentary time (ST) over the first 10 months following a youth sport-related knee injury in comparison to uninjured youth. As a secondary objective, differences by sex were explored.

### Methods

Ninety youth (11-20 years) who suffered a sport-related knee injury within the past 3-months and 53 uninjured controls completed Tampa Scale for Kinesiophobia (TSK-17 and TSK-11), MVPA, and ST (accelerometer measured average daily minutes). Descriptive statistics [median (range), proportion] were calculated for all participant characteristics, outcomes and change in outcomes from baseline to follow-up by study group and sex. Unadjusted logistic regression (odds ratio; 95%CI) was used to assess the odds of high TSK score (TSK-17>37 or TSK-11≥17) by study group and sex at baseline and follow-up. Spearman's rho was used to examine the association between TSK score and MVPA or ST at baseline and follow-up. The difference in change in TSK score, MVPA, and ST between baseline and follow-up between study groups and sex were evaluated with Wilcoxon rank sum tests.

### Results

Participant median age was 16.5 years (range 10.9-20.1) and 68.5% were girls. Median time from injury to baseline and injury to follow-up was 1.3 months (range 0.3-4.5) and 7.7 months (range 5.9-10.8), respectively. The injured at baseline had 3.96 (OR; 95%CI 1.9,8.1; p<.001) times greater odds of high TSK-17 score and 13.54 (OR; 95%CI 1.6,113.4; p=.016) times greater odds of high TSK-11 score. Injured girls had higher TSK (17: z=-4.277, p<.001; 11: z=-4.553, p<.001) scores and lower MVPA (z=3.279, p=.001) at baseline and higher TSK-11 scores (z=-2.408, p=.016) and lower MVPA (z=2.377, p=.017) at follow-up compared to uninjured girls. At baseline, injured girls had greater ST than injured boys (z=2.131, p=.033) and uninjured girls had greater ST than uninjured boys at follow-up (z=2.292, p=.022). There was no evidence of differences in change in TSK score, MVPA or ST from baseline to follow-up by study group or sex nor a correlation between TSK and MVPA or ST.

### Conclusion

We found no evidence of a relationship between TSK score (TSK-11 or TSK-17) and MVPA or ST at baseline or 10 months following a youth sport-related knee injury. Further, we saw no improvement in TSK score, MVPA, or ST over the first 10 months following injury. We found evidence that TSK scores are higher in youth within three months of a knee injury and that girls are less physically active than boys. These findings suggest that TSK scores may not be associated with physical activity levels after a youth sport-related knee injury and that sex and/or gender differences needs to be considered when managing physical activity after injury. A larger sample, and a longer follow-up period should be used to further investigate these findings.

Funded by Women & Children's Health Research Institute Summer Studentship

The Power of Partnership

Abstract # 141  
Presenter: Boyd, Kassi  
Supervisor: Phelan, Shanon  
Title: Engaging dis/abled children in critical qualitative research: Rights, dignity and 'voice(s)'  
Authors: Kassi Boyd, Emma Peters, Joy Munroe, Shanon Phelan

### **Introduction**

Participatory research methods have garnered much attention for their capacity to actively, responsibly, and ethically engage with children in research, particularly when exploring sensitive and complex research topics. In response to a new era of children's rights and the new sociology of childhood, children are being valued as autonomous agents that are capable of contributing to the research process as co-researchers. Some of the most prominent challenges to this approach include perceptions of competence, power differentials, and protection of a 'vulnerable' group. Engaging disabled children in research adds another layer of complexity that needs to be considered in relation to disability rights, inclusivity of methods, and participatory strategies. Task-based methods, or tool-kit approaches that offer diverse and dynamic data collection strategies that are responsive to each individual child are important. Although promising work has emerged, these methods are underdeveloped, particularly with children who experience disability.

### **Methods**

The purpose of this research is: 1) To develop an adaptable approach to actively, responsibly, and ethically engage disabled children as co-researchers in critical qualitative research and 2) To pilot methods identified by children that have the potential to address complex research questions about disability, inclusion, child-driven culture, and the interplay between the three. Children were invited as co-researchers to set the research agenda, refine the research question, and discuss potential interview questions and data collection methods that would provide the researchers some insights into the complexities of children's worlds.

### **Results**

The researchers will present on their experience with developing a child-driven research advisory group (ages 10-15 years, self-identified as experiencing disability) to inform an ongoing qualitative study investigating the intersections of child-driven culture, inclusion, and disability. Critical reflexivity will be discussed as a means to foster a deeper understanding of how to effectively and ethically engage disabled children throughout the research process in ways that emphasize children's rights, dignity and 'voice(s)' in research. Emphasis will be placed on researcher reflexivity, ethical moments in research practice, participatory methods (interview and visual), and practical considerations.

### **Conclusion**

This research contributes to our understanding of how to effectively and ethically engage disabled children throughout the research process and has implications for children's rights and voice in research. Implications for the adoption of existing, or creation of new, methodological approaches and methods for use with and by disabled children will be discussed.

Funded by SSHRC- Insight Development Grant; Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute; WCHRI Trainee Travel Grant

The Power of Partnership



Abstract # 142  
Presenter: Fan, Lu'an  
Supervisor: Thompson-Hodgetts, Sandra  
Title: **The effectiveness of preventive disclosure in influencing peer engagement for the child with ASD in summer camps: A within case study**  
Authors: McKillop, Ashley; Shire, Stephanie; Couture, Melanie; Weiss, Jonathan; Zwaigenbaum, Lonnie.

### **Introduction**

Children with Autism Spectrum Disorder (ASD) are at high risk of experiencing exclusion, stigma and bullying, especially in community programs. Planned sharing of a child's diagnosis and information about behaviours (preventive disclosure + explanation) might be one way to counteract stigma and increase social inclusion by increasing peers' understanding of the child with ASD. However, no study has evaluated the effects of preventive disclosure in real life contexts, including community programs.

### **Methods**

This poster presents a sub-analysis of data from a larger mixed-method study, rooted in evaluating outcomes of disclosure versus non-disclosure on inclusion of children with ASD in one type of community program, inclusive week-long summer camps. We provide an in-depth evaluation comparing outcomes for one child who participated in two different summer camps, one in which he disclosed and one in which he did not disclose. For both conditions, 15-minute videos were collected on the first (baseline; pre-disclosing for that condition), second (post-disclosing for that condition) and last day of the program (follow-up). The primary outcomes were peer engagement states and reciprocal interactions (initiations and responses), coded by a blinded observer for the child with ASD and his peers using a time-interval behavioral-coding system, the Playground Observation of Peer Engagement (POPE). The Child Behavior Scale, Excluded by Peers subscale (CBS-EP) was completed by the camp leader on the same days as video was collected to assess a gestalt impression of the child's inclusion with peers over the whole day. Parents' completed the Adaptive Behavior Assessment System, third edition (ABAS-3) to describe the functional abilities of the child. Semi-structured qualitative interviews about perceived outcomes of disclosure were completed with one camp leader, the child with ASD, and 5 peers (disclosure condition only). These data were thematically analyzed.

### **Results**

According to the interviews, positive outcomes have been found toward preventive disclosure among different groups of people. The child with ASD indicated acceptance to disclose his diagnosis to others. The camp leader perceived that preventive disclosure had a positive effect on changing his, and the peers', understanding of behaviours and acceptance of the child with ASD in that summer camp. Peers noted that preventive disclosure increased their understanding of some autism-related behaviors. Data analysis of the ABAS-3, CBS-EP and POPE are underway.

### **Conclusion**

Preventive disclosure plus explanatory information may be a simple intervention to improve peer engagement and inclusion of children with ASD in community programs.

Funded by Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute

The Power of Partnership



Abstract # 143  
Presenter: Lopresti, Sabrina  
Supervisor: Willows, Noreen  
Title: **IYMP principal investigator perspectives on essential characteristics of multi-sited Community-University Partnership with Indigenous communities**  
Authors: Lopresti S, Willows N, Storey K, McHugh T, IYMP National Team

## Introduction

The Indigenous Youth Mentorship Program (IYMP) is a peer-led school-based healthy living program grounded in the teachings of Indigenous scholars, Drs. Verna Kirkness and Martin Brokenleg. IYMP is delivered as a multi-sited community-university partnership (CUP) with 13 Indigenous communities across Canada. IYMP aims to reduce risk factors for obesity and diabetes and empower youth and communities. The purpose of this qualitative study was to describe the essential characteristics of this multi-sited CUP as perceived by the IYMP principal investigators. The identified key characteristics resulting from this research may be used to inform future multi-sited CUPs in Indigenous communities.

## Methods

A descriptive qualitative method guided this research. Key informant interviews were conducted with 5 IYMP principal investigators (2 male and 3 female; 2 Indigenous and 3 non-Indigenous). Interview transcripts were analyzed using content analysis. Research adhered to Ownership, Control, Access and Possession (OCAP) principles developed by The First Nations Information Governance Centre. Principal investigators prioritized community voice in decision-making using OCAP principles. To enhance rigor, findings were reviewed with the IYMP National Advisory Council which includes Indigenous knowledge keepers and by several IYMP investigators.

## Results

Essential characteristics emerged as foundational in this IYMP multi-sited CUP. Preliminary findings suggested the overarching theme was forming a community of practice (CoP) as described by Wenger-Trayner & Wenger-Trayner, 2015. This is a group of people who share a concern or a passion for something they do, and learn how to do it better as they interact regularly. There were 4 sub-themes: shared interest for Indigenous health/wellbeing; relationships, mentorship, and taking a decolonizing research approach.

## Conclusion

This study contributes to the sparse literature about the essential characteristics involved in the implementation of multi-sited CUPs with Indigenous communities. Firstly, those with shared interests in Indigenous health and partnership with Indigenous communities could consider forming a CoP. Within this CoP relationships and mentorship can be developed through discussion and activities. For CoP with Indigenous communities, it is important to acknowledge the impact that colonial policies and practices have had on generations of Indigenous communities. In the context of IYMP, the CoP that was formed permitted new relationships to be developed and existing ones to be sustained. This allowed mentorship to occur across regions contributing to the successful implementation of IYMP. Results of this research may be used to inform other multi-sited CUPs with Indigenous communities and future IYMP CUPs.

Funded by CIHR, Diabetes Canada, PolicyWise, and the generous support of the Stollery Children's Hospital Foundation through WCHRI. KS is supported as a Distinguished Researcher.

The Power of Partnership



Abstract # 144  
Presenter: Raza, Sarah  
Supervisor: Zwaigenbaum, Lonnie  
Title: **The role of emotion regulation in the emergence of Autism Spectrum Disorder**

Authors: **Sarah Raza, Lori Sacrey, Vickie Armstrong, Azadeh Kushki, Lonnie Zwaigenbaum, Susan Bryson, Jessica Brian, Isabel M. Smith, Peter Szatmari, Tracy Vaillancourt, & Louis Schmidt**

### **Introduction**

Autism Spectrum Disorder (ASD) is associated with impaired emotion regulation (ER), the ability to maintain homeostasis in response to positive and negative events. Prospective research has shown that infants at risk for ASD have difficulty regulating their emotional states by 12 months of age, and this ability is critical to the development of later social-communicative skills and may affect the onset of ASD. This research proposes a unique, novel model of ASD symptom development by focusing on ER as an early risk marker. Given that ER is a multicomponent process, a behavioral-physiological approach is used, where behavioral assessments will be supplemented with physiologic indices of autonomic arousal to examine how early impairments in ER predict ASD symptom expression and later diagnoses. The aim of this study are to (1) determine the relation between behavioral affect and heart-rate during an ER task, and (2) whether behavioral affect and/or heart-rate predict later social-communication and ASD symptoms in infants at risk for ASD.

### **Methods**

Participants: High-risk (HR) infants (i.e., have an older sibling diagnosed with ASD) were assessed at 12 and 18 months of age.

Emotion Regulation: Infants were tested at 12 months on an ER task, comprised of activities designed to elicit positive (bubbles, toy play) and negative (toy removal, masks, grooming) emotions. Behavioral affect was coded for valence (positive, negative, or neutral) and intensity (to differentiate mild/moderate displays from intense displays of affect). Raw heart-rate was recorded and extracted from an electrocardiogram signal. The data were processed and transformed into a metric of average change in heart-rate from baseline.

Social-Communication Symptoms: The Early Social Communication Scales (ESCS) examined an infant's ability to initiate and respond to social requests with an examiner during toy play (i.e., coordinated joint attention) at 18 months. Initiating joint attention and responding to joint attention was coded.

ASD Symptoms: The Autism Diagnostic Observational Assessment - Toddler Module (ADOS-T) was used to measure early signs of ASD at 18 months.

### **Results**

The analyses are currently ongoing, but the relationship between behavioral affect and heart-rate will be explored using Spearman rank-order correlations. Regression analyses will also be used to estimate how ER (i.e., integrated behavior-physiologic responses) at 12 months predict social-communication (ESCS scores) and ASD symptoms (ADOS-T) at 18 months of age.

### **Conclusion**

This research has the potential to identify infants likely to develop ASD in the first year. By integrating behavioral and physiological data, the developmental pathways by which ER emerge in HR infants will be characterized, and how these processes give rise to later ASD symptoms. This research may not only lower the age of initial detection and diagnosis, but also identify novel treatment targets and inform the development of interventions that can be applied clinically.

Funded by **WCHRI (Graduate Studentship), Stollery Children's Hospital Foundation, Kids Brain Health Network, Alberta Innovates, Brain Canada, Azrieli Foundation, CIHR**

The Power of Partnership



Abstract # 145  
Presenter: Singh, Simran  
Supervisor: Petrovskaya, Olga  
Title: "I love it, but more clinics should use it!": Parents' experiences with MyChart electronic patient portal in the Stollery respirology clinic  
Authors: Singh S., Singh N., Ali S., Amirav I., Graham T., Hicks A., Makhinova T., Petrovskaya O.

### Introduction

In November 2019, AHS will launch a province-wide clinical information system, Connect Care, which includes the implementation of an electronic patient portal MyAHSCoconnect (aka MyChart). MyChart provides patients with online access to their health providers (via secure messages), test results, medication lists, doctor's notes and visit summaries, and in some cases appointment self-scheduling. Although MyChart has been piloted in several adult clinics in Edmonton Zone since 2016, the Stollery Respirology clinic is the only pediatric setting that offered MyChart to parents of children with chronic breathing conditions, starting in January 2018. This poster will address a Research question: What are parents' experiences of using MyChart portal to access their children's health information? Data for this poster were generated from a larger ongoing qualitative study examining the implementation of MyChart in this clinic.

### Methods

In September 2019, an online survey was administered to all parents (n=214) who accepted clinic's offer to sign up for MyChart during the 18-month pilot period. To date, we received 21 response (10% response rate): 10 from portal users and 9 from non-users. (Two records were deleted to enhance data quality, one incomplete and the other clearly showing acquiescence bias.) Data are being analyzed using thematic analysis and results will be summarized in the poster. The survey has been housed at the REDCap database at the U of Alberta.

### Results

The poster will address the following questions: What are the demographic characteristics of portal users versus non-users? What difficulties did parents face when signing up for the portal? How do parents use MyChart, for example, what portal functions do they find useful? What benefits of the portal do they perceive? Do they understand information they access? Why some parents intensely dislike MyChart? What changes do parents like to see?

### Conclusion

The poster will present food for thought for everyone who will be affected by Alberta's Connect Care and its patient portal. Methodological recommendations will benefit researchers interested in Health Information Technologies. Clinicians, administrators, and others will be invited to grapple with the question, How to make the portal REALLY useful for diverse patient populations?

Funded by WCHRI CRISP grant

The Power of Partnership



Abstract # 146  
Presenter: PHAM, Thanh-Tu  
Supervisor: LE, H. Lawrence and LOU, H. Edmond  
Title: **Correlating ultrasonic soft tissue-bone reflection coefficients with curve severity in adolescent idiopathic Scoliosis: A preliminary study**  
Authors: Thanh-Tu Pham, Lawrence H. Le, Mahdieh Khodaei, Rui Zheng, and Edmond H. Lou

### **Introduction**

Adolescent idiopathic scoliosis (AIS) is a spinal abnormality with a lateral curve of the spine. Cobb angle technique using radiographs is the current gold standard to assess the severity and progression of the curves. However, exposure to ionizing radiation due to accumulative visits may increase the risk of cancer, which is undesirable to adolescents. Ultrasound has been applied to AIS to image the spinal deformity and therefore measure the severity of scoliosis. AIS is commonly associated with low bone quality. Using ultrasound to evaluate bone quality of spine and correlating ultrasound parameters with curve severity are novel and innovative. This preliminary study investigates the feasibility of determining the ultrasonic reflection coefficient (RC) measured from spinal scans and correlating them with the scoliotic severity quantified by Cobb angle (CA).

### **Methods**

The RC of the soft tissue-bone interface is obtained from ultrasound echoes reflected from vertebrae. Large RC-value suggests stiff and strong bone, thus indicating better bone quality. Thirty-seven AIS patients (aged  $13.8 \pm 1.6$  years old) were recruited for the study and were scanned in the standard upright posture. Their curves were divided into two groups: mild curve (CA  $10^\circ$ - $24^\circ$ ) and moderate curve (CA  $25^\circ$ - $45^\circ$ ). RCs were measured and correlated with the CAs. Linear regression was used to best fit the data.

### **Results**

The average RC values for the mild-curve and moderate-curve groups are  $0.51 \pm 0.02$  and  $0.47 \pm 0.02$ , respectively. Also, moderate correlation between RC and curve severity is found with  $R^2$  (coefficient of determination) of 0.42. The best-fitting line shows that the RC decreases with the increasing CA, indicating that bone quality declines with the severity of AIS.

### **Conclusion**

This preliminary study shows that bone quality of the spine assessed by ultrasound can be associated with scoliotic severity. RC has promising potential to be a prognostic indicator to predict the progression of scoliosis with non-ionizing radiation imaging.

Funded by Natural Sciences and Engineering Research Council of Canada (NSERC) and Scoliosis Research Society.

The Power of Partnership



Abstract # 147  
Presenter: Watson, Adrienne  
Supervisor: Voronova, Anastassia  
Title: Understanding the role of fractalkine signalling in neural and oligodendrocyte precursor cells in the developing brain  
Authors: A. Watson, B. Wang, Y. Li, T. Footz, A. Voronova

### **Introduction**

During brain development, neural stem cells generate diverse progeny, including neurons, astrocytes and oligodendrocytes. Oligodendrocytes are glial (non-neuronal) cell types that generate myelin, a fatty substance that coats and protects nerve projections. The ability to form healthy myelin, which comprises white matter, is critical for proper brain development and function; however, in children with neurodevelopmental disorders (NDDs), white matter formation is abnormal (Fields et al. 2008, Trends in Neurosciences). Moreover, oligodendrocytes and myelin are lost in pediatric disorders such as leukodystrophies. Neural stem and precursor cells (collectively termed NPCs) in the subventricular zone (SVZ) and oligodendrocyte precursor cells (OPCs) in brain parenchyma have the ability to produce oligodendrocytes throughout life. Thus, if we can understand the environmental signals that instruct NPCs and OPCs to become oligodendrocytes, we may then be able to utilize this information to engage endogenous precursor cells to regenerate oligodendrocytes and myelin for proper brain development and function. My project focuses on fractalkine, a chemokine that is known to regulate oligodendrocyte formation from embryonic NPCs (Voronova et al. 2017 Neuron). However, its ability to regulate postnatal and adult NPC and OPC differentiation into oligodendrocytes is currently not known. The aim of my project is to determine if fractalkine has a pro-oligodendrogenic effect on NPCs and OPCs postnatally.

### **Methods**

We cultured NPCs isolated from murine postnatal SVZ niche as neurospheres, where the only cells that propagate are precursors, and other cells such as microglia, neurons and astrocytes do not survive. We differentiated neurosphere-derived NPCs into monolayers or secondary neurospheres in the presence or absence of FKN. Immunocytochemistry was used to quantify the proportion of oligodendroglial cells in monolayer cultures, and the number of secondary neurospheres was used as a measure of NPC proliferation. To test the direct effect of FKN on OPCs, OPC monolayer cultures were incubated in the presence of vehicle-control or FKN and analyzed for differences in differentiation, survival, migration, and phagocytosis.

### **Results**

We showed that FKN may increase NPC differentiation to OPCs and oligodendrocytes, without affecting NPC proliferation or OPC differentiation. FKN also prevented OPC apoptotic cell death, and may increase OPC migration and phagocytosis of myelin debris.

### **Conclusion**

Our study started to unveil FKN's role in modulating NPC and OPC function in the developing brain. Future studies will investigate the role of FKN signalling in the developing and adult NPCs and OPCs in vivo. This information may give us clues as to the cellular processes underlying white matter developmental disorders, as well as potential therapies for these disorders.

Funded by 75th Anniversary Graduate Scholarship, NSERC, MS Society of Canada, CIHR

The Power of Partnership





Abstract # 148  
Presenter: Almubarak, Asra  
Supervisor: Berry, Fred  
Title: Foxc1& Foxc2 are required for the development of the vertebral column & intervertebral discs  
Authors: Asra F. Almubarak1, Fred B. Berry1,2

### **Introduction**

Endochondral ossification is a skeletal development process where mesenchymal progenitors differentiate into chondrocytes that will be eventually replaced by bone. Disrupting this process causes skeletal dysplasia. Foxc1 and Foxc2 are two transcription factors of the forkhead box family that express at early stages of endochondral ossification. Given the similar expression pattern and similar endochondral ossification phenotype observed in Foxc1 or Foxc2 mutant mice, which indicates a possible compensation between the two genes. Compound Foxc1 and Foxc2 mutant mice die before any skeletal elements are formed

### **Methods**

In order to study the role of Fox1 and Foxc2 in endochondral ossification, we generated conditional mutant that deletes Foxc1 and Foxc2 in the chondrocytes.

### **Results**

These mutant mice exhibited an overall skeletal dysplasia with shorter limbs and a reduced formation of the vertebral column. In this study, we focus on the phenotypes observed in the vertebral column. Histological assessment with Safranin O showed less cartilage formed in mutant mice with only small mesenchymal condensations formed in the region of cervical vertebrae, while small thoracic vertebrae were observed. In the intervertebral discs, anulus fibrosus was not formed and the nucleus pulposus was irregularly shaped. SOX9, SOX6, COL2, COLX and COL1 localization in the vertebral region of the mutant mice was not detected by Immunofluorescence, indicating that chondrocyte differentiation was blocked. In the thoracic vertebrae, these chondrocytes differentiation markers were detected, although at lower level

### **Conclusion**

Our findings suggest that Foxc1 and Foxc2 are essential for regulating endochondral ossification in the vertebral column and shaping intervertebral discs.

Funded by 1-Women and Children's health research institute.2-Gilbert K Winter.  
3-The Natural Sciences and Engineering Research Council of Canada

The Power of Partnership

Abstract # 149  
Presenter: Herzog, Jens  
Supervisor: Waskeiwicz, Andrew  
Title: TSC2 required for mTOR regulation in the developing upper eye

Authors: Jens A. Herzog, Kevin H. Yoon, Andrew J. Waskeiwicz

### **Introduction**

Superior coloboma is a genetic congenital blinding disorder, which is caused by aberrant embryonic morphogenesis of a fissure in the upper eye. Our lab has identified many genetic variants from whole genome sequencing of patients presenting superior coloboma, which can be used to detect causal mutations. A promising candidate mutation was found in Tuberous Sclerosis Complex 2 (TSC2), a known regulator of mTOR signaling, involved in cell growth and proliferation. We propose that *tsc2* functions as a critical regulator of superior fissure morphogenesis, with the aim of discovering the cellular mechanism involved in the process.

### **Methods**

Eye development amongst vertebrates is highly conserved. This permits the use of zebrafish (*Danio rerio*), as a genetic model organism to study human eye development. As an initial study of *tsc2* function, we utilized gene-specific morpholino oligonucleotides to block *tsc2* translation. These experiments will be followed up with CRISPR-Cas9 mutagenesis to delete *tsc2* exon 1 in zebrafish. This would provide an excellent model for further experiments assessing the effect on mTOR activity and to identify the mTOR outputs that are perturbed. mTOR is involved in two complexes mTORC1 and mTORC2 the first step will be determining which one is involved. TSC2 has been shown to interact primarily with mTORC1, which can also be suppressed by addition of rapamycin. By indicating which mTOR complex is involved we can start to investigate specific outputs, so future experiments will focus on the testing these in *tsc2*<sup>-/-</sup> fish.

### **Results**

Other individuals who present with tuberous sclerosis complex caused by mutations of *tsc2*, are concomitantly diagnosed with atypical coloboma. We have demonstrated that *tsc2* knock-down by morpholino in zebrafish, causes a 60% incidence of superior fissure closure delay. The specific functional role of mTOR in the superior eye, though remain largely unknown, beyond the multiple general roles it plays in cell proliferation and growth as the outputs in the superior eye have yet to be assessed.

### **Conclusion**

The preliminary data indicates that *tsc2* knockdown increases the incidence of superior coloboma in zebrafish, suggesting that the human *tsc2* mutations cause the developmental defect. With current genetics techniques we have the capability of creating a useful model of superior coloboma in zebrafish, and the role of mTOR signalling on eye development. As the superior coloboma is genetic, understanding the other factors involved are very likely to present interventions that will decrease incidence during development.

Funded by NSERC, WCHRI, CIHR

The Power of Partnership

Abstract # 150  
Presenter: Dzierlega, Kasia  
Supervisor: Yokota, Toshifumi  
Title: **Increased expression of water channels aquaporin 1 and 5 in mouse and dog models of Duchenne muscular dystrophy**  
Authors: **Kasia Dzierlega, Kenji Rowel Lim, Toshifumi Yokota**

### **Introduction**

Duchenne muscular dystrophy (DMD) is the most common lethal genetic disease affecting children. A water channel aquaporin 4 (AQP4) is selectively expressed at the cell membrane in fast-twitch skeletal muscle fibres and known to be significantly reduced in Duchenne muscular dystrophy (DMD) patients; however, its function in healthy and diseased muscle fibres is poorly understood. In contrast, the expression of AQP1, which is located in epithelial cells of capillaries, has been previously reported to be upregulated in DMD muscle biopsies. We hypothesized that other aquaporin family members are also upregulated and compensate for the role of AQP4 in dystrophic muscles.

### **Methods**

Immunohistochemistry, Western blotting, and quantitative PCR were performed to examine the expression levels of 12 aquaporins (AQP1-12) in mouse and dog models of DMD.

### **Results**

Surprisingly, a significant increase in AQP5 expression was observed in mdx muscle fibres, a mouse model of DMD, compared to healthy control. AQP4 expression was significantly reduced in dystrophic dog muscle fibres, while significant elevation of AQP1 expression was detected in both transcript and protein analysis.

### **Conclusion**

We were able to identify elevated expression of AQP1 and AQP5 in DMD animal models for the first time. These results provide insight into aquaporin characteristics and suggest compensatory mechanisms for AQP4 deficiency by other water channel family members, including AQP1 and AQP5, in dystrophic muscle fibres.

Funded by **Natural Sciences and Engineering Research Council (NSERC)**

The Power of Partnership

Abstract # 151  
Presenter: Yoon, Kevin  
Supervisor: Waskiewicz, Andrew  
Title: A key eye patterning gene, *vax2*, affects the closure of superior ocular sulcus, a novel developmental feature of eye development  
Authors: Kevin Yoon, Jennifer C. Hocking, Ordan Lehmann, Andrew J. Waskiewicz

## Introduction

Congenital ocular coloboma is a genetic disorder that is typically observed as a cleft formation in the inferior aspect of the eye due to the failure of the choroid fissure to close during eye development. Recently, identification of individuals with coloboma in the superior aspect of the iris led to the discovery of a novel developmental structure, referred to as the superior ocular sulcus (SOS), that is transiently present on the dorsal aspect of the optic cup during early zebrafish eye development. Previous research in our lab demonstrated that manipulation of BMP signaling results in SOS closure delay. We aim to elucidate the role of a key dorsoventral (DV) eye axis patterning gene identified in patient-derived exome sequencing data, *VAX2*, a transcription factor regulated by Shh signaling that is expressed in the ventral eye.

## Methods

Using zebrafish, we created a *vax2* null allele, resulting in deletion of 83 base-pairs upstream of the homeodomain region, which subsequently produces a truncated protein. In addition, wildtype and variant human *VAX2* mRNA were microinjected to investigate the effects of overexpression on SOS-related phenotypes. Gene expression changes were assessed using in situ hybridization and quantitative real-time PCR.

## Results

The *vax2* null mutant embryos display increased incidences of SOS closure delays when compared to that of wildtype and heterozygous embryos. Conversely, overexpression of wildtype *VAX2* mRNA in wildtype zebrafish embryos leads to a strong phenotype in which there is delay in SOS closure in a dosage-dependent manner. Overexpression of *VAX2* also leads to perturbed expression of DV-axis patterning genes, including that of *tbx5a* and *efnb2a*. In addition, overexpression of the nonsynonymous *VAX2* variant (p.Leu139Met) identified in the patient appears to result in decreased incidences of SOS closure delay when compared to wildtype *VAX2* mRNA injections, indicating that the patient variant is likely to be a loss-of-function allele. Additionally, *VAX2* overexpression results in abnormal vasculature formation around the developing eye, which is consistent with our previous finding that normal SOS closure is required for proper eye vasculature formation.

## Conclusion

SOS closure appears to require a tightly-regulated expression of *vax2*, wherein both loss of and increase in *vax2* expression can result in aberrant closure. Overall, our results provide support for a model in which proper DV eye axis patterning is essential for SOS closure, in which loss of dorsally-expressed BMP signaling molecules and increase of ventrally-expressed Shh-induced factors results in aberrant closure of SOS. Using our existing exome sequencing data, future research will aim to further elucidate the genetic factors that lead to this novel ocular disorder.

Funded by WCHRI, CIHR, NSERC, and AITF

The Power of Partnership

Abstract # 152  
Presenter: Sanderson, Matthea  
Supervisor: Wevrick, Rachel  
Title: Elucidating the function of MAGEL2 through its protein-protein interaction network defined by proximity labeling (BioID) and mass spectrometry: A novel role RNA processing  
Authors: Matthea Sanderson, Richard Fahlman, and Rachel Wevrick

### Introduction

Mutations in the MAGEL2 gene cause Schaaf-Yang syndrome, a neurodevelopmental disorder. MAGEL2 is also one of six genes inactivated in Prader-Willi syndrome, which shares many clinical features with Schaaf-Yang syndrome. In mice, loss of Magel2 affects brain development and function, disrupts circadian cycles and causes other phenotypes that recapitulate endophenotypes in Schaaf-Yang and Prader-Willi syndromes. Mice lacking Magel2 have region-specific reduction in brain volume and altered brain chemistry. The MAGEL2 protein functions as an adapter protein for E3 ubiquitin ligases and deubiquitinases. However, little else is known about the role MAGEL2 plays in physiology during development or in cell biology. We used proximity-dependant labeling (BioID) combined with mass spectrometry to elucidate the molecular and cellular pathways in which MAGEL2 participates.

### Methods

We identified proteins that interact with MAGEL2 using BioID and mass spectrometry. Flp-In 293 cells were stably transfected with plasmid constructs expressing a biotin ligase (BirA\*) MAGEL2 fusion protein. Proximity-labeled biotinylated proteins were recovered by streptavidin affinity purification and identified by mass spectrometry. Two MAGEL2 constructs were analyzed: FL-MAGEL2 encodes the 1249 amino acid full length human MAGEL2 protein, while Cterm-MAGEL2 encodes the C-terminal portion of the protein containing the MAGE homology domain. The C-terminal region has been previously studied, whereas this is the first study to examine protein interactions with the N-terminal region of the MAGEL2 protein.

### Results

We identified sets of MAGEL2-interacting proteins that included both known interactors and novel interactors. We compared the interactome of the FL-MAGEL2 protein with that of Cterm-MAGEL2. This revealed a set of proteins in the FL-MAGEL2 interactome that were absent in the Cterm-MAGEL2 interactome, suggesting that they interact with the N-terminal region of MAGEL2. We identified two families of proteins that interacted with FL-MAGEL2 (TNRC6 and YTHDF) that function in RNA silencing and mRNA stability respectively.

### Conclusion

We are now investigating whether MAGEL2 acts as an adapter protein for ubiquitin-related processes that could modify the stability or function of these newly identified interacting proteins. These results suggest a novel function for MAGEL2 in RNA biology through specific interactions with the N-terminal region of the MAGEL2 protein.

Funded by CIHR, the WCHRI Graduate Studentship and the Foundation for Prader-Willi Research

The Power of Partnership

Abstract # 153  
Presenter: Dicipulo, Renee  
Supervisor: Waskiewicz, Andrew J.  
Title: Evidence for cross talk between Taz and Wnt signaling in brain ventricle morphogenesis  
  
Authors: Renee Dicipulo, Lyndsay G. Selland, Andrew J. Waskiewicz

### Introduction

The brain ventricle system (BVS) is a vertebrate-specific innovation that is necessary for the proper regulation of cerebrospinal fluid and nutrient and waste cycling in the brain. Aberrant development can result in a series of neurodegenerative defects, including hydrocephaly. While morphogenesis of the cavities that form the brain ventricle system are well known, the signaling pathways that govern the proper development of the BVS are poorly understood. Our laboratory has identified a novel role for Taz, canonically a co-transcriptional regulator of the Hippo signaling pathway. We have found evidence of crosstalk between the WNT and Hippo signaling pathways in the regulation of brain ventricle morphogenesis.

### Methods

To understand the role of Taz in the development of the BVS, Transcription Activator-Like Effector Nucleases (TALENs) were used to generate zebrafish taz knockouts. In addition, transgenic zebrafish lines and fluorescence microscopy were used to assay changes in ventricle structure and signaling pathway activity. Taz immunohistochemistry as well as in situ hybridization were used to assay protein stabilization and gene expression. To modulate WNT signaling, pharmacological agents were used to manipulate WNT and Taz interactions.

### Results

Zebrafish taz mutants display a decreased BVS due to failure of ventricle midline separation, the first step in ventricular morphogenesis. In addition, molecular assays have shown that taz mutants have aberrant apicobasal polarity in the hindbrain ventricle. In wild-type zebrafish, we have noted that Taz protein is localized to hindbrain segment boundaries, where WNT signaling is known to be active. When wild-type animals are treated with pharmacological inhibitors of WNT, there is a loss of Taz localization at these segment boundaries, showing that the intrasegmental stabilization of Taz is WNT-dependent. In addition, pharmacologically agonizing WNT results in an increase in Taz stabilization at the rhombomere boundaries. This is in accordance to Azzolin et al. 2014, showed in vitro that TAZ interacts with the  $\beta$ -catenin destruction complex, and is subsequently degraded in WNT-off cells.

### Conclusion

Our work has demonstrated that Taz is required for proper morphogenesis of the brain ventricle in zebrafish, and loss of Taz affects apicobasal polarity of the ventricle midline. From our work, we suggest a model where Taz is regulated by WNT signaling, wherein in WNT-on cells, Taz is stabilized.

Funded by WCHRI, NSERC, Alberta Innovates

The Power of Partnership

Abstract # 154  
Presenter: Roshmi, Rohini Roy  
Supervisor: Yokota, Toshifumi  
Title: Development of novel genome editing therapy for Duchenne muscular dystrophy  
Authors: Rohini Roy Roshmi, Quynh Nguyen, Rika Yokota Maruyama, Toshifumi Yokota

### Introduction

Duchenne muscular dystrophy (DMD) is the most common lethal genetic disorder, characterized by progressive muscle loss and cardiorespiratory complications. Most children with DMD start exhibiting symptoms by the time they are 2-4 years old. It is caused by a lack of dystrophin protein due to mutations in the DMD gene that can disrupt the reading frame of the gene. The N-terminal region of the DMD gene, specifically exons 3-9, is a hotspot for mutations. Skipping of exons 3-9 can theoretically treat 7% of DMD patients. In addition, exons 3-9 skipping is associated with very mild phenotype in patients with Becker muscular dystrophy, a milder form of muscular dystrophy. We hypothesised that clustered regularly interspaced short palindromic repeats (CRISPR)-Cas9 mediated non-homologous end-joining (NHEJ) restores dystrophin expression in immortalized dystrophic dog muscle cells carrying a splice site mutation in intron 6 by removing frame-disrupting exons i.e. exons 3-9.

### Methods

We designed guide RNAs (gRNAs) that target introns 2 and 8 as exon 9 is known to be skipped spontaneously with exon 8 skipping. The gRNAs were inserted into AAV vectors. The activity of the gRNAs was assessed by T7 endonuclease 1 assay. gRNAs specific to canine DMD gene were transfected into immortalised dog muscle cells with the canine X-linked muscular dystrophy (CXMD). RNA was extracted from these cells ten days after differentiation and RT-PCR was done to confirm exon skipping.

### Results

Sanger sequencing of the plasmids showed successful insertion of gRNAs into the plasmid. The T7 endonuclease 1 assay identified gRNAs, targeting introns 2 and 8, with cutting efficiency. In the RT-PCR results, the gRNAs exhibited successful exons 3-9 skipping in immortalised CXMD dog muscle cells.

### Conclusion

We demonstrated successful genome editing and restoration of in-frame dystrophin expression in a dog model of DMD. CRISPR-Cas9 genome editing is a promising therapeutic option as it can restore dystrophin expression permanently at the genomic level.

Funded by Alberta Innovates: Health Solutions (AIHS) and Canadian Institutes of Health Research (CIHR)

The Power of Partnership

Abstract # 155  
Presenter: Fox, Sabrina  
Supervisor: Waskiewicz, Andrew  
Title: Bmp3 regulates ocular fissure closure via TGF- $\beta$  signalling

Authors: Sabrina C. Fox, Sonya A. Widen, Lisa B. Prichard, Ordan J. Lehmann and Andrew J. Waskiewicz

### Introduction

The ocular fissure is a transient structure in the ventral eye that serves as an entry point for the developing ocular vasculature and an exit for the optic nerve. Failure of ocular fissure closure results in ocular coloboma, which is characterized by gaps in ocular tissues. Previous work has identified Transforming Growth Factor-Beta (TGF- $\beta$ ) and Bone Morphogenetic Protein (BMP) as major regulators of fissure closure, and sequencing of human patients with microphthalmia/coloboma revealed potentially deleterious variants in BMP3 (a known TGF- $\beta$  ligand). Therefore, we hypothesize that *bmp3* is an important regulator of optic fissure closure.

### Methods

CRISPR/Cas9 genome editing was used to create a frameshift mutation in zebrafish *bmp3*, and the presence of open optic fissure in these mutants was assessed using laminin antibody staining at 65 hours post fertilization (hpf). In-situ hybridization was used to determine the spatial expression of *bmp3* and dorsal/ventral gene expression markers in zebrafish embryos. Antibody staining for phosphorylated Smad3 (pSmad3) was used to assess TGF- $\beta$  signalling in the ventral eye. The pharmacological treatment Specific Inhibitor of Smad3 (SIS3) was used to inhibit TGF- $\beta$  signalling, and treated embryos were scored for the presence of open fissures at 65 hpf and compared to control embryos.

### Results

We have shown that *bmp3* is expressed in the zebrafish head mesenchyme and forebrain during early ocular development, and *bmp3* <sup>-/-</sup> fish display delayed ocular fissure closure, suggesting that *bmp3* has a critical role in early eye morphogenesis and ocular fissure closure. Additionally, we have found that TGF- $\beta$  signalling is active adjacent to the ocular fissure, further strengthening a role for *bmp3* in fissure closure. This is consistent with other findings that *bmp3* <sup>-/-</sup> embryos are sensitized to a suboptimal dose of TGF- $\beta$  inhibitor, resulting in an increased penetrance of fissure closure defects. Spatial expression of dorsal (*tbx5a* and *aldh1a2*) and ventral (*vax2* and *aldh1a3*) markers in *bmp3* <sup>-/-</sup> mutants was not disrupted, indicating that *bmp3* signalling does not affect overall patterning of the eye.

### Conclusion

These results suggest that *bmp3* is a novel regulator of optic fissure closure. Further studies will focus on the contribution of other TGF- $\beta$  signalling ligands in optic fissure closure. Additionally, we hope to explore the role of periocular mesenchyme cells in optic fissure closure.

Funded by WCHRI, CIHR, NSERC, Glaucoma Research Society of Canada

The Power of Partnership



Abstract # 156  
Presenter: Sosa-Alvarado Carla  
Supervisor: Chan Catherine  
Title: **Antibiotic administration at early stages of life affects pancreatic islet morphology and function**  
Authors: **Carla Sosa-Alvarado, Carina Yang, Janelle M. Fohse, Steven Qiu, Benjamin P.Willing and Catherine.B.Chan**

### Introduction

Early life antibiotic exposure has been associated with adverse metabolic outcomes later in life, including obesity and diabetes. We previously demonstrated alterations in islet development and function in a piglet model of antibiotic exposure that resulted in reduced  $\beta$ -cell area and proliferation weeks after antibiotic withdrawal. The aim of the present work was to identify early-life gut microbiota perturbations induced by amoxicillin antibiotic that could be associated with potential mediators of insulin secretion, such as incretins, metabolites and antimicrobial peptides. We examined amoxicillin-induced changes in gut microbiota composition and potential mediators in newborn piglets at postnatal days (PND) 7, 14 and 49.

### Methods

A piglet model was chosen due to similarities to human infant gastrointestinal function and structure. 42 Crossbred newborn piglets (Duroc x Large White/Landrace) were randomly assigned to an oral therapeutic dose of amoxicillin (30mg/kg/day) (ANT; n=7) or placebo (CON; n=7) throughout the first 14 days of life. The termination and sample collection was done at PND 7, 14 and 49. RNA extraction from isolated islets, ileum and distal colon was used to measure gene expression. Plasma insulin and active glucagon-like peptide-1 (aGLP-1) concentrations were assayed by ELISA. Pancreatic  $\beta$ - and  $\alpha$ -cell proliferation and apoptosis rates were measured in fixed pancreatic tissue by using Ki67 and TUNEL immunohistochemistry. Insulin content and insulin release was measured from isolated islets challenged with 2.8-22 mM glucose by radioimmunoassay. Changes in microbial composition were assessed by 16 rRNA gene (hypervariable regions V3-V4) amplicon sequencing on the MiSeq platform. Short chain fatty acid (SCFA) concentrations were analyzed by gas chromatography. Plasma lipopolysaccharide (LPS) concentration was measured by PYROGENT-5000 Kinetic Turbidimetric LAL Assay

### Results

PND49 ANT presented an increase in plasma insulin but a decrease in islet insulin content and  $\beta$ -cell area, which was not seen at earlier time points. Islet TCF7L2, INS, PDX-1 and IGF-2 gene expression were decreased only in PND14 ANT compared with CON piglets whereas at PND 7, ANT islets had higher gene expression of GCG, GLP-1R, PSCK1/3, PSCK2 and DPPIV, TNF $\alpha$  and the antimicrobial peptide protegrin. Pancreatic  $\beta$ - and  $\alpha$ -cell area, proliferation and apoptosis rates were not different in PND7 piglets of ANT or CON groups. PND7 ANT piglets had higher plasma aGLP-1 concentration. SCFA concentration in cecum was not changed by the administration of amoxicillin at any time point. At PND7 a trend for higher LPS (p=0.080) was found in ANT, which corresponded with an increased abundance of Escherichia coli in the ileum, cecum and colon.

### Conclusion

Administration of amoxicillin in early life induced changes in islet behaviour as reflected by differences in the expression of important regulators of islet development. These changes may be a response to the inflammatory environment suggested by the increase in expression of TNF $\alpha$  and protegrin. The increased inflammation is likely a product of a bloom in E. coli and increase in serum LPS. Further studies are needed to confirm the role of E coli in the altered islet development which will provide

Funded by **CONACYT and WCHRI Graduate Students Award**

The Power of Partnership

Abstract # 157  
Presenter: Sanchez Enkerlin, Annette  
Supervisor: Clugston, Robin  
Title: **Transfer of vitamin A into breast milk: Dissecting the molecular retinoid pathway**

Authors: **Annette Sanchez Enkerlin, Timothy Dalmer, Tianna Clarke, Robin D. Clugston**

### **Introduction**

Vitamin A is one of the essential micronutrients, therefore during nursing the developing infant relies on maternal breast milk to meet its demands for vitamin A. The infant's intake during lactation is necessary to establish vitamin A stores that can be utilized post-weaning. Adequate vitamin A status is essential in children to maintain a healthy body, particularly in regard vitamin A's role in vision and immunity. A better understanding of the mechanisms that facilitate the transfer of maternal vitamin A into breast milk is significant in populations with marginal vitamin A status, as well as in people with otherwise impaired vitamin A homeostasis. The aim of the following study was to characterize the retinoid metabolic pathway in mammary tissue collected from mice during three unique developmental stages: virgin, lactation, and involution. We predicted that the differential expression of components in the retinoid metabolic pathway during lactation would indicate the central players in vitamin A transfer into breast milk. The goal described above is part of our ongoing research and the following preliminary results reflect our work in progress.

### **Methods**

Mammary gland tissue was collected from female mice differing in reproductive stages: virgin, lactation and involution. Messneger RNA extracted from the tissue was converted into cDNA for appropriate analysis using qPCR. The data obtained from this analysis allowed us to decipher the relative expressions of central genes in the retinoid metabolic pathway.

### **Results**

Results obtained so far indicate that there is significant differential expression within the retinoid metabolic pathway that coincides with increased demand for vitamin A transfer into breast milk during lactation. This includes significantly increased expression of the retinyl ester-synthesizing enzyme Lrat (lecithin:retinol acyltransferase), as well as decreased expression of enzymes involved in retinoic acid synthesis (Raldh). Our results indicate that during lactation, mammary tissue shifts the retinoid metabolic pathway away from retinoic acid synthesis, toward retinyl ester synthesis. This pattern is consistent with the fact that retinyl esters are the predominant form of vitamin A found in breast milk. As well as characterizing the molecular mechanisms of vitamin A transfer into breast milk, our preliminary data suggests an unexpected role for maternal vitamin A status in the maturation of mammary tissue.

### **Conclusion**

In summary, the present study demonstrates a shift in mRNA expression in mammary gland tissue to favor production of retinyl ester, while decreasing retinoic acid production. This on-going research should yield a better understanding of how vitamin A is transferred into breast milk, as well as the importance of vitamin A status in maturation of mammary tissue.

Funded by **NSERC CRSNG**

The Power of Partnership

Abstract # 158  
Presenter: Orsso, Camila  
Supervisor: Haqq, Andrea; Prado, Carla  
Title: Variations in body composition in children with similar degrees of obesity based on body mass index: Preliminary results from the Metabolic Load-Capacity study  
Authors: Orsso CE, Hamilton J, Matkowski A, MacLeod M, O'Neill M, Pakseresht M, Ansarian M, Ball GDC, Rubin DA, Field CJ, Prado CM, Haqq AM

## Introduction

Body mass index (BMI) z-score is a widely used anthropometric measure that approximates body fatness in childhood. However, several studies have shown a poor sensitivity of BMI to identify excess fat mass (FM) at the individual level, as children may exhibit varied body composition influencing disease risk and physical functioning. What is less clear is whether BMI is a surrogate of FM in children with obesity. In this study, we evaluated the extent to which body composition varied among degrees of obesity in children using preliminary data from the Metabolic Load-Capacity study.

## Methods

Children (10-16 years old; BMI >95th percentile) had anthropometrics and body composition assessed on the same day after an overnight fast. Weight and height were measured using standardized procedures. BMI z-score was computed using WHO AnthroPlus and participants were categorized as BMI <3SD, BMI  $\geq 3$  and <4SD, and BMI  $\geq 4$ SD. Air-displacement plethysmography was used to assess FM and fat-free mass (FFM). The metabolic load-capacity index was calculated as FM (in kg; metabolic load) divided by FFM (kg; metabolic capacity). Children completed a validated pubertal status questionnaire. The Spearman correlation coefficient was used to evaluate the associations between anthropometric and body composition variables.

## Results

Among fifteen children who completed the study to date, nine (60%) were males; median age was 12.0 (IQR, 10.8-13.5) years; and most of the children were at early puberty (66.7%; Tanner stages 2 or 3). Although BMI z-score was positively correlated with FM% ( $r=0.807$ ,  $p<0.0005$ ) and negatively with FFM% ( $r=-0.807$ ,  $p<0.0005$ ), a wide range of FM% and FFM% within BMI z-score categories was observed. For example, children with BMI z-score <3SD (46.7%) had FM% ranging from 30.2-42.3% and FFM% between 57.7-69.8%. Children with BMI z-score  $\geq 3$  and <4SD (33.3%) had FM% ranging from 40.2-50.3% and FFM% 49.7-59.8%. Moreover, children with BMI  $\geq 4$ SD (20%) had FM% between 45.1-53.6% and FFM% between 46.4-54.9%. At an individual level, FM% and FFM% overlapped between BMI z-score categories. There was a strong and positive association between the load-capacity index and BMI z-score ( $r=0.807$ ;  $p<0.0005$ ), but the range also varied between categories (BMI <3SD: 0.42-0.73; BMI  $\geq 3$  and <4SD: 0.67-1.01; BMI  $\geq 4$ SD: 0.82-1.16).

## Conclusion

Our preliminary analyses suggest that BMI z-score was strongly correlated with FM in children with obesity. We also found that children with similar degrees of obesity based on BMI z-score categories had a wide range of FM%, FFM%, and load-capacity indices. In fact, some children in the lowest degree of obesity had FM similar to those in higher BMI z-score categories. Future analyses that include our final sample size goal ( $n=90$ ) are needed to substantiate these findings.

Funded by This research has been funded by the Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute.

The Power of Partnership

Abstract # 159  
Presenter: Tan, Qiming  
Supervisor: Haqq, Andrea  
Title: An atypical case of Prader-Willi syndrome caused by a microdeletion at 15q11.2 that includes the SNORD116 gene cluster  
Authors: Qiming Tan\*, Kathryn Potter\*, Lisa Cole Burnett, Rudolph Leibel, Davis Ryman, Andrea Haqq  
\*co-first authors

### Introduction

Prader-Willi syndrome (PWS) is a neurodevelopmental disorder due to the lack of expression of paternal alleles in 15q11.2-q13. Beginning in early childhood, affected individuals develop hyperphagia and excessive weight gain, which often leads to obesity. Major characteristics of PWS also include infantile hypotonia causing poor feeding and failure to thrive, hypogonadism, short stature, delayed development, minor facial abnormalities, cognitive impairment, and behavioral and psychiatric disturbance. Although most cases of PWS are caused by large deletions of 5 MB or greater, recent research shows that PWS can occur by deletion of a small critical region of chromosome 15. Here we report a 17-year-old boy who presents a rare type of PWS, in which a microdeletion at 15q11.2 encoding the SNORD116 complex results in the disease phenotype.

### Methods

Genomic DNA was analyzed by next-generation sequencing technology.

### Results

Genetic analysis identified a homozygous microdeletion of 71 kb on chromosome 15 (25296613-25267633). Southern analysis using methylation-sensitive restriction enzymes and SNRPN or PW71B probes did not detect this variant of PWS. This deletion does not affect the SNURF-SNRPN locus but results in the loss of several of the PWS-associated non-coding RNA species, including the SNORD116 cluster. From birth to 3 years of age, the patient required tube feeding due to extreme lethargy and prominent hypotonia. He exhibited global developmental delay and at age 3, he became hyperphagic. His history is also significant for central sleep apnea, autism, obsessive compulsive disorder, and intellectual disability. Of note, unlike many children with PWS, he had spontaneous onset of puberty. Puberty was complete at the time that he was assessed in our clinic. The patient had Tanner 5 pubic hair and his testes were 20 ml bilaterally. Without the use of growth hormone replacement therapy, he reached a tall adult stature, which is atypical for PWS. From age 4 onward, his height followed the 90-95th percentiles and his body mass index (BMI) remained above the 97th percentile for age. At age 15, his height was above the 97th percentile. At age 17, his BMI was 28.45 kg/m<sup>2</sup> (percentile: 95%). Most recent laboratory results showed normal HbA1c level, thyroid function, AM cortisol, and fasting lipid profile, and his testosterone level was consistent with puberty.

### Conclusion

The present case shows that deletion of 71kb critical region encompassing the SNORD116 gene cluster is sufficient to cause PWS. To our knowledge, this is the smallest deletion described to date. Consistent with recent literature, this finding strongly suggests that lack of SNORD116 expression plays a significant role in the etiology of PWS. Standard genetic testing for PWS may miss this microdeletion. To prevent missed diagnosis, targeted analysis of the SNORD116 gene cluster in addition to SNRPN methylation analysis is recommended for patients with symptoms suggestive of PWS. This case also illustrates that the phenotype of rare cases of PWS that involve mutation of the SNORD116 complex may have atypical features, such as tall stature and spontaneous progression through puberty.

Funded by The W. Garfield Weston Foundation and the University of Alberta

The Power of Partnership

Abstract # 160  
Presenter: Morin, Sarah  
Supervisor: Chui, Linda  
Title: **Characterizing Clostridioides difficile found in paediatric populations**

Authors: **Sarah Morin, Colin Lloyd, Taryn Stokowski, Stephen Freedman, Bonita Lee, Xiao-Li Pang and Linda Chui on behalf of the APPETITE team**

### **Introduction**

Clostridioides difficile infection (CDI) is primarily characterized by loose stool induced by toxins released from C. difficile that colonize the large intestine. In infants, there exist high rates of asymptomatic C. difficile carriage, suggesting that the presence of C. difficile alone does not necessarily lead to disease in this age group. A study on children with diarrhea conducted by the Alberta Provincial Pediatric EnTeric Infection TEam (APPETITE) detected C. difficile in both sick and healthy cohorts. The purpose of our investigation was to determine whether a number of pathogen-specific factors varied between sick children and healthy control children that were both positive for this bacterium.

### **Methods**

APPETITE had previously characterized stool samples of healthy and sick children as having either 1) mono-detection of C. difficile or 2) co-detection of C. difficile with another gut pathogen. Stool samples from all cohorts were tested for the presence of toxins using the C. DIFF QUIK CHEK COMPLETE® enzyme immunoassay (EIA), followed by confirmation of the toxin gene with an in-house quantitative PCR assay. C. difficile load was estimated using an established standard curve that correlates quantitative PCR crossing points to bacterial cell counts. Fingerprint profiles were generated by either directly-from-stool or isolate PCR ribotyping to determine whether specific strains were associated with symptomatology.

### **Results**

We found no significant differences in toxin detection, bacterial load and ribotypes between sick vs. healthy children, regardless of co-detection of C. difficile with another gut pathogen.

### **Conclusion**

It has yet to be established whether C. difficile is likely a likely pathogen in this group of children. Since CDI depends on a complex interplay of both the pathogen and host, future direction would include investigating host-specific factors such as co-morbidities and medications.

Funded by **WCHRI Summer Studentship; Alberta Innovates**

The Power of Partnership

Abstract # 161  
Presenter: van der Leek, Aaron  
Supervisor: Kozyrskyj, Anita  
Title: **Fecal immunoglobulin A and asthma/wheeze in the first 5 years of life in the CHILD cohort**  
Authors: Aaron P. van der Leek, Catherine J Field, Anne Hicks, Yarden Yanishevsky, Dean Befus, Meghan B. Azad, Allan B Becker, Piushkumar J Mandhane, Diana L. Lefebvre, Malcolm R Sears, Stuart E Turvey, Theo Moraes, Padmaja Subbarao, James A Scott and Anita L Kozyrskyj and CHILD

### **Introduction**

Evidence has been accumulating on the impact of aberrant early immune maturation and gut microbial composition on the development of asthma in children. Previous studies by Kukkonen et al., (2010) show low gut mucosal immunoglobulin A levels in infancy to be associated with the development of atopic disease. Dzidic et al., (2017) found that secretory Immunoglobulin A (sIgA) responses to gut microbiota predicted future asthma and allergy. In our study, we determined whether lower levels of the primary gut mucosal immunoglobulin (sIgA) during infancy was associated with the development of atopic and non-atopic wheeze.

### **Methods**

From the Vancouver, Edmonton and Winnipeg sites of the CHILD Cohort Study, 951 infants with a stool collection at  $\leq 5.5$  months were analyzed to limit the known effects of food introduction on mucosal immunity. Child asthma/wheeze was determined from parent report of physician-diagnosed asthma at 1, 2, 3, 4 and 5 years of infant age. Atopic sensitization status at age 1 and 3 years was determined by skin prick test. Fecal sIgA was quantified using the Immundiagnostik sIgA ELISA kit. A 3-category variable was created as: breastfed (with low or high fecal sIgA levels), not breastfed with low sIgA levels (lowest tertile) and not breastfed with fecal sIgA levels in the highest 2 tertiles. Using STATA v16, logistic regression models determined the association (Odds Ratio, OR) between low fecal sIgA levels in non-breast fed infants and child asthma/wheeze, adjusting for confounding factors identified from a directed acyclic graph: maternal pre- and post-natal depression, maternal age and breastfeeding status.

### **Results**

About 6% of infants had asthma/wheeze by age 3, increasing to 11% at ages 4-5. Low fecal sIgA levels were found in 68% of infants who were not breastfed, 31% of infants who were partially breastfed and 14% of infants who were exclusively breastfed ( $p < 0.001$ ). When compared to breastfed infants, infants not breastfed with low fecal sIgA levels had 2.20 times the odds of having asthma/wheeze in the first three years of life (OR: 2.20; 95%CI: 1.12, 4.34) when controlling for confounding factors. No associations were found between asthma/wheeze at age 1-3 and higher fecal sIgA if not breastfed or between asthma/wheeze at ages 4-5, and low or higher fecal sIgA in the absence of breastfeeding. Infants not breastfed with low fecal sIgA were at increased risk for non-atopic wheeze at age 1-3 years (OR: 1.89; 95%CI: 1.18, 3.04), whereas not breastfed, high fecal sIgA infants were at increased risk for atopic wheeze (OR: 3.17; 95%CI: 1.08, 9.29) when compared to breastfed infants. Child asthma/wheeze was not associated with fecal sIgA levels in exclusively or partially breastfed infants.

### **Conclusion**

Low levels of innate production of fecal sIgA was associated with increased risk for asthma and non-atopic wheeze in the first three years of life, whereas high levels were associated with increased risk for atopic wheeze. Due to these associations, sIgA production in non-breastfed infants may be an important biomarker for early-onset non-atopic/atopic wheeze.

Funded by CIHR

The Power of Partnership

Abstract # 162  
Presenter: Toohey, Alexander W.  
Supervisor: Funk, Gregory D.  
Title: **Intracellular adenosine metabolism is important for maintaining baseline inspiratory rhythm in the preBötzing complex of neonate mice in vitro**  
Authors: **Alexander W. Toohey, Robert J. Reklow, and Gregory D. Funk**

### **Introduction**

Breathing in premature infants often stops briefly (apnea) due to an immature brainstem network that controls the process. During apneas, oxygen levels fall (hypoxia) triggering a rapid increase in breathing that is followed by a life-threatening depression of breathing. During hypoxia ATP is released in the key brain site that underlies inspiration, the pre-Bötzing Complex (preBötC), where it stimulates breathing and reduces the depression. ATP, however, is broken down into adenosine (ADO), which depresses preBötC activity by acting at A1 or A2 ADO receptors (Rs). Thus, the balance between ATP and ADO actions is emerging as key in determining the size of the hypoxic respiratory depression. Methylxanthines (i.e. caffeine) block ADO receptors and are used to stimulate breathing in premature infants with apneas. However, 20% do not respond to therapy highlighting the importance of discovering alternate therapies. In other regions of the adult brain, two enzymes (adenosine kinase (ADK) and adenosine deaminase (ADA)) metabolize intracellular ADO and are important in controlling this ATP-ADO balance. ADK is the most important of the two enzymes, but it is immature at birth. If the same is true in the breathing network, this could contribute to the profound hypoxic respiratory depression in premature mammals.

### **Methods**

To test the role of these enzymes in controlling preBötC inspiratory network activity during development, I compared the effects of ADK (5-ITC & ABT-702) or ADA (EHNA) inhibitors on baseline inspiratory activity generated by medullary slices from 0-3 and 9-12 day-old mice.

### **Results**

ADK inhibitors had no effect on either age group. In contrast, ADA inhibition reduced basal frequency in 0-3 day-old mice by  $12.8\% \pm 2.4\%$  ( $P < 0.0005$ ). Time restrictions prevented testing ADA inhibition in 9-12 day-old mice. Inhibition in 0-3 day-old mice was reversed by caffeine, an A1/A2R blocker, but not by DPCPX, an A1R blocker.

### **Conclusion**

These data suggest that ADK does not influence ADO levels in the preBötC before day 12, while ADA activity increases basal preBötC rhythm by limiting A2R-mediated ADO inhibition. The next step is to determine whether ADA activity can be manipulated to reduce the hypoxic depression of breathing.

Funded by **WCHRI Summer Studentship; AIHS Summer Studentship**

The Power of Partnership

Abstract # 163  
Presenter: Elawad, Dalia  
Supervisor: Hicks, Anne  
Title: Pseudomonas in pediatric tracheostomy patients: Incidence, prevalence and risk factors

Authors: Dalia Elawad, Gregory Tyrrell, Anne Hicks

### Introduction

Physical barriers that prevent microbial colonization of the airways are bypassed by tracheostomy. Short-term studies have demonstrated changes to the lung microbial population in patients with tracheostomy. Pseudomonas in chronically colonized patients often develops multidrug resistance, with limited oral treatment options. Patients with suspected Pseudomonas infection can require hospital admission and intravenous antibiotic therapy. This study describes a 5-year cohort of tracheostomy patients at a single site and the incidence and prevalence of Pseudomonas aeruginosa in these patients.

### Methods

This is a descriptive analysis of a retrospective cohort chart review of children under 18 years who had tracheostomy and were followed at the Stollery Children's Hospital between January 1, 2012 and May 30, 2017. Clinical and demographic data (age, reason for tracheostomy, GT and fundoplication) was obtained from a previous unpublished chart review. Microbial culture results were provided by the Alberta Provincial Laboratory.

### Results

Of the 113 participants identified by the chart review, 29 participants received a tracheostomy for isolated upper airway obstruction, 17 patients for ventilator access only, and 28 participants for a combination of both, while 39 participants did not have enough data recorded. The average age at the time of tracheostomy was 5 years. G tube placement was confirmed for 42 participants, not present in 12 participants and unknown for the remaining 59 participants. Of the 42 participants with G tubes, 29 had a confirmed fundoplication; status was unknown for 65 participants with only 6 participants confirmed to have no fundoplication. There were no cases of fundoplication in the absence of G tube. Of the 42 patients with a G tube, 79% were ventilated while 42% of the participants with no G tube were ventilated. There were 56 participants who had a Pseudomonas aeruginosa positive culture, 49 participants with no positive cultures and 10 participants for which no microbial data was available.

39% of the participants with isolated obstruction grew Pseudomonas compared with 35 % of participants with isolated ventilation and 61 % of participants with combined obstruction and ventilation need. Only 25% of participants who had no G tube grew Pseudomonas while 33% of participants with G tube without fundoplication compared with 62% of participants with G tube and fundoplication.

### Conclusion

Over the study period of 5 years, there were 113 recorded tracheostomy procedures at our site, of which half of them required ventilation. The average age at the time of tracheostomy was 5 years. Almost 40% of participants had isolated airway obstruction, while 62% of those requiring ventilation also had airway obstruction. Patients with G tube and fundoplication were more likely to grow Pseudomonas than patients with a G tube alone; those not dependent on tube feeding had the lowest risk, suggesting a possible link with swallowing and other gastrointestinal system issues. Participants with isolated need for upper airway bypass or ventilation were less likely to grow Pseudomonas than those requiring both respiratory support.

Funded by WCHRI

The Power of Partnership



Abstract # 164  
Presenter: Bird, Melissa  
Supervisor: Storey, Kate  
Title: **Sleeping Soundly: Understanding the translation of sleep promotion at school to sleep behaviours at home**  
Authors: **Bird, M., Storey, K., Montemurro, G.**

### **Introduction**

Sleep is increasingly recognized as an essential component of a healthy lifestyle and is crucial to children's development. However, children's sleep has been declining in recent decades. Inadequate sleep has been associated with obesity, physical inactivity, poor nutrition, anxiety, depression, suicide risk, and poor academic performance. These health deficits present a public health concern and additional research is required to explore children's sleep behaviour. School and home environments are recognized as critical settings to shape healthy behaviours among children. School-based health promotion efforts have recently adopted holistic models, such as the comprehensive school health (CSH) approach, to address student health across these critical environments. This approach is utilized by health promotion initiatives such as APPLE Schools (A Project Promoting healthy Living for Everyone in schools). Given that sleep behaviours learned at school are carried out in the home, it is necessary to explore student understandings of school-based sleep education and the accompanying contextual knowledge of sleep behaviour that exists in the home environment. The objective of this research is (1) examine children's perceptions of their own sleep behaviour and determine if and how they act as change agents and initiate sleep behaviour changes in the home. (2) Explore parents' perspectives on sleep behaviours and understand how parenting practices facilitate and support, or act as a barrier, to healthy sleep behaviours.

### **Methods**

This research utilized photovoice as both a qualitative method and data generating strategy. Focused ethnography was used to explore contextual meanings of sleep behaviour within participating APPLE schools. Fifty grade 4 & 5 students from participating APPLE schools with a school-based sleep education initiative were recruited in Winter 2019. Students were given cameras and asked to take photos of sleep behaviours in their home. Photos were then discussed during semi-structured interviews using an established protocol. Interviews aimed to examine if and how children act as change agents and initiate sleep behaviour changes in the home. Data collection and latent content analysis occurred concurrently, with students participating in the analytic process during interviews and through follow-up classroom presentations.

### **Results**

In progress. Expected data analysis completion is September 2019.

### **Conclusion**

This research will increase our understanding of the translation of school-based sleep education to the home environment among students. Results can help to inform and improve existing approaches, including future CSH implementation related to sleep.

Funded by **CIHR, WCHRI**

The Power of Partnership

Abstract # 165  
Presenter: Louie-Poon, Samantha  
Supervisor: Scott, Shannon D.  
Title: Comparing the usability evaluation results of three parental tools for bronchiolitis

Authors: Samantha Louie-Poon, Tabatha Plesuk, Alyson Campbell, Hyelin Sung, Anne Le, Hannah Brooks, Lisa Hartling, Shannon Scott

### **Introduction**

Bronchiolitis is an acute infection of the lower respiratory tract that predominantly affects children less than two years old. Although self-limiting, symptoms of bronchiolitis can be distressing for young children. Research has demonstrated that parents may not have the necessary information to be able to identify bronchiolitis symptoms, resulting in emergency department (ED) visits and hospitalizations. Parents have expressed that they feel unprepared, afraid, and that they lack information on their child's condition. Digital knowledge translation (KT) tools have the potential to convey complex health information to parents.

### **Methods**

We worked with parents of children with bronchiolitis to develop and evaluate three digital tools on bronchiolitis (whiteboard animation video, infographic, and e-Book). Following prototype completion, usability testing was conducted using iPads in two Alberta ED waiting rooms. Parents were asked to complete a 9-item, 5-point Likert scale survey that assessed usability, aesthetics, language, length, and future use. Data were analyzed using SPSS.

### **Results**

Overall, the three tools were highly rated, with parents providing scores of 3.97-4.58 (out of 5.00) on each usability item. Using SPSS, we ran an analysis of variance (ANOVA) to compare usability item scores between the tools. Results revealed a significant difference in parents' scores for length appropriateness ( $p < 0.00$ ), with the e-Book being rated the lowest at 3.33, followed by the infographic (4.09) and video (4.27). There were no significant differences for the other usability items.

### **Conclusion**

These high scores from parents suggest that digital tools are useful in delivering complex health information to parents.

Funded by NCE, CIHR

The Power of Partnership

Abstract # 166  
Presenter: Campbell, Alyson  
Supervisor: Scott, Shannon D  
Title: Our experience conducting an environmental scan (ES) on knowledge translation (KT) tools for pediatric concussion  
Authors: Alyson Campbell, RN, PhD Student; Shannon D. Scott, RN, PhD

### **Introduction**

Environmental scans (ESs) originated in business as tools for retrieving and organizing data for decision-making. In healthcare however, ESs remain relatively undefined, unevaluated and underutilized. While individual studies in healthcare indicate the utility of ESs, there are no quality standards or guidelines for conducting an ES, resulting in wide variations of methods used across studies. This lack of guidance can present challenges for those intending to conduct an ES as a method for knowledge synthesis. We report on our experience and lessons learned conducting an ES on knowledge translation (KT) tools for pediatric concussion.

### **Methods**

Phase 1 of my doctoral research is to conduct an ES with the purpose of identifying and gaining an understanding of all Canadian-based, publicly available knowledge tools about pediatric concussion. This ES incorporates systematically searching the Internet/App Stores and conducting interviews with key informants from health organizations providing identified knowledge tools.

### **Results**

The following lessons were learned conducting an ES: 1) ESs are a good “first step” for research projects, resulting in a snapshot of the environment under study, 2) pertinent data and information was collected from a variety of sources in a timely and manageable way, providing vital information in moving forward with the project, 3) ESs provide more flexibility as opposed to other knowledge synthesis methods, 4) scanning the environment to understand what is already known and available allows for more targeted research to be conducted or interventions to be developed.

### **Conclusion**

Conducting an ES without methodological guidance is challenging, particularly when it comes to making decisions about how to robustly and comprehensively collect data. ESs have considerable potential to be a creative, responsive and comprehensive tool for knowledge synthesis in healthcare. However, further application and review are necessary for making ESs an established research methodology.

Funded by Stollery Children's Hospital Foundation, Women and Children's Health Research Institute

The Power of Partnership

Abstract # 167  
Presenter: Cunningham, Chentel  
Supervisor: Scott, Shannon  
Title: Using patient engagement to evaluate the usability of two pediatric fever tools  
  
Authors: Chentel Cunningham, Anne Le, Lisa Hartling, Shannon Scott

## Introduction

Childhood fever is one of the most common reasons parents seek emergency care for their children. Lack of parental knowledge about fever and its associated symptoms (e.g., rashes, lethargy, discomfort and tachycardia) provoke anxiety in parents, leading to several unwarranted emergency care visits. Parental knowledge translation (KT) tools (e.g., videos and infographics) have shown positive outcomes by effectively communicating complex health information in understandable formats for parents, empowering parental decision making, facilitating parental knowledge retention, and reducing unwarranted ER visits. Our team has developed a suite of parent KT tools for common childhood conditions as part of a Networks of Centres of Excellence Knowledge Mobilization Initiative, TREKK (Translating Emergency Knowledge for Kids) with fever being identified to have significant parental knowledge gaps. Therefore, we developed two parental tools (infographic and video) on childhood fever. The purpose of this study was to provide parental evaluation comparing the usability of both tools.

## Methods

Parents were recruited from urban and rural Canadian emergency department waiting rooms to evaluate one of the two KT tools on innovative iPad technology. After randomization to either tool, parents responded on a 5-point Likert scale to evaluate one of two KT tools in 8 different aspects: 1) usefulness; 2) relevance; 3) simplicity; 4) length; 5) aesthetics; 6) future use; 7) influence on health decisions 8) recommendation to others. Data were analyzed using descriptive statistics and measures of central tendency.

## Results

58 parents evaluated the KT tools (video, n=27; infographic, n=31). Participants gave overall favorable responses for both KT tools with the exception of length and future use. Participants slightly preferred the length of the infographic (M=4.20, SD=+0.85) compared to the video (M=3.93, SD=+1.04). Participants also reported more future utilization of the infographic (M=4.16, SD=+0.69) compared to the video (M=3.96, SD=+0.59).

## Conclusion

Overall, both KT tools were evaluated favourably by parents, illustrating the usefulness of both KT strategies. Scores were slightly more favorable when tools had features that allowed quicker access of health information. This study provides valuable insight for constructing useable parental KT tools in a health care setting and provides a platform for future research on parental input for refinement on these arts-based tools.

Funded by WCHRI, Stollery Children's Hospital, Networks for the Centres of Excellence, University of Alberta, TREKK, Arche

The Power of Partnership

## Strategies to enhance patients' adherence to orthodontic treatments:

### A systematic review

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### Objective

Non-adherence to orthodontic treatments is a critical population health issue both from the perspective of quality of life and health economics. The aim of this systematic review aimed to critically analyze the strategies developed and applied to Enhance Patient's Adherence to orthodontic treatments using removable appliances.

### Methods

Comprehensive electronic searches of Medline via OVID, PubMed, EMBASE, and Web of Science as well as a hand search of references were undertaken to identify relevant studies. Google Scholar was the engine elected to search for grey literature. The New Castle Ottawa quality assessment tool evaluated the level of evidence. The patient's adherence during active orthodontic treatment defines as appointment keeping, cooperating in the use of removable appliances, and oral hygiene.

### Results

Through the electronic searches, 681 article were identified. Fourteen articles were finally included in the review reporting three main types of programs to enhance patients' adherence. The first involved specific strategies for targeted health behaviors (i.e., oral hygiene). The second was patient-education modules, and the third strategy was individual-patient focused counseling techniques (e.g. motivational interviewing).

### Conclusions

This paper reveal the need for development and implementation of a comprehensive patient-centered program to enhance adherence to the treatment among orthodontic patients. Patient's social support (e.g. family and peers' endorsement) should also be considered while developing strategies to improve adherence.

**Keywords:** Adherence, Orthodontics, Oral hygiene, Appointment keeping, Appliance wearing

Abstract # 169  
Presenter: Wine, Osnat  
Supervisor: Osornio Vargas, Alvaro  
Title: What does it take to implement and shape integrated knowledge translation in an interdisciplinary research project  
Authors: Osnat Wine, Katharina Kovacs Burns, Michael van Manen, Jude Spiers, Alvaro Osornio Vargas, and on behalf of the DoMiNO project

### **Introduction**

Research on health and children's environments is complex. It requires the collaboration of diverse disciplines and knowledge users in the research process and in knowledge translation. The application of collaborative approaches, such as integrated knowledge translation (iKT), is often challenging for interdisciplinary teams. Much can be learned from an in-depth study of such processes. Based on the DoMiNO Project experience our objective is to portray what it takes to implement and shape an iKT approach.

### **Methods**

As part of a qualitative case study of the DoMiNO project iKT process, designed to learn about the essential components of iKT, data were collected using different methods over five years. Observation and project logbook were used to identify and describe the major iKT activities. Data evaluation informed the ongoing iKT process, and thematic analysis of surveys, project documents, interviews and focus groups with DoMiNO team members identified the contribution of these activities to the iKT process and the project success.

### **Results**

Different activities were required for the operation of the iKT in DoMiNO in order to ensure rapport, engagement, learning, reflection and the creation of an inclusive environment. The DoMiNO project iKT framework included: four annual face-to-face two-day meetings, multiple steering committee meetings, newsletters, webinars, evaluation and reflection activities, as well as ongoing emails, small group meetings, and informal and social meetings. Some of these activities were part of the original project plan, while others were developed in response to the project needs as identified by reflective activities and the ongoing evaluation of the iKT process. Some of the latter for example, included the design of specific discussions, workshops, webinars or tools to support joint knowledge creation and translation. Applying these activities required sufficient time, an engaged team, and an attentive management of the project, in order to plan and make changes as needed and set the tone for collaborative research.

### **Conclusion**

The findings highlight some of the aspects required for the implementation of iKT in an interdisciplinary research project. These include designated activities, on-going evaluation, responsive management, engaged team and flexibility in the iKT framework. The findings reflect the context of the DoMiNO project. However, these lessons can inform leaders, team members and knowledge users about incorporating iKT in their research practice.

Funded by WCHRI: Graduate Studentship, Patient and Community Engagement Training (PaCET), Trainee Travel; CIHR/NSERC: Collaborative Health Research Program (CHRP)

The Power of Partnership

Abstract # 170  
Presenter: Flynn, Rachel  
Supervisor: Scott, Shannon and Stevens, Bonnie  
Title: Developing rigorous evaluation approaches for the sustainability of child health interventions: Findings from an integrative review  
Authors: Rachel Flynn, Bonnie Stevens, Arjun Bains and Shannon Scott

## Introduction

Extensive research and financial efforts are spent on the development and implementation of research based interventions to improve various aspects of child healthcare. Yet little research has been done on how to sustain these research interventions to improve child health. Sustainability is the degree to which a research-based intervention continues to be used in practice after efforts of implementation have ended. There is a lack of consolidated evidence on what approaches (methods, models, theories and frameworks) are used to evaluate and measure sustainability, and lack of understanding on the instruments to measure sustainability. The aim of this integrative review is to identify and synthesize the peer-reviewed research evidence on what approaches currently exist to measure and evaluate the sustainability of health interventions. The findings from this review will inform the development of a framework to evaluate sustainability outcomes of a research-based intervention for infant pain management practices.

## Methods

An integrative review following Whittemore and Knalf's five stage methodological process was used. Using a defined inclusion and exclusion criteria, two reviewers completed a two-phase screening process. We used the Mixed Methods Appraisal Tool (MMAT) to assess the methodological quality of the included studies. Published studies in peer reviewed journals were included.

## Results

Forty-nine primary research studies were included. 57% of included studies used a qualitative research design to evaluate sustainability. There was variability in approaches to evaluate sustainability. Of the 51 included studies, 17 used methods, 15 used a framework, 10 used a model, 4 used a tool, 3 used a theory and 2 used an instrument as the selected approach to evaluate sustainability. The most commonly reported theories were: Normalization Process Theory (NPT) (n=3), NHS Sustainability Model (NHS SM) (n=3), the Dynamic Sustainability Framework (DSF) (n=3). Only two frameworks were used in more than one study, the DSF (n=2) and CFIR (n=2). The NHS SM was the most applied model to evaluate sustainability (n=4). The PSAT was the most reported tool (n=3). There was high variation in the approaches, methods and timing of sustainability evaluations, indicating the absence of standard practices. The most reported barriers to sustainability were: Lack of resources (human, financial, infrastructure) (n=15) staff workload and/or turnover (n=10), complexity (n=5) and competing priorities (n=5). The most reported facilitators to sustainability were: Resources (human, financial, infrastructure) (n=16), leadership approach & commitment (n= 16), observed patient benefits and program efficacy (n=13), compatibility "fit" "integration" of initiative to current ways of working/ context (n=14).

## Conclusion

This evidence will contribute to the methodological advancement of sustainability for implementation research. This research will also inform the sustainability evaluation of a research-based intervention to improve infant pain management. This research is important to help develop more rigorous approaches to evaluate the sustainability of interventions.

Funded by WCHRI Postdoctoral Fellowship and Faculty of Nursing Postdoctoral Fellowship, University of Alberta

The Power of Partnership

Abstract # 171  
Presenter: Zare, Alaa  
Supervisor: Postovit, Lynne and Dyck, Jason  
Title: RIPK2 role in promoting inflammatory breast cancer tumorigenesis  
  
Authors: Alaa Zare

### **Introduction**

Inflammatory breast cancer (IBC) is a rare and aggressive form of breast cancer that accounts for approximately 1–5% of all breast cancers but 10% of all breast cancer specific mortality. Approximately, 20-30% of IBC patients are presented with distant metastasis at diagnosis. Despite improvements in identifying IBC as a different subtype of breast cancer, the intricate cellular mechanisms underlying the aggressiveness of this disease is still unknown. Thus, elucidating the biologic and molecular characteristics of IBC should aid in earlier diagnosis and improve patient overall outcome. Given the role of the receptor tyrosine kinase (RIPK2) in many inflammatory diseases including cancer, my aim is to understand the function of RIPK2 in IBC tumorigenesis. I hypothesize that RIPK2 promotes cell growth, invasion, metastasis, and cytokine increase in IBC.

### **Methods**

Utilizing IBC cell models and patient tumor samples, I have determined the presence of an increased level of active RIPK2 using western blot and immunohistochemistry, respectively.

### **Results**

As a result of the activation of RIPK2 (and most likely others), elevated production of pro-inflammatory cytokines and growth factors were found in IBC cell culture supernatant suggesting a contribution to molecular inflammation and metastasis of IBC.

### **Conclusion**

To fully understand the importance of RIPK2 in my IBC cell model, I'm working on constructing stable Ripk2 knockout using Cas9/gRNA Ribonucleoproteins (RNPs) genome engineering. Successful clones with Ripk2 deletion will be examined for (a) cell proliferation, (b) invasion, (c) metastasis and (d) cytokine level. All of these functional assays will elucidate the role of RIPK2 in the invasion-metastasis cascade that is known to correlate with cancer poor prognosis.

Funded by Saudi Arabia ministry of higher education

The Power of Partnership



Abstract # 172  
Presenter: O'Reilly, Amanda  
Supervisor: Kelly, Erin  
Title: **Effectiveness of pelvic floor muscle injections for chronic pelvic pain: A systematic review and narrative analysis**  
Authors: **A. O'Reilly, S. Zhu, S. Campbell, L. Sadownik, E. Kelly**

### **Introduction**

Chronic pelvic pain is a very complex, debilitating condition for women. One recognized etiology is myofascial pelvic pain, which refers to pain in the muscles, connective tissue, and surrounding fascia of the pelvic floor. Intramuscular injections with local anesthetics or botulinum toxin have emerged as a novel treatment strategy for this condition. While initial reports have been positive, there are no standardized guidelines for treatment with injectable therapies. Our aim was to establish an evidence-based synthesis of what is known about this treatment to inform clinical practice and future research.

### **Methods**

Participants included women with chronic pelvic pain. The intervention was any regimen of injectable medication infiltrated into pelvic floor muscles. The primary outcome was improvement in pelvic pain. A medical librarian searched 8 databases from inception through April 2019. Hand searches of abstracts from research meetings, reference lists from relevant review articles, and reference lists of the included studies were performed. After removal of duplicates, citations retrieved from the search were screened by title and abstract. Two independent reviewers assessed full texts for eligibility. Disagreements were resolved by consensus. Relevant data were collected from each included study using a standardized data extraction form. Risk of bias assessment was performed. Data were synthesized qualitatively.

### **Results**

841 articles were identified by the database search. After removal of duplicates, 692 abstracts were reviewed for eligibility. After excluding review articles and irrelevant abstracts, 187 full text articles were reviewed. Of these, 37 studies met our inclusion criteria. In addition, 12 studies were retrieved from hand searching, for a total of 49 articles. 9 studies were randomized controlled trials, 30 were cohort studies, and 10 were case reports. Of the included studies, 10 involved local anesthetics, 31 botulinum toxin, and 8 involved injections of both. Varying injection regimens were used. Overall, significant improvements in chronic pain were reported by all but three of the articles. Of note, the randomized controlled trials of both injectable local anesthetics and botulinum toxin reported statistically significant improvements in pain scores compared with each group's baseline scores. However, none of the trials demonstrated statistically significant differences in pain scores when compared with placebo treatments (most commonly saline injections). Adverse effects were generally mild and of limited duration and the treatments were well tolerated. The studies were of variable quality.

### **Conclusion**

Emerging evidence suggests that intramuscular injections of either local anesthetics or botulinum toxin may be effective interventions for the management of chronic pelvic pain. The treatment appears to be safe and well tolerated. Future research should aim to clarify the effectiveness of these injectable medications in comparison to that of placebo injections into the pelvic floor.

Funded by **None**

The Power of Partnership

Abstract # 173  
Presenter: Mevawala, Aynah  
Supervisor: Richter, Solina  
Title: A Transition theory perspective of menopause in a developing context

Authors: Aynah Mevawala and Solina Richter

## Introduction

Women experience several physiological changes during the midlife. These are mainly related to the pre-, peri- and post-menopausal symptoms that have an impact on their physical and psychological well-being, as well as their quality of life. Midlife women from diverse cultures differ in behaviors, values and beliefs related to their life experiences, and management of menopausal symptoms. Pakistani women tend to use a combination of modern medicine and self-care practices to promote health and prevent disease. There is limited research in the Pakistani context related to the management of menopause. The purpose of this study was to explore Pakistani, urban, Muslim midlife women's experiences of menopause and to acquire a deeper understanding of menopause and associated management strategies. This presentation will discuss the Transition theory as the most relevant theoretical approach to the study on Pakistani, urban, Muslim midlife women's experience of menopause.

## Methods

A focused ethnography research design was used. 20 Pakistani, Muslim midlife women were recruited through purposive and snowball sampling between December 2017 and March 2018. All participants were residents of urban Karachi. In-depth, semi-structured interviews were conducted. Mandatory ethical considerations were followed in the study. The data were managed using Quirkos qualitative data management software. Thematic content analysis was conducted.

## Results

The Transition theory by Meleis, Sawyer, Im, Schumacher, and Messias (2000) was found most relevant to the study. Menopause is a transition phase of life and cannot be experienced in isolation. The experience is based on multiple factors including, the women's cultural, religious, familial, and social beliefs and understanding. Menopause has multiple, related and simultaneous patterns of transitions. Menopause is a complex process as it brings about changes in different aspects of women's life. Women in this study experienced menopause in their own unique ways depending on several factors such as their sociocultural and religious understanding of menopause; the nature of their work, their work environment and position at work, the level of their physical, mental, emotional and social support system through family, friends, colleagues and significant others; their role change, and their experiential perception associated with menopause. Transition has various important properties i.e. awareness, engagement, change and difference, time span of transition, and critical points and events. In this study, women's level of awareness varied based on the degree of freedom of speech or silence they observed related to their menopause experience, their transition time span differed according to the length of time they experienced menopause symptoms. Women's critical points and events were contingent upon their personal, familial and societal circumstances.

## Conclusion

Each woman is unique and so are their experiences. The robust socio-cultural, religious and familial ties that are strongly ingrained in the Pakistani setting influenced Pakistani women's beliefs, perceptions and actions. Menopause experiences of Pakistani urban midlife Muslim women were multiple and complex in nature that did not occur in isolation. These were in combination with other developmental situational

Funded by -

Abstract # 174  
Presenter: Manz, Joren  
Supervisor: Hyakutake, Momoe  
Title: Cannabis use among women with chronic pelvic pain  
  
Authors: Joren Manz, Momoe Hyakutake, Erin Kelly

### **Introduction**

Chronic pelvic pain (CPP) is a debilitating condition affecting women worldwide that is characterised as non-cyclical pelvic pain lasting a minimum of 6 months. Its management requires a bundle approach of various pain modulators, including cannabinoids. Cannabis has been shown to reduce pain levels in various studies and has shown effectiveness in treating chronic pain conditions, as well as lowering the dosing and prescribing of other analgesics, including opioids. Unfortunately, there is no literature on the use and efficacy of cannabis in women with CPP.

### **Methods**

Outpatients in the CPP clinic were contacted in clinic and emailed an online questionnaire to survey their pain experience and use of cannabis.

### **Results**

Of the 23 responses received, 35% reported using cannabis and 39% of non-users reported wanting to try it. Among users, 71% reported pain relief, 80% an improvement of sleep, and 51% reported a positive effect on their quality of life. Effect on friendships/social life, mental health, and work/studies all reported either a positive or no effects. Side effects were reported in 57% of patients and included cough, anxiety, and increased appetite. 29% of those using cannabis reported decreasing their use of opioid and non-opioid based analgesics, antidepressants, and NSAIDs.

### **Conclusion**

Many women use cannabis to deal with CPP and related issues. Our outpatient survey reported minimal side effects when using cannabis. Benefits included improvement in sleep, chronic and acute pain, mood, social/family life, and quality of life. Cannabis should be considered for women suffering from CPP, and further research into this area is required and encouraged.

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The Power of Partnership

Abstract # 175  
Presenter: Babyn, Katherine  
Supervisor: Yuksel, Nese  
Title: Exploring cannabis use in women's health: A scoping review

Authors: Katherine Babyn, XueQing Jiang, Pat Mayo, Nese Yuksel

## Introduction

At each reproductive health stage, from menstruation to menopause, a woman may experience medical conditions or symptoms requiring therapeutic interventions. With the recent Canadian legalization and increased promotion of products, cannabis is quickly becoming a socially accepted substance with increased patient interest to use for symptom management. Clinical guidelines on the use of medical cannabinoids currently do not address women's health conditions. Our objectives were to explore existing scientific literature to summarize published evidence on cannabis use in adult women, identify findings related to efficacy and safety of cannabis use, and describe related women's perspectives.

## Methods

We completed a scoping review using the PRISMA-ScR checklist. Electronic databases were systematically searched, including MEDLINE, EMBASE, CINAHL, and Cochrane Library, from inception to September 2018 for relevant articles. Grey literature was searched including ProQuest Dissertations & Theses Global and Google Scholar. Keywords were derived from cannabis and women's health topics, including "cannabis, marijuana, cannabinoids" and "women's health, menstruation, perinatal, maternal, menopause". Recreational and medical cannabis was included within the search process. Hand search of bibliographies for additional articles was completed. Exclusion criteria included: non-English articles, review articles or conference abstracts without full-text publishing, infant/pediatric populations, and studies specific to cannabis use disorder, withdrawal effects or policy development. Screening involved title/abstract, followed by full-text review. Data extraction provided narrative summaries and categorization of evidence to date.

## Results

After screening, 46 articles met the inclusion criteria and were categorized into three topic areas: efficacy of cannabis use, safety/risks of cannabis use, and perspectives/beliefs of women who use cannabis. Studies were published between 1976 and 2018, with the majority from the United States (n=37) or Canada (n=6). The reproductive health stages investigated were menstruation (n=9), pregnancy (n=25), breastfeeding (n=2), menopause (n=3), and remaining did not specify or were studies investigating sex-differentiating effects. Adverse outcomes from cannabis use during pregnancy was the most common area explored in literature. Five studies mentioned medical cannabis use specifically.

## Conclusion

There is a lack of evidence on cannabis for therapeutic use in women's health. Future work in understanding the experiences of women who use cannabis for symptom management of their women's health-related conditions will provide user insight to cannabis efficacy.

Funded by Faculty of Pharmacy and Pharmaceutical Sciences

The Power of Partnership

Abstract # 176  
Presenter: Lee, Lara  
Supervisor: Postovit, Lynne  
Title: Characterization of epigenetic and transcriptomic alterations in hypoxia induced breast cancer cell plasticity  
Authors: Lee, L., Postovit, L.

### **Introduction**

Breast cancer is the second leading cause of death from cancer in Canadian women and metastasis is the primary cause of cancer mortality. Phenotypic plasticity affords cancer cells with the ability to metastasize and resist therapies, leading to reduced survival in patients. Dynamic regulation of gene expression can be mediated through the epigenome, which is essential for establishing cell fate both in contexts of developmental biology and disease. A tumor micro-environmental factor that can alter the epigenome and transcriptome, as well as lead to an induction of plasticity is hypoxia, a condition of low oxygen.

### **Methods**

Here we apply a combination of imaging and high through-put sequencing methods to address how the epigenomes of breast cancer cells respond to hypoxia by examining the alterations in histone modifications in concert with the resulting transcriptional response. T47D and MDA-MB-231 breast cancer cell lines, epithelial and mesenchymal-like respectively, were used.

### **Results**

We observed an enrichment of heterochromatin, both through electron spectroscopic imaging and immuno-fluorescence imaging, particularly near the nuclear periphery in response to hypoxia (0.5% O<sub>2</sub>, 48 hours). Furthermore, at epithelial-to-mesenchymal transition markers and stem cell markers, surrogates for measuring cancer cell plasticity, there is an increase in active histone (H3K4me3) marks upstream of the TSS with concordant transcriptional up-regulation post hypoxia treatment.

### **Conclusion**

Taken together, our findings indicate that global epigenetic reprogramming accompanies the hypoxic response, and further suggests the association of epigenetic alterations with the induction of plasticity. Elucidating the nuanced cellular response to hypoxia and the role of the epigenome in this response will better our understanding of hypoxia induced cancer cell plasticity.

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The Power of Partnership

Abstract # 177  
Presenter: Prachi Shah  
Supervisor: Beate Sydora  
Title: **The Walk-and-Talk app: Physical and mental health benefits of a social app for menopausal women**  
Authors: Prachi Shah, Orest Cokan, Dr. Eleni Stroulia, Dr. Sue Ross, Dr. Beate Sydora

### **Introduction**

Menopause is the end of a woman's menstrual cycle and reproductive years. Some women struggle with various symptoms during the menopause transition. Regular walking exercise can be an easy way to maintain physical and mental health during and after menopause. Previous focus groups with women recruited from Edmonton Menopause clinics revealed that women enjoy and want the social aspect of walking groups. We have developed a mobile application (the Walk-and-Talk app) through which women can connect with each other and schedule walks around Edmonton and track changes to their menopause symptoms. The overall goals of this participatory research study are (a) to evaluate the usability of the app, and (b) its effectiveness in terms of mitigating mental health and menopausal symptoms. Results from the focus groups are presented.

### **Methods**

We invited women previously interested in menopause walking therapy to attend focus groups. At the focus groups, attendees were presented with the app features. During the focus group discussions, participants provided feedback on possible changes/additions. Data were collected from audio-recorded discussions and surveys. Women were invited to test the restricted login, walk-scheduling feature and complete initial surveys and questionnaires including menopause-specific symptom and validated quality of life (QOL) questionnaires. The study was approved by the UofA Research Ethics Board (Pro00091271).

### **Results**

Out of 80 women contacted, 55 (69%) responded and 31 (56% of respondents) expressed an interest in the app. Nine women were available for focus groups. Focus group attendees found the app useful and were eager to try it. They especially liked the social aspect of it and being able to track their symptoms. The main suggested change was adding reviews on walking locations that could be seen by other users. Focus groups revealed what features women want to see in the app and changes were made accordingly.

### **Conclusion**

The Walk and Talk app was well appreciated by focus group participants in menopause transition and postmenopause as a means to connect for walking exercises. Women believed the app would be useful and effective to track symptom changes and facilitate improved menopause symptom management. We plan to track app use and follow women's progress on physical and mental health through the data collected from the questionnaires. The app is undergoing further development and has the potential to help women start and maintain an exercise habit, and ultimately of generating a positive impact on women's health.

Funded by AIHS Summer Studentship Award, WCHRI Summer Studentship Award

The Power of Partnership

Abstract # 178  
Presenter: Panigrahi, Rashmi  
Supervisor: Glover, Mark  
Title: **INSIGHT into the nucleosomal dynamics- the first step in DNA damage response signaling**  
Authors: **Rashmi Panigrahi, MdTohidul Apu Islam, Morenike Ajidagba, Ayodeji Kulepa, Ross Edwards, Mark Glover**

### **Introduction**

Cancer, specifically that affect the ovary and the breast, is a public health problem of critical proportions that affects Albertan women. DNA damage response and histone modifications in chromosomes are frequently altered in cancer, thus contributing to the etiology and progression of tumors. The orderly recruitment and disassembly of DNA damage repair (DDR) proteins at the damage foci are conserved in eukaryotes. However, the intricate mechanism of this cascade remains to be defined. Developing therapeutic approaches to combat cancer necessitates a deeper mechanistic understanding of the interaction of DNA repair proteins with nucleosomes (the basic unit of a chromosome). In human, H2AX, a histone variant exists in the nucleosomes, which is necessary for the recruitment of DDR factors. This variant has a C-terminal motif that is phosphorylated by DNA protein kinases on serine 139 (forming  $\gamma$ H2AX), an indication of DNA double-strand break (DSB) recognition. Formation of  $\gamma$ H2AX leads to recruitment of the Mediator of DNA damage checkpoint protein 1 (MDC1), an early player in the DDR pathway. MDC1 knockout phenotypes present significant genomic instability. Structural details underlying the interaction of the phosphorylated C-terminal tail of H2AX with BRCT domain of MDC1 has been previously studied by our lab.

This study aims at investigating the nucleosome dynamics underlying MDC1 and  $\gamma$ H2AX containing nucleosome interaction.

### **Methods**

We have used bacterial cloning and protein purification techniques for large-scale production of recombinant nucleosomes. We have accessed the homogeneity of the assembled complexes using size exclusion chromatography assisted with multi-angle light scattering detector (SEC-MALS). Further, we are using the small-angle X-ray scattering technique to visualize the dynamics of the complexes.

### **Results**

Other labs have previously prepared nucleosomes using refolding technique. In this project, firstly, we have developed a novel bacterial co-expression system to produce milligram quantities of nucleosomes. Secondly, we developed a protocol to prepare nucleosomes containing H2AX, which contain phosphorylated serine 139. Thirdly, we have identified conditions necessary for the homogeneous assembly of MDC1 BRCT domain-phosphorylated nucleosome complex. Finally, solution scattering studies are being undertaken to visualize the dynamics.

### **Conclusion**

We have successfully prepared macromolecular assembly of the nucleosome bound to MDC1, suitable for structural studies. This focused study aims to unravel the enigmatic link between nucleosome phosphorylation followed by its interaction with the DDR associated player, MDC1 and the consequential nucleosome dynamics. The current study will add to existing knowledge on nucleosome dynamics during DDR and thus provide targets for the design of DDR specific inhibitors.

Funded by **Canadian Institutes of Health Research (CIHR)**  
**National Institutes of Health (NIH)**

The Power of Partnership

Abstract # 179  
Presenter: Choi, Won-Shik (Daniel)  
Supervisor: Godbout, Roseline  
Title: Investigating retinoic acid resistance in HER2-enriched breast cancer: The role of MYC  
  
Authors: Won-Shik Choi, Rong-Zong Liu, Roseline Godbout

## Introduction

HER2-positive (HER2+) breast cancers express high levels of the growth-promoting HER2 protein on their cell surface. The development of a targeted drug, trastuzumab, has greatly improved the clinical outcome for HER2+ patients. However, intrinsic and acquired resistance to trastuzumab are common, with cancer stem cells known to drive resistance to trastuzumab treatment. Retinoic acid (RA) induces cancer stem cell differentiation, suggesting possible synergistic action with trastuzumab for the elimination of HER2+ breast cancer stem cells. A number of genes regulate RA activity, including RA receptors which function as transcription factors (e.g. RARalpha and PPARbeta), and RA binding proteins CRABP2 and FABP5, which deliver RA to RARalpha and PPARbeta, respectively. RARalpha and PPARbeta have opposite functions, with RARalpha promoting differentiation and PPARbeta promoting proliferation in response to RA. The HER2 gene (ERBB2) is frequently co-amplified with the gene encoding RARalpha in HER2+ breast cancer. It is surprising, therefore, that HER2+ breast cancers are refractory to RA treatment.

MYC is an oncogene that inhibits RARalpha activity in leukemia cells. MYC also upregulates the RA-binding protein FABP5. Importantly, MYC is preferentially amplified and overexpressed in HER2+ breast cancers. My research aims to elucidate the mechanism underlying RA resistance in HER2+ breast cancers, with a special focus on the role of MYC. Hypothesis: MYC regulates RA action through inhibition of the CRABP2-RARalpha pathway and activation of the FABP5-PPARbeta pathway.

## Methods

RNA levels of MYC, RARalpha, and HER2 were examined in a panel of 20 human breast cancer cell lines. Using TCGA gene profiling datasets, correlations between the expression of MYC and that of HER2, RA transcription factors, and RA binding proteins were investigated. MYC levels were manipulated in selected HER2-enriched breast cancer cells using expression vectors and siRNAs. These cells were then subjected to RA treatment. Cell proliferation was measured using the crystal violet assay. RAR activation was measured using the luciferase reporter assay.

## Results

MYC is preferentially amplified in HER2+ breast cancers and its RNA levels are positively and negatively correlated with FABP5 and CRABP2 expression, respectively. Depletion of MYC in HER2+ breast cancer cells decreases FABP5 levels, and upregulates CRABP2. These results support a role for MYC in promoting the pro-tumourigenic FABP5-PPARbeta pathway, while inhibiting the anti-tumourigenic CRABP2-RARalpha pathway. Furthermore, depletion of MYC also sensitizes RA-resistant HER2+ breast cancer cells to RA-induced cell killing.

## Conclusion

MYC attenuates the anti-cancer effects of RA by inhibiting CRABP2-RARalpha pathway in HER2+ breast cancer cells. This study will shed light on the role and mechanism of MYC in governing RA resistance in HER2+ breast cancer cells. Our results may support the use of RA and trastuzumab for the treatment of subsets of patients with HER2+/low MYC breast cancers.

Funded by Food and Health Innovation Initiative, Canadian Cancer Society Research Institute, and Women & Health Research Institute

The Power of Partnership



Abstract # 180  
Presenter: Thompson, Alexa  
Supervisor: Dacks, Joel  
Title: Candidate gene discovery for pregnancy-associated malaria using RNA sequencing

Authors: L. Alexa Thompson, Sedami Gnidehou, Joel B Dacks.

### Introduction

Malaria infects millions of people every year worldwide. Caused most severely by the parasite *Plasmodium falciparum*, pregnant women and children are especially susceptible to infection and the life-threatening complications that accompany it. A specific subset of malaria called pregnancy-associated malaria occurs when the parasite infects maternal erythrocytes (red blood cells) and then travels to and infects the placenta. Binding and adhesion of the infected erythrocytes to the placenta is mediated by a protein called VAR2CSA. As the main virulence factor in pregnancy-associated malaria, VAR2CSA is a widely accepted vaccine candidate against this disease. However, knockout of VAR2CSA doesn't inhibit total binding of infected erythrocytes to the placenta, indicating that there are still other proteins involved in the process. Our research focuses on identifying other proteins that are co-expressed and upregulated with VAR2CSA during placental infection in an attempt to uncover other potential therapeutic targets

### Methods

Here we propose to utilize high-throughput RNA sequencing and advanced bioinformatics in a comparative approach between *P.falciparum* infected erythrocytes and non-placental bound *P.falciparum* infected erythrocytes to identify candidate genes involved in VAR2CSA mediated placental infection.

### Results

RNA from placental-bound *P.falciparum* infected erythrocytes demonstrated a high level (>99%) of human RNA contamination, leading to an under-represented amount of genes able to be mapped to the *P.falciparum* genome for comparison. Conversely, a high level (>99%) of RNA from non-placental bound *P.falciparum* infected erythrocytes was mapped to the *Plasmodium* genome and expressed a different *Plasmodium var* family gene, as expected.

### Conclusion

Further research is required to identify transcripts that are upregulated and co-expressed with *var2csa* in placental-bound infected erythrocytes. Future experiments will need to include re-selection of placental bound strains and qPCR analysis to confirm the upregulation of *var2csa* and subsequent candidate target genes, prior to further RNA sequencing. Once *Plasmodium* gene enrichment occurs in the selected strains, RNA sequencing and analysis can be carried out and the differential expression between placental-bound and non-placental bound infected erythrocytes can be deduced.

Funded by WCHRI Summer Studentship and Faculty of Medicine and Dentistry Studentship in Placental Research.

The Power of Partnership

Abstract # 181  
Presenter: Wooldridge, Amy  
Supervisor: Davidge, Sandra  
Title: Effects of prenatal hypoxia exposure on pregnancy outcomes in offspring later in life

Authors: Amy Wooldridge, Nataliia Hula, Raven Kirschenman, Floor Spaans, Christy-Lynn Cooke, Sandra Davidge

### Introduction

Maternal exposure to a hypoxic environment during pregnancy causes pregnancy complications such as maternal preeclampsia and intrauterine growth restriction. Adverse effects on offspring neurodevelopmental, metabolic and cardiovascular health have been well-studied. Recent reports indicate that female offspring of rat dams exposed to hypoxia in utero show signs of accelerated aging within their ovaries and oviducts. This suggests that the fertility and reproductive outcomes of female rats dams exposed to maternal hypoxia are worsened, however this has not been directly confirmed. We hypothesized that the female offspring from hypoxia dams would have poorer pregnancy outcomes than adult female offspring from normoxia dams.

### Methods

Pregnant Sprague-Dawley rats were exposed to either hypoxia (11% oxygen) or normoxia (21% oxygen) from gestational day (GD) 15-21 (term=GD22). After weaning, female offspring (n=4/group) were aged to four months (i.e. young adult age) and mated. At GD20, pregnancy outcomes were recorded in the adult female offspring born to hypoxic and normoxic (control) pregnancies.

### Results

To date, breeding success for female offspring born from hypoxic pregnancies was reduced compared to control female offspring born from normoxic pregnancies. We have had n=4 control rats carry pregnancies, but only n=2 of the n=4 mated female offspring from hypoxic pregnancies were carrying pregnancies on GD20. Due to low numbers of pregnancies in female rats from hypoxic pregnancies, we can only report descriptive results. The two female offspring from hypoxic pregnancies that were not pregnant after positive plug testing had no reabsorption sites and both had fluid in their uterus – one was confirmed pyometria. Of the rats that did carry pregnancies, control dams had a median litter size of 16 (range 15-17), whereas dams from hypoxic pregnancies had litter sizes of 13 and 5. One pregnant dam from a hypoxic pregnancy had a left ovarian cyst and the left side of the uterus appeared like a non-pregnant uterus, including small uterine arteries. Fetal and placental weight, and fetal:placental weight ratios appeared similar between groups. Average crown-rump lengths of fetuses carried by dams from hypoxic pregnancies were both 3.8 cm, were smaller than from those carried by control dams, which had median crown-rump lengths of 4.7 cm (range 4.5-4.8 cm). Average fetal abdominal girths from dams from hypoxic pregnancies were 4.5 and 4.7 cm, and were larger than those from control dams, which had a median of 3.7 cm (range 3.6-3.9 cm).

### Conclusion

Our preliminary results support that there are poor fertility and pregnancy outcomes in rat dams exposed in utero to maternal hypoxia, and our results thus far emphasize the striking effect of a single in utero insult on later-life reproductive health. Increasing our n-numbers will enable us to statistically confirm these observations. Lack of reabsorption sites and uterine fluid in hypoxia rats that were not successfully pregnant may inform on mechanisms behind poor reproductive outcomes. We are assessing vascular function and structure to determine if these contributed to the poor fertility and pregnancy outcomes.

Funded by CIHR, WCHRI

The Power of Partnership

Abstract # 182  
Presenter: Nguyen, Jasmine  
Supervisor: Riddell, Meghan  
Title: **Vibratome sectioning of term placenta for analysis of epithelial cell polarity in the intact syncytium**  
Authors: Jasmine Nguyen, Saba Saadat, Collete Watkins, Meghan Riddell

### **Introduction**

The placenta is a vital organ that develops during pregnancy and provides nutrients to and removes waste from the growing fetus. This essential exchange occurs at the placenta's epithelium, which lines the outer surface of the placenta and is composed of a single, giant, multinucleated epithelial cell called the syncytiotrophoblast (ST).

While the epithelium of most organs is composed of a dense population of individual cells, the placental epithelium differs greatly in that it consists entirely of the singular ST with no lateral borders. Lateral borders are typically crucial in the maintenance of cell polarity in other tissues and thus, they are essential for the proper exchange of waste and nutrients. The ST, despite lacking lateral borders, is highly polarized in order to support fetal life, but the mechanisms that control this polarity remain completely unknown.

The aim of this project was to optimise a novel technique that will allow for analysis of the 3D localisation of proteins in the placenta for future examination of the mechanisms governing cell polarity in the ST.

### **Methods**

In order to visualise the 3D structure of the placenta, sectioning using a vibratome was optimised for analysis with immunofluorescent staining and confocal microscopy. Fixation, blocking buffer conditions, and embedding medium were optimised for thick placental sections. Vibratome blade frequency, speed, angle, and section size were also refined alongside this. The sections were then stained with antibodies and imaged with confocal microscopy.

### **Results**

Through optimisation of this technique, we have been able to consistently generate reproducible images of the ST through confocal microscopy and analysis via Volocity. These images allow for the direct visualization of both the placental villi in the intact syncytium and the expression and colocalization of placental proteins in situ.

### **Conclusion**

Combining vibratome sectioning and confocal microscopy will be a powerful tool in understanding both the colocalization of different proteins in intact tissue and how the activation or expression of these proteins changes under different treatment conditions or maladies. In the future, this technique will be used in combination with placental explants to test further hypotheses regarding epithelial cell polarity in the syncytium.

Funded by Women and Children's Health Research Institute, Royal Alexandra Hospital Foundation, Stollery Children's Hospital Foundation, UAlberta Faculty of Medicine and Dentistry

The Power of Partnership

Abstract # 183  
Presenter: Kang, Jimmy  
Supervisor: Hornberger, Lisa  
Title: **Impact of biological sex on the surgical outcomes for congenital heart disease patients with adverse early life events**  
Authors: Jimmy Kang, Amanda Cao, Deliwe Negwezi, Daniel Garros, Dominic Cave, Luke Eckersley, Lisa Hornberger

### **Introduction**

Infants with adverse early life exposures (AELEs) have worse surgical outcomes associated with congenital heart disease (CHD). Although never shown in humans, animal investigations suggest AELEs contribute to cardiac remodeling and impaired post ischemic recovery more pronounced in males. Whether worse ischemic reperfusion injury (IRI) occurs in infants with AELEs undergoing cardiopulmonary bypass (CPB) has not yet been explored. Therefore, we sought to evaluate the impact of AELEs and biological sex on early operative outcomes associated with CPB surgery for CHD at <1 year.

### **Methods**

Methods: We identified Albertan infants who underwent CPB for CHD at <1 year between 2007-2018 at our institution. AELEs included birth to a diabetic mother (IDM), preterm birth (<37 weeks), and/or small for gestational age (birth weight <5%ile). We included infants with and without (controls) AELE. Prenatal, birth and surgical outcomes were reviewed. We compared Pediatric Risk of Mortality Scores (PRISM) (higher=worse), a measure of hemodynamic instability in the 1st 24 hours post CPB, total CPB and cross-clamp (CC) times and 20 other hemodynamic measures in the first 24-48 hours of surgery.

### **Results**

528 infants were included, 209 with (49.3% male) and 319 without (59.9% male) AELEs. Overall, AELE infants demonstrated marginally higher PRISM scores (AELE 8.47+/-5.20 vs control 7.94+/-5.18, p=0.15). However, among infants with a CPB time of >100 minutes, AELE males (n=55) had significantly higher PRISM scores compared to AELE females (n=70) (10.9+/-5.62 vs 8.71+/-5.18, respectively p=0.03). When examining lesions individually, atrioventricular septal defect had the largest number of patients and showed male AELE (n=14) having significantly higher PRISM scores compared to female AELE patients (n=21) (10.07+/-4.04 vs 7.38+/-4.63, respectively p=0.03).

### **Conclusion**

AELEs potentially contribute to increased IRI in CHD which may be worse in males exposed to longer CPB times. Further analyses are underway exploring other measures of hemodynamic stability and surgical outcomes associated with AELE in CHD.

Funded by N/A

The Power of Partnership

Abstract # 184  
Presenter: Stretch, Kendyl  
Supervisor: Bell, Rhonda C.  
Title: Women in Alberta are surpassing iron recommendations during pregnancy

Authors: Kendyl Stretch, Taylor Clements, Michelle Mackenzie, Megan Jarman, Rhonda C. Bell and the APrON study team

### Introduction

Iron is an important nutrient during pregnancy as it is required for expanding maternal red blood cell mass and for the growth and development of the fetus. Inadequate iron intake can result in the development of iron deficiency anemia, which is associated with adverse pregnancy and birth outcomes. In order to meet iron needs, it is recommended that women consume 27 mg of iron/day from a combination of diet and supplements. How much iron Canadian women consume is not known. The aim of this study is to describe the contributions of diet and supplements to total iron intake in a cohort of pregnant women who participated in the Alberta Pregnancy Outcomes and Nutrition (APrON) study.

### Methods

Diet and supplement information was collected during each trimester from pregnant women in the APrON study, a prospective cohort study. Dietary iron intake was collected using 24 hour recalls and calculated using Food Processor. Foods were categorized according to whether they contained heme and/or non-heme iron. Iron intake from supplements was collected using questionnaires and iron content was determined using the Licensed Natural Health Product Database (LNHPD) and manufacturer's websites. Descriptive statistics (mean and standard deviation) were calculated using Excel.

### Results

Data was included from women who provided both diet and supplement information in the first (T1; n=535), second (T2; n=2043) and third trimester (T3; n=1753). The average iron intakes from food (mg/d) were  $14.2 \pm 5.6$  in T1,  $15.2 \pm 6.0$  in T2 and  $15.5 \pm 6.0$  in T3. Non-heme iron made up 89%, 84% and 87% of total iron intake, in T1, T2 and T3 respectively. In all trimesters ~95% of women were taking iron containing supplements. The average intakes of supplemental iron (mg/d) were  $23.7 \pm 17.3$  in T1,  $27.2 \pm 20.1$  in T2 and  $34.0 \pm 28.4$  in T3. The average intakes of supplemental and dietary iron (mg/d) combined were  $37.9 \pm 18.8$  in T1,  $42.4 \pm 21.1$  in T2 and  $49.5 \pm 28.9$  in T3. With diet and supplements combined 76%, 86% and 88% of women exceeded the recommendations of 27 mg/day in T1, T2 and T3 respectively.

### Conclusion

Very few women in the APrON study were meeting iron recommendations from food alone. However, nearly all of the women were taking iron containing supplements which led to the majority of women exceeding the recommendations of 27 mg/day. In the future we will combine this data with iron-related biomarkers and pregnancy/ birth outcomes to understand the effects iron intake has on iron status and maternal and fetal health.

Funded by APrON was funded by Alberta Innovates Health Solutions

The Power of Partnership

Abstract # 185  
Presenter: Webster, Kirsten  
Supervisor: Hemmings, Denise  
Title: Sphingosine 1-phosphate as a mediator of tumour necrosis factor- $\alpha$  signalling in placental development  
Authors: Kirsten Webster, Yuliya Fakhr, Denise G. Hemmings

### Introduction

Preeclampsia (PE) is a multisystem pregnancy disorder characterized by hypertension and end organ damage. In PE, low fusion rates and increased apoptosis of trophoblasts leads to poor placental barrier formation and hence poor oxygen transfer to the fetus. One factor that leads to this poor syncytialization, or barrier formation, is the inflammatory cytokine, tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ). In endothelial cells, TNF- $\alpha$  mediates its apoptotic effects through a bioactive sphingolipid, sphingosine 1-phosphate (S1P). At increased concentrations, each factor independently induces apoptosis of placental trophoblasts and inhibits syncytialization. While we know that both factors are elevated in the plasma and placentas of mothers with PE, we do not know if TNF- $\alpha$  signals through S1P to mediate its effects in placental cells. Because TNF- $\alpha$  blockers cannot be used during pregnancy due to detrimental side effects, we are investigating SK1, the S1P synthesizing enzyme, and S1PR1, an anti-apoptotic S1PR, as potential downstream factors to target to improve syncytialization in PE. We hypothesize that elevated levels of TNF- $\alpha$  will decrease syncytialization, increase SK1 expression, and decrease S1PR1 expression in term placental chorionic explants, a physiological placental tissue culture model.

### Methods

To evaluate the role of TNF- $\alpha$  and S1P in syncytialization, we needed to determine how many days of incubation were needed for the multinucleated syncytium to fully shed. Chorionic explants were first incubated at 37°C for up to 8 days without treatment (n=2). Explants were then fixed and visualized with immunofluorescence microscopy using DAPI, a nuclear stain, and E-cadherin, a cell membrane stain. The syncytium was fully shed at day 4. Thus, explants were treated with or without 1 ng/mL of TNF- $\alpha$  for up to 48 hours after 4 days of incubation (n=2). SK1 and S1PR1 mRNA expression in the cultured explants was quantified using qRT-PCR, relative to the expression of the housekeeping gene HPRT1. To examine the effect of TNF- $\alpha$  on syncytialization, we treated chorionic explants with 0 to 10 ng/mL of TNF- $\alpha$  for up to 48 hours after incubating for 4 days. Explants were fixed and visualized with immunofluorescence microscopy using DAPI and E-cadherin stains (n=3).

### Results

TNF- $\alpha$  appears to initially decrease S1PR1 expression by 2-fold at 24 hrs, followed by recovery at 36 hrs. We did not observe a change from 0 to 24 hrs. SK1 expression appears to increase 2.5-fold after 36 hrs in untreated cultures. TNF- $\alpha$  treatment visually increases SK1 expression by 1.5-fold compared to untreated samples at 36 and 48 hrs. Data from immunofluorescence microscopy analysis suggests that TNF- $\alpha$  decreases syncytium formation in chorionic explants with 0.1-10 ng/mL TNF- $\alpha$  after 24-48 hrs of treatment, with the most dramatic results seen with 10 ng/mL TNF- $\alpha$  after 48 hrs of treatment.

### Conclusion

More replicates are needed to confirm findings; however, TNF- $\alpha$  appears to decrease syncytialization and affect S1PR1 and SK1 expression as predicted. This means that S1PR1 and SK1 could in fact mediate TNF- $\alpha$  signaling. Next, we will assess syncytialization in the presence of S1PR1 and SK1 antagonists.

Funded by CIHR, WCHRI

The Power of Partnership

Abstract # 186  
Presenter: Noble, Ronan  
Supervisor: Bourque, Stephane  
Title: **Perinatal iron deficiency leads to systolic dysfunction in neonatal rat hearts**

Authors: **Ronan Noble, Andrew Woodman, Jason Li, Richard Mah, Sareh Panahi, Ferrante Gragasin, Luke Eckersley, Stephane Bourque**

### **Introduction**

Iron deficiency (ID) is the most common nutritional deficiency worldwide, and affects an estimated 23% of pregnant women in Canada. ID causes organ-specific patterns of hypoxia, mitochondrial dysfunction and oxidative stress in the fetus, although the effects on offspring heart function have not been studied. By virtue of iron's role in ensuring oxygen delivery to the body, we sought to determine how reduced oxygen carrying capacity associated with anemia would affect heart function.

### **Methods**

Sprague Dawley rats were fed an iron-restricted or iron-replete diet (control) 2 weeks prior to and throughout pregnancy. After birth, all dams were fed an iron-replete diet. On postnatal day (PD)14, offspring cardiac function was assessed by echocardiography.

### **Results**

ID offspring exhibited growth restriction (-19%;  $P < 0.001$ ), which persisted through PD14 (-32%;  $P = 0.0014$ ). At PD14, when normalized to body weight, ID pups had increased right ventricle weights (+56%;  $P = 0.0023$ ), combined left ventricle and ventricular septum weights (+51%;  $P = 0.0049$ ), left ventricular internal diameters (49%;  $P = 0.016$ ), as well as anterior and posterior wall thickness (+47%;  $P < 0.034$  +48%;  $P < 0.021$ ). Furthermore, ID offspring had reduced ejection fraction (-22%;  $P < 0.0025$ ), and increase in pulmonary artery ejection time (+11%;  $P = 0.025$ ). After adjusting for bodyweight, no changes in cardiac output or stroke volume were observed. Finally, there were no changes in diastolic function of any parameter analyzed.

### **Conclusion**

These results show that perinatal ID causes structural and functional changes in the neonatal heart, which, in the absence of increased cardiac output, suggest the development of systolic dysfunction. These findings may have important implications for short and long-term cardiac health in the offspring.

Funded by **WCHRI graduate studentship, CIHR CGSM, Maternal and Child Health Scholarship Program, CIHR, WCHRI.**

The Power of Partnership

Abstract # 187  
Presenter: Fellus, Sapir  
Supervisor: Kaul, Padma  
Title: **Socioeconomic determinants of preeclampsia in Alberta**

Authors: **Sapir Fellus, Maria Ospina, Radha Chari, Padma Kaul**

### **Introduction**

Preeclampsia is a hypertensive disorder of pregnancy affecting 3-8% of women worldwide, and is classically characterized by elevated blood pressure and end-organ damage. Progression of preeclampsia may lead to devastating effects on both mother (e.g., eclampsia, death) and child (e.g., intrauterine growth restriction, abnormal fetal heart rate, and stillbirth). It is becoming increasingly clear that living conditions and social contexts, in addition to advances in medical treatments, are the major factors that shape and exacerbate illness. The aim of this study is to characterize preeclampsia using a social determinants lens in order to increase and complement our molecular understanding of this disease. The primary objective is to assess the influence of maternal area of residence, socioeconomic status, ethnicity, and immigrant status on the incidence of preeclampsia in Alberta. The secondary objective is to elucidate how these socioeconomic determinants are associated with obstetrical and neonatal outcomes among women with preeclampsia.

### **Methods**

This retrospective cohort study will utilize data from an Alberta pregnancy and birth cohort, which includes maternal demographics, clinical and obstetrical outcomes, delivery information, and maternal and neonatal clinical data pertinent to preeclampsia. These data are obtained from Alberta Health administrative health records, and will be linked to census data that will be used to determine rural/urban status, and to incorporate neighborhood-level information on maternal socioeconomic status at the time of pregnancy. Maternal ethnicity and immigrant status will be obtained through the use of established naming algorithms for the former and information on the previous country of residence for the latter. All pregnancies of women aged 15 – 49 years who were residents of Alberta with live births between 2005 and 2018 will be included in the study. The principal outcome of interest is the incidence of preeclampsia, and the secondary outcomes of interest are obstetrical and neonatal outcomes (e.g., C. section, preterm birth, low birth weight) among women with preeclampsia. A Chi-Square test for categorical variables will be performed for each of the four exposures of interest. All exposures which are significant at  $p < 0.20$  as well as clinically important covariates, such as maternal age, pre-existing diabetes, hypertension, and previous history of preeclampsia, will be included as candidates for a multiple logistic regression model.

### **Results**

A total of 481,903 pregnancies were included in the study. Of these, 6,863 cases of preeclampsia or eclampsia occurred during the length of the study (1.42% of pregnancies). Data is currently undergoing statistical analysis.

### **Conclusion**

Uncovering data about the interplay between preeclampsia and rural/urban status, ethnicity, immigrant status, and socioeconomic status, may reflect, complement, and enrich etiologic preeclampsia research, as well as potentially provide important information for clinicians about socioeconomic risk factors associated with preeclampsia. In addition to sharing results with clinicians, knowledge translation of this study's results will include dissemination to relevant local Alberta Health decision-makers.

Funded by

The Power of Partnership



Abstract # 188  
Presenter: Palmer, Sophie  
Supervisor: Chandra, Sue  
Title: Development of a clinical decision support tool and order set for stillbirth and second-trimester fetal death using knowledge translation principles  
Authors: Palmer S; Guyon G; Young W; Belbeck D; Chandra S

### **Introduction**

Our objective is to analyze the development of an order set and paired clinical decision support tool for management of stillbirth and second-trimester fetal death, using knowledge translation (KT) principles. KT is part of the Canadian Institutes for Health Research's (CIHR) core mandate and is an iterative process that strengthens health services through synthesis, dissemination, exchange, and application of knowledge into practice. KT tools include point-of-care clinical decision support tools that assist in evidence-based clinical decision making. Order sets, when used in conjunction with clinical judgement, can be powerful clinical decision support tools—they have been shown to improve adherence to practice guidelines, reduce practice variations, and improve patient safety.

### **Methods**

The process and initial implementation steps of the above order set and clinical decision support tool is reviewed, to analyze the how the tool fits within the knowledge-to-action KT framework. Process steps within the framework included engaging the provincial perinatal quality assurance committee in a needs assessment, use of a pan-provincial, multidisciplinary working group to adapt knowledge to local context, and planning for outcome evaluation and future research.

### **Results**

Challenges to KT tool development identified in the investigation of stillbirths and second-trimester fetal deaths in Alberta included existing practice variations, resource variations, and the deterministic effect of vital statistics definitions on both research and practice. Strengths included existing provincial perinatal leadership, multidisciplinary collaboration, investment in technology, and the iterative process used for tool development.

### **Conclusion**

We demonstrate the theoretical basis for utilizing an order set with a paired clinical decision tools as a KT tool for investigation of stillbirth and second-trimester fetal death, and explore system challenges and strengths encountered in its development. Ultimately, this case highlights broader interactions in obstetrics and medicine between KT, health technology and health systems, and quality improvement.

Funded by Alberta Health Services

The Power of Partnership

Abstract # 189  
Presenter: Shaha, Sumaiyah  
Supervisor: Yanow, Stephanie & Hemmings, Denise  
Title: Developing a physiological assay to measure Plasmodium falciparum infected erythrocyte adhesion to syncytiotrophoblast in vitro  
Authors: Shaha S, Fakhr Y, Mitran C, Wiebe M, Hemmings DG, Yanow SK

### Introduction

Erythrocytes infected with the malaria parasite Plasmodium falciparum bind to the placenta via VAR2CSA, an erythrocyte membrane protein 1, which binds to chondroitin sulfate A (CSA) glycosylated syndecan-1 (SDC-1) on the placental syncytiotrophoblast (ST). The resulting damage to ST causes placental malaria leading to poor birth outcomes. Pregnant women develop antibodies to VAR2CSA that prevent adhesion to ST during subsequent pregnancies. Current in vitro assays to test antibodies for adhesion-blocking activity have major limitations and are not physiological. Our goal is to develop and optimize an assay to test antibodies elicited by immunization and assess their adhesion-blocking activity under more physiological conditions. Further, antibodies isolated from pregnant individuals exposed to malaria could be used to determine better epitopes for vaccine development.

### Methods

The presence of SDC-1 on ST was confirmed by digesting CSA from fixed placenta sections of normal term pregnancies and staining with anti-SCD-1 antibody using immunofluorescence. Primary human term cytotrophoblasts were cultured in 21% O<sub>2</sub> with cAMP to induce differentiation into multinucleated ST. Cultured ST were fixed followed by the addition of P. falciparum infected red blood cells (iRBC). After washing to remove unbound iRBC, bound iRBC were fixed to ST and bound RBC were stained for glycophorin A (transmembrane protein) using immunohistochemistry. iRBC bound to the ST were counted using brightfield microscopy with a polarized filter.

### Results

SDC-1 staining was seen primarily on the apical side of the ST in placenta sections. Chondroitinase treatment of ST to remove CSA reduced iRBC bound to cultured ST by 40% (n=3, SEM=0.15) -56% (n=3, SEM=0.16) depending on washing techniques used. Preincubation of iRBC with decorin (soluble VAR2CSA receptor) reduced binding by 35% (n=5, SEM=0.19) – 38%(n=3, SEM=0.27) depending on washing techniques used. Preincubation with soluble CSA reduced binding by 42%(n=4, SEM=0.32).

### Conclusion

Once optimized, this assay will allow researchers to assess vaccine efficacy by testing how well antibodies produced inhibit iRBC binding and protect against placental malaria. This will improve our ability to select for antibodies that are protective against placental infection and direct us to determine the best vaccine targets using molecular and biochemical approaches.

Funded by CIHR, WCHRI, NSERC

The Power of Partnership

Abstract # 190  
Presenter: Latif, Asna  
Supervisor: Bhavsar, Amit  
Title: **Investigating mechanisms of chemotherapy-induced permanent hearing loss in childhood cancer patients**  
Authors: **Asna Latif, Ghazal Babolmorad, Amit P. Bhavsar**

### **Introduction**

Cisplatin is a chemotherapy drug used in the treatment of a multitude of cancers including cervical, gallbladder, pancreatic, head and neck, and solid tumours in children. It is highly effective, approaching 90% success rates in some cases, but it leads to permanent hearing loss in over half of treated children. Not only does this have devastating long-term impacts on their quality of life but it also limits the dosage of cisplatin that can be administered, thereby interfering with outcomes of cancer treatment. While mechanisms of cisplatin-induced hearing loss are not well understood, there may be a connection to nickel contact-hypersensitivity which has been shown to interact with an innate immune receptor, Toll-like Receptor 4 (TLR4). Chemical similarities between cisplatin and metals like nickel, palladium, or cobalt implicate TLR4 in cisplatin-induced hearing loss and this opens avenues for protective therapies.

### **Methods**

A human embryonic kidney (HEK) cell line that expresses TLR4 and its co-receptors was used as an in vitro model of cisplatin-induced toxicity and compared to HEK cells that don't express these receptors. They were treated with cisplatin, nickel, or a known TLR4 ligand, LPS. Responses to these treatments were then measured through cell viability assays or secretion of a pro-inflammatory cytokine as an indicator of cell toxicity. In order to further ascertain the involvement of TLR4 in cisplatin-induced toxicity, a TLR4 inhibitor was used to suppress receptor activity prior to cisplatin treatment. Cell responses were also measured in the absence of the TLR4 co-receptor, MD2, to investigate mechanistic similarity of cisplatin-TLR4 interactions to nickel-TLR4 interactions.

### **Results**

HEK cells that expressed TLR4/MD2 were found to release the pro-inflammatory cytokine IL-8 significantly more than cells lacking these receptors. In fact, HEK-TLR4/MD2 cells showed dose dependent IL-8 secretion in response to cisplatin. Inhibition of TLR4 with small molecule inhibitor TAK242 resulted in effective suppression of IL-8 signaling in response to cisplatin. Furthermore, treating cells with cisplatin in the absence of the MD2 co-receptor demonstrated that cisplatin-TLR4 interactions work independently of MD2, similar to nickel-TLR4 interactions and distinct from LPS-TLR4 interactions.

### **Conclusion**

TLR4 is involved in cisplatin-induced toxicity and the mechanism of interaction is similar to that seen in nickel-TLR4 hypersensitivity reactions. Additionally, the effectiveness of TAK242 in preventing cisplatin-TLR4 signaling implicates small molecule inhibitors as valuable candidates for protective therapies in the future.

Funded by **WCHRI Summer Studentship through Stollery Children's Hospital Foundation, CIHR**

The Power of Partnership

Abstract # 191  
Presenter: Kim, Chan  
Supervisor: Hammond, James  
Title: **Effect of tyrosine kinase inhibitors on 6-mercaptopurine cytotoxicity: Interactions with equilibrative nucleobase transporter 1**  
Authors: Kim C, Jabilona K, Ruel N, Nguyen KH, Eisenstat D, Hammond JR

### Introduction

Acute lymphoblastic leukemia (ALL) is the most common childhood cancer. Standard chemotherapy of ALL includes 6-mercaptopurine (6-MP), a purine nucleobase analog which is transported by Equilibrative Nucleobase Transporter 1 (ENBT1), a purine-selective nucleobase transporter encoded by the SLC43A3 gene. In some cases (e.g. Ph+ ALL) tyrosine kinase inhibitors (TKIs) are also included in combination with 6-MP. This is of interest as recent studies have shown that TKIs can inhibit the uptake of adenine, a purine nucleobase, in human kidney epithelial cells. This raises the possibility of potential drug-drug interactions between TKIs and 6-MP at ENBT1. We hypothesize that TKIs can inhibit ENBT1 and thereby affect the therapeutic efficacy of 6-MP.

### Methods

[3H]adenine was used to assess ENBT1-mediated uptake activity in SLC43A3-transfected HEK293 cells in the presence and absence of TKIs. To determine impact on 6-MP toxicity, cells were incubated with a range of 6-MP concentrations (78 nM – 1.28 mM) with and without a predetermined concentration of TKI for 48 hours and assessed for their viability via the MTT assay.

### Results

An initial screen showed significant inhibition of ENBT1-mediated adenine uptake by TKIs at 10  $\mu$ M: gefitinib >> imatinib = dasatinib (n=6). Gefitinib concentration response and inhibition curves showed that 3  $\mu$ M gefitinib does not affect MOLT-4 cell viability and inhibits ENBT1-mediated adenine uptake by ~30% (n=5). Co-administration of 6-MP and 3  $\mu$ M gefitinib in MOLT-4 cells resulted in a significant 2-fold increase in the cytotoxicity of 6-MP (n=5).

### Conclusion

Our results show that TKIs can significantly inhibit ENBT1. However, contrary to expectations, gefitinib increased the cytotoxicity of 6-MP. Additional work is needed to determine the mechanism(s) underlying this synergistic effect of gefitinib on 6-MP cytotoxicity. Furthermore, these results justify investigating the effect of imatinib and dasatinib on the cytotoxic activity of 6-MP.

Funded by NSERC - Undergraduate Student Research Award

The Power of Partnership

Abstract # 192  
Presenter: Mohseni, Mahsa  
Supervisor: Brandwein, Joseph M  
Title: Combination of siRNA and chemotherapeutic agents in acute leukemic cells  
  
Authors: Mahsa Mohseni, Cezary Kucharski, Remant Bahadur KC, Hasan Uludag, Joseph M Brandwein

### Introduction

Acute lymphoblastic leukemia (ALL) is the most common type of leukemia in children, accounting for 29% of all pediatric cancers. Non-viral gene therapy with specific small interfering RNAs (siRNAs) can be an alternative and/or supportive therapy of ALL due to its specificity and high degree of safety. In addition, combination of small interfering RNA (siRNA) therapy and the most common chemotherapeutics used for ALL could improve treatment outcomes of current therapies by targeting oncogenic mechanisms. However, an effective siRNA therapy requires efficient delivery systems since polynucleotides are highly unstable in serum, and their anionic nature prevents them from traversing cellular membranes. Among molecular targets for acute leukemia, transcription factors including Signal Transducer and Activator of Transcription (STAT)- protein family members are highly important, since they can activate expression of oncogenes leading to aberrant proliferation of cancer cells. In hematological malignancies, downregulation of STAT5 can decrease proliferation of leukemia cells. In this study, we evaluated therapeutic role of STAT5 inhibition by polymeric siRNA delivery systems in combination with drugs in ALL cell lines.

### Methods

Acute lymphocytic RS4; 11 and SUP-B15 leukemia cells were used. Lipid-modified low molecular weight polyethyleneimine (PEI) polymers were used as siRNA carriers. Doxorubicine, dexamethasone and vincristine were used as chemotherapeutics. Cell proliferation was assessed by MTT assay, Cellular uptake by Flow Cytometry and STAT5 knockdown at mRNA level by RT-qPCR.

### Results

Specific lipid substituted 0.6, 1.2 and 2 kDa PEI (0.6PEI, 1.2PEI and 2PEI) displayed excellent complexation properties with siRNAs to form nanoparticles and gave high siRNA uptake in cells with negligible toxicity. STAT5 gene expression was downregulated (60-90%) in SUP-B15 and (32%) in RS4; 11 cells using 1.2PEI and 2PEI-lipid polymer. In addition, siRNA complexes in combination with vincristine (10 nM) resulted in a significant growth inhibition in RS4;11 cells.

### Conclusion

We demonstrated effective delivery of STAT5 siRNA by polymeric nanoparticles into leukemia cells, accompanied by marked inhibition of STAT5 gene. Cell growth was reduced significantly by combinational strategies involving drug-siRNA combinations. Further experiments will be directed at evaluating STAT5 protein silencing by siRNA therapy and exploring the effect of STAT5 downregulation on leukemic patient samples.

Funded by This research has been funded by the generosity of Hair Massacure and Innovation foundations through the Wemon and Children's Health Research Institute as well as CIHR.

The Power of Partnership

Abstract # 193  
Presenter: Ruel, Nicholas  
Supervisor: Hammond, James  
Title: SLC43A3 as a biomarker for 6-mercaptopurine cytotoxicity in leukemia cells

Authors: Nicholas M Ruel, Khanh Hoa Nguyen, James R Hammond

### Introduction

6-Mercaptopurine (6-MP) is a nucleobase analog drug used in the maintenance treatment phase of acute lymphoblastic leukemia (ALL). Our lab has established that transfection of cells with SLC43A3, which encodes equilibrative nucleobase transporter 1 (ENBT1), increases 6-MP influx and cytotoxicity in a heterologous transfection model. SLC43A3 is known to be expressed in leukemia cells, but its relationship to 6-MP therapeutic activity has not been defined. We hypothesize that the level of SLC43A3 expression in leukemia cells relates directly to the degree of 6-MP uptake and cytotoxicity.

### Methods

A panel of leukemia cell lines was assessed for SLC43A3 expression, ENBT1 function, and sensitivity to 6-MP cytotoxicity. SLC43A3 transcript was determined using RT-qPCR. 6-MP cytotoxicity was assessed using the MTT assay. ENBT1 function was evaluated by measuring the 2 sec uptake of [<sup>14</sup>C]6-MP by these cells. SLC43A3 knockdown was achieved using the SMARTvector Lentiviral shRNAi inducible vector.

### Results

SLC43A3/ENBT1 expression and function varied widely across leukemia cell lines. We found significant correlations between SLC43A3 expression, 6-MP uptake, and toxicity to 6-MP. Furthermore, knockdown of SLC43A3 with shRNAi in the RS4:11 cell line led to a significant decrease in 6-MP uptake (3-fold) and cytotoxicity (Log EC50: ALL-1 =  $-6.45 \pm 0.11$ ; ALL-1\_shRNAi =  $-4.242 \pm 0.14$ )

### Conclusion

Changes in expression and activity levels of SLC43A3/ENBT1 lead to concurrent changes in 6-MP cytotoxicity. These data suggest that ENBT1 is the primary transporter for 6-MP in leukemia cell lines and SLC43A3 may be a genetic biomarker for 6-MP dosage efficacy in ALL.

Funded by The Cancer Research Society

The Power of Partnership

Abstract # 194  
Presenter: Greenwell, Amanda  
Supervisor: Ussher, John  
Title: **Cardiac glucose oxidation rates are impaired and a possible pharmacological target for mitigating heart failure in Barth syndrome**  
Authors: Amanda A. Greenwell, Keshav Gopal, Tariq Altamimi, Malak Almutairi, Jennifer Kruger, Farah Eaton, Rami Al Batran, John R. Ussher

### **Introduction**

Heart failure (HF) presents as the leading cause of infant mortality in individuals with Barth syndrome (BTSH), a rare genetic disorder first described by Peter Barth and colleagues in 1983. The causative mutation underlying the BTSH phenotype has been definitively mapped to the tafazzin (TAZ) gene, which encodes for a phospholipid transacylase critical in the remodelling of the mitochondrial phospholipid, cardiolipin. Despite well-characterized mitochondrial dysfunction, information regarding perturbations of cardiac energy metabolism in individuals with BTSH remains limited. Hence, our objective was to identify potential metabolic perturbations and determine whether optimization of cardiac energetics may be a novel approach to attenuate cardiomyopathy development in BTSH children.

### **Methods**

Cardiac function in a mouse model of BTSH (tetracycline-inducible Taz knockdown (TAZKD) mice) was assessed via ultrasound echocardiography in mice ~2 months of age. Hearts were subsequently extracted from ~2.5-month-old TAZKD mice and their wild-type littermates for mRNA/protein expression profiling, or for isolated working heart perfusions to assess energy metabolism.

### **Results**

TAZKD mice exhibited early development of a hypertrophic cardiomyopathy as evidenced by increased left ventricular (LV) anterior ( $0.95 \pm 0.04$  vs.  $0.82 \pm 0.03$  (mm)) and posterior ( $0.85 \pm 0.05$  vs.  $0.79 \pm 0.09$  (mm)) wall thickness during diastole, and impaired LV volumes during both systole and diastole. Conversely, no signs of systolic dysfunction or HF were apparent. Of interest, inhibitory phosphorylation of pyruvate dehydrogenase (PDH), the rate-limiting enzyme for glucose oxidation, was increased in hearts from TAZKD mice. This change coincided with increased protein expression of PDH kinase 4 (PDHK4, gene name Pdk4), the primary PDHK isoform in the heart inhibiting PDH activity, but did not coincide with an increase in Pdk4 mRNA expression. Moreover, TAZKD mouse hearts exhibited a marked reduction in glucose oxidation rates.

### **Conclusion**

Our findings point to a marked reduction in myocardial glucose oxidation prior to the development of overt HF in TAZKD mice, which may represent a pharmacological target for mitigating HF development/progression in BTSH.

Funded by WCHRI, CIHR

The Power of Partnership

Abstract # 195  
Presenter: Kaur, Amanpreet  
Supervisor: Hornberger, Lisa K  
Title: **Trends in (2003-2018) and barriers to the prenatal detection of congenital heart disease in Alberta**  
Authors: Kaur Amanpreet, Eckersley Luke, Ngwezi Deliwe, Hornberger Lisa

### **Introduction**

We have previously shown that modifications to ultrasound screening guidelines have led to a significant increase in prenatal detection of certain forms of congenital heart disease (CHD) in Alberta. Unfortunately, there are still many infants (20-30%) with critical CHD not identified prenatally. Lower socioeconomic status (SES) and greater distance of residence (DOR) from a tertiary care center have been shown to importantly impact prenatal detection in the United States. Whether lower SES and greater DOR impact rate and timing of prenatal detection of CHD in Canada is unclear. In the current study we examine the impact of SES and DOR on the prenatal detection of major CHD over a well-defined era of increasing prenatal detection rates (2003-2018). We hypothesize maternal SES, more remote DOR from tertiary care ultrasound and fetal echo practices are associated with the timing and rate of prenatal detection of CHD.

### **Methods**

This is a retrospective population-based study of fetal and pediatric patients resident at birth in Alberta encountered or born, respectively, with CHD from January 1, 2003 to December 31, 2018. Patients with major CHD requiring an intervention within the first 12 months will be identified through the Western Canadian Children's Heart Network, provincial echocardiography and surgical databases. Pregnancies diagnosed with major fetal CHD and encountered in the same years will also be identified through two provincial databases and linked with the pediatric database, identifying those with and without a prenatal diagnosis and fetal cases not resulting in a live birth. Postal codes will be acquired for each pediatric and fetal case, and SES scores generated by quintiles using a recently validated, Stats-Canada based method (Chan et al). Postal codes will be used to calculate the DOR to the two tertiary referral obstetric units and the two pediatric cardiac programs in the North (Edmonton) and South (Calgary) of the province. DOR will also be analysed according to metropolitan, regional and remote ordinal categories. Multivariate logistic modeling will be used to explore whether SES, DOR and diagnostic category contribute to lack of prenatal detection.

### **Results**

To date all patients with CHD born in Alberta during the study period have been identified. We are currently removing simple defects and are linking the fetal with postnatal cases. We expect over 2200 cases with major CHD.

### **Conclusion**

A better understanding of the influence of SES and DOR on the rate and timing of prenatal detection may allow the development of more effective strategies to enhance detection of CHD for pregnancies within lower SES and living more remotely.

Funded by No external funding

The Power of Partnership



Abstract # 196  
Presenter: Ahmad, Attila  
Supervisor: Eckersley, Lucke  
Title: Validation of knowledge-based cardiac chamber volumes against 3D echo and MRI datasets  
Authors: Dr. Luke Eckersley, MBBS PhD, Dr. Attila Ahmad, MBChB, Dr. Jonathan Windram BSc (Hons), MBChB, MRCP (UK), Dr. Timothy Colen, MD

### Introduction

Ultrasound imaging is used to assess the heart's structure, size and function in children and adults. Accurate measurement of cardiac chambers is useful in a variety of conditions that affect the heart's structure and function. Traditionally two-dimensional ultrasound (2DE), three-dimensional ultrasound (3DE) and cMRI (cardiac magnetic resonance imaging) has been used to measure cardiac chamber size. 2D echo tend to be limited by the fact that it is measuring the volume of a three-dimensional structure in two dimensions. On the other hand, 3DE and cardiac MRI are more accurate but time consuming, expensive and require specific training in these imaging modalities. Our study aims to use a novel method of 3D reconstruction volumetric measurement software created by Ventripoint to measure heart chamber volumes, specifically left ventricle (LV) and left atria (LAV), and compare them to conventional 2D and 3D echo, and cMRI volumetric measurements

### Methods

General hypothesis: we hypothesis that assessment of left atrial and left ventricular volumes using 3D reconstruction using 2D images is a time efficient method, with an accuracy comparable to 3DE, cMRI and favorable to 2D-echocardiography. Inclusion Criteria: healthy control patients aged 0 to 18 years who were included in previous 3D echo study (n=214). Consecutive MRI studies that are acquired on patients aged 0 - 18 years in 2017 – 2019 at the Mazanowski Heart Institute clinical MRI department will also be used for the MRI part of the study. We will measure LA and LV volumes on a single dataset using two measurement techniques, and two observers. To adequately assess technique differences according to subgroup (age range, sex, BSA) with a power of 0.8 and alpha of 0.05, and assuming a standard deviation of 15% within techniques, 20 patients are required per age range. As MRI is not dependent on echocardiographic acoustic window quality (i.e. not affected by BSA or sex), a smaller number (n=10) per subgroup is estimated to be required Exclusion Criteria: anyone with single ventricle physiology or poor image quality that preclude measurement using the software. Study procedures: Involves importing the images obtained from previous studies completed above to the Ventripoint software. Then, we will select the images required to measure 3D reconstruction volumes of LA and LV using 2D images obtained from each imaging study. Statistical methods will be used to analyze intra-observer, interobserver variability. The relationship between 3DRE-derived and conventional 3D/2D LA/LV volumes will also be evaluated.

### Results

Still in data collection process.

### Conclusion

We anticipate the finding of this study will help us validate the accuracy of using this novel method to measure heart chamber volumes quickly with accuracy that is comparable to more time-consuming methods such as conventional 3D echo and cardiac MRI.

Funded by

The Power of Partnership



Abstract # 197  
Presenter: Harake, Danielle  
Supervisor: Khoo, Nee  
Title: **Does ventricular dyssynchrony in pre-bidirectional cavopulmonary anastomosis palliation stage children with hypoplastic left heart syndrome predict morbidity and mortality?**  
Authors: Danielle Harake, Lily Lin, Luke Ekersley, Edythe Tham, Nee Khoo

## Introduction

Ventricular mechanical dyssynchrony, as demonstrated by strain imaging patterns is associated with worse heart function. While many quantitative measures of mechanical dyssynchrony have been proposed and studied, there remains no single dyssynchrony parameter associated with patient outcome. More recently, Risum et al. (Am Heart Journal 2012) showed that in structurally normal hearts the presence of a "classical" patterns is predictive of clinical response to cardiac resynchronization therapy (CRT). Our group published in 2018 on several potential RV function predictors of HLHS using both advance and conventional measures to show that right ventricular function before bidirectional cavopulmonary anastomosis (BCPA) palliation in children with hypoplastic left heart syndrome (HLHS) to predict death or need for heart transplantation. Since that publication, the single ventricle database at the primary study site has grown significantly. We propose to revisit this cohort and determine whether the presence of ventricular dyssynchrony at the pre-BCPA stage, as demonstrated by ECG, echocardiographic, or MRI data, can improve predictions of death or need for heart transplantation.

## Methods

This is a prospective single-center study analyzing clinical and imaging data collected on HLHS patients enrolled in the Single Ventricle Study at the University of Alberta since 2007. The study involves the collection of additional clinical information and functional echocardiographic data at pre-neonatal surgery, pre-BCPA, pre-Fontan and post-Fontan stages. All collected patient information is stored securely in RedCap. We intend to look for any ECG, echocardiographic or MRI evidence of ventricular dyssynchrony in any of the 150 prospectively recruited patients with HLHS who have pre-BCPA stage functional echocardiograms available. The composite end point will be death or heart transplant. Receiver operating characteristic analysis will be performed, and cutoff values optimizing sensitivity and specificity will again be derived for post-BCPA outcomes.

## Results

As of September 2019, there are 150 HLHS patients enrolled in the Single Ventricle Study at our institution. Based on data from the Western Canadian Children's Heart Network (WCCHN), 110 are alive at the present time, 7 have been transplanted (2 subsequently died), and 33 have died without being transplanted (40 have met the primary endpoint of death or transplant).

## Conclusion

If a clear ECG, echocardiographic or MRI pattern of ventricular dyssynchrony can be identified in this single ventricle cohort, it might help improve predictions of clinical outcomes in HLHS patients following the BCPA surgical stage. If the presence of ventricular dyssynchrony in this cohort does correlate with increased risk of death or need for heart transplantation, it is possible that, like their structurally-normal heart failure counterparts, single ventricle patients exhibiting signs of dyssynchrony may have improved clinical outcomes with the initiation of cardiac resynchronization therapy.

Funded by WCHRI team grant and Stollery Children's Foundation

The Power of Partnership

Abstract # 198  
Presenter: Lin, Lily  
Supervisor: Khoo, Nee Scze and Freed, Darren  
Title: Tricuspid valve responds to chronic right ventricular pressure and volume load stress by rapid leaflet expansion: 3DE study in a novel recovery piglet model  
Authors: Lily Lin, Sanaz Hatami, Richard Thompson, Consolato Sergi, James Yashu Coe, Timothy Colen, Elena Di Martino, Walter Herzog, Ziad Abu Sara, Darren H. Freed, Nee Scze Khoo

### Introduction

Tricuspid valve (TV) failure is a risk factor for mortality in children with hypoplastic left heart syndrome (HLHS). Durability of surgical repair is modest while the mechanisms underlying TV failure is not well understood. We aim to study TV adaptive changes when exposed to chronic preload and afterload stress in a novel piglet model simulating HLHS first surgical interstage single right ventricular physiology

### Methods

Twenty piglets (4-5weeks, infant equivalent) underwent left thoracotomy. Intervention piglets (IP, n=10) had their pulmonary valve torn to produce moderate to severe pulmonary regurgitation (volume loading) and pulmonary artery band placed to increase RV pressure. Age and gender-matched control piglets (CP, n=10) had sham surgery. Following 4-week recovery period, we performed RV pressure measurements and 3D Echocardiography (3DE) of the TV. TV annulus and leaflet geometry at mid and end-systole were measured using custom MATLAB 3DE software. Ex-vivo unstretched TV leaflet area was photographed and measured.

### Results

All IP had severe pulmonary regurgitation, significantly elevated RV systolic pressure, thicker RV free wall and anterior papillary muscle, confirming an effective model [see Table]. IP had larger and more circular annulus, but similar bending angle to CP. IP in-vivo 3DE TV leaflet surface area was 43% greater than CP, especially in the posterior leaflet. Coaptation index was similar while IP TV leaflet tethered volume and TR was greater. No difference in ex-vivo TV pathologic specimen (unstretched) area was detected, however correlation with 3DE TV leaflet area persisted ( $r=0.60$ ,  $p=0.02$ ).

### Conclusion

Upon exposure to chronic RV volume and pressure stressors, TV adapts by annular dilation while maintaining "saddle" shape and total coaptation surface area. This is mostly achieved through a process of rapid leaflet expansion. Further study of TV leaflet growth and its modulation may provide novel insights into the pathophysiology of TV failure in HLHS.

Funded by WCHRI Graduate Studentship Award, WCHRI Innovation Grant

The Power of Partnership

Abstract # 199  
Presenter: Olugbuyi Oluwayomi  
Supervisor: Hornberger, Lisa  
Title: **Does disparities in proximity to care and socioeconomic class influence congenital heart disease (CHD) outcome in Canada?**  
Authors: Resident Dr Oluwayomi Olugbuyi ; Primary Supervisor: Dr Lisa Hornberger; Co-investigators: Dr Padma Kaul, Dr Douglas Dover, Dr Luke Eckersley.

## Introduction

Greater geographic DOR from the cardiology care center has been shown to importantly contribute to the discontinuation of care of adolescents with CHD in the US suggesting greater DOR potentially adds a barrier to care which could impact outcomes. This study will evaluate the impact of distance from residence (DOR) on lesion specific mortality in infant requiring surgical intervention in the first year of life Canada. Objective AIM 1: To investigate the association between DOR from a central pediatric cardiology or cardiac surgical program (postal codes) and residence on in-hospital mortality (primary outcome) in children with CHD warranting intervention in the first year born between 2004 and 2018 across Canada, examining differences between provinces and for different CHD. AIM 2: To investigate the impact of DOR from a Pediatric Cardiology Center (SCH, ACH, Providence) and a Pediatric Cardiac Surgical Center (SCH) on mortality, frequency of outpatient cardiology clinic visits and hospital-based recourse utilization for children with CHD necessitating intervention in the first year encountered from 2004-2018, For both studies we will focus on 10 categories of CHD requiring intervention in the first year among infants and children born between 2004 and 2018. Hypothesis: DOR may impact outcome in infants requiring surgery for congenital heart disease

## Methods

### Method

This retrospective study will evaluate the effect of DOR on lesion specific mortality in infants with CHD requiring surgical intervention in the first year of life. Using Canadian-wide administrative data, we will identify, based on ICD10 diagnostic codes, all patients born with CHD between 2004 and 2018. Demographic data (age, birth weight sex, gestational age and nature of delivery) will be obtained from the administrative database. Mortality will be compared based on DOR from the closest cardiac center (presence of  $\geq 3$  pediatric cardiologists on site, 11 total in 6 provinces) and cardiac surgical center (7 total in 5 provinces). CHD types will be classified using the complexity classification (Boston group RACHS-1). Statistical analysis: Data will be analyzed using Stata 15 (Stata Corp, Lakeway Drive, Texas, USA). We will analyze continuous variables by measures of central tendency including student t-test and will analyze nonparametric variables with Chi squared test. Bivariate analysis will be conducted where appropriate using of Fisher's exact test for comparing simple proportions and the nonparametric Mann-Whitney U test for assessing differences in median age, weight. We will analyses confounding variables with Mantel Hanzel test. We will use multiple logistic regression models to measure associations between independent and dependent variables

### Results

The result may help in driving policy to care for children with cardiac disease.

### Conclusion

This study will provide foundation for future socioeconomic data for future studies

Funded by None

The Power of Partnership

Abstract # 200  
Presenter: Mangat, Avneet  
Supervisor: Schmolzer, Georg  
Title: **Does a respiratory function monitor during positive pressure ventilation in the delivery room reduce infant mortality? A systematic review and meta-analysis**  
Authors: **Avneet K. Mangat BSc, Georg M. Schmolzer, MD, PhD,**

### **Introduction**

The current neonatal resuscitation guidelines recommend positive pressure ventilation (PPV) if a preterm infant does not initiate breathing at birth. During PPV, a set pressure is used with the assumption that it will deliver an adequate tidal volume (VT). However, the VT is never actually measured. Several animal studies and observational studies in the delivery room reported that high VT delivery can cause lung and brain injury. Using a respiratory function monitor (RFM) to guide VT delivery during PPV, might reduce lung and brain injury. We aimed to perform a systematic review and meta-analysis of available randomized controlled trials (RCT) comparing a RFM that is visible or masked during PPV in the delivery room in premature infants.

### **Methods**

Articles were systematically searched in PubMed, Google Scholar, and EMBASE, and Clinical Trials.gov for ongoing trials. Risk of bias was assessed using the Covidence Collaboration Tool and disagreements were resolved by discussion. Results were pooled into a meta-analysis using a random effects model with the primary outcome being death prior discharge. The meta-analysis was conducted using Cochrane Collaboration tool RevMan V.5.2.

### **Results**

Two RCTs were identified and combined in a meta-analysis. The pooled analysis showed no difference in death before discharge for PPV with RFM visible or masked (RR 0.01 (-0.11 to 0.13), I<sup>2</sup>=0%). However, the pooled analysis identified a trend to reduced brain injury in infants receiving PPV with an RFM visible versus RFM masked (RR -0.09 (-0.19 to 0.02), I<sup>2</sup>=0%). Similarly, the pooled analysis identified a trend to reduced air leaks in infants receiving PPV with an RFM visible versus RFM masked (RR -0.09 (-0.19 to 0.01), I<sup>2</sup>=0%).

### **Conclusion**

Although, infant mortality was similar between groups, there is a trend to less brain injury and air leaks if PPV is provide with an RFM. However, further studies are needed before this technology can be translated into routine care.

Funded by **Northern Alberta Clinical Trials and Research Centre Summer Student Award, Heart and Stroke Foundation**

The Power of Partnership

Abstract # 201  
Presenter: Mustofa, Jannatul  
Supervisor: Schmolzer, Georg  
Title: Development of non-contact video-based heart rate monitoring in newborn infants

Authors: Jannatul Mustofa, Kyle E. Mathewson, Georg Schmolzer

### Introduction

Measurement of heart rate (HR) is a critical assessment in the Delivery Room to evaluate the wellbeing of an infant and to guide neonatal resuscitation. Current neonatal resuscitation guideline include recommendations for contact-based methods such as electrocardiography (ECG) or pulse oximetry (PO). However, these methods may cause injury or infection to premature infants who have fragile skin where the electrodes can cause discomfort, stress, pain and epidermal stripping. A new approach might be non-contact video-based HR recording, which translates video images into HR, will be a feasible method of monitoring in the delivery room.

The primary aim of our study was to examine if HR can be reliably measured in newborn infants using non-contact video-based HR monitoring. The secondary aim was to assess if non-contact video-based HR monitoring compared to the ECG will (a) improve accuracy of HR assessment, (b) decrease delay in obtaining HR signals, and (c) reduce the need for contact-based monitoring.

### Methods

Newborn infants born at the Royal Alexandra Hospital delivery rooms were included. Video-based HR monitoring uses photoplethysmography, an optical technique that is used to detect blood volume changes in tissues microvasculature. HR is detected by the emitting wavelengths of light. Video-based HR data was collected and compared to ECG HR measurements.

Statistical analysis was performed using Bland-Altman comparison between ECG and video-based HR monitoring measurements. Two-way mixed absolute agreement intraclass correlation coefficient was computed to assess intra-rater reliability between ECG and average video-based HR monitoring for the HR.

### Results

Newborn infants (n=40, mean birthweight 1225g, gestational age 28.6 weeks gestation, Apgar 1 min 4.8, Apgar 5 min 6.8) were included in the study.

The mean (SD) HR for video-based monitoring was 146.0 (6.3) bpm and ECG was 146.4 (8.3) bpm. Bland-Altman analysis showed the mean HR was similar to the gold standard, with a mean difference (95% levels of agreement) of 0.38 (-7.99 to 8.74) bpm between video-based HR monitoring and ECG [ICC = 0.83, 95% CI (0.70, 0.91)].

### Conclusion

Our study demonstrated that non-contact video-based HR monitoring has similar accuracy compared to ECG. Video-based HR monitoring is feasible in the delivery room and randomized trials are warranted.

Funded by WCHRI Summer Studentship

The Power of Partnership

Abstract # 202  
Presenter: Ghoman, Simran K  
Supervisor: Schmölzer, Georg M  
Title: Game-based summative assessment of neonatal resuscitation competence using the RETAIN board game  
Authors: Simran K Ghoman, Maria Cutumisu, Matthew RG Brown, Georg M Schmölzer

## Introduction

One million infants around the world each year die at birth during neonatal resuscitation. Alarming, 50% of this mortality is caused by deficiencies in healthcare professionals' (HCPs) competence. Therefore, HCPs must be frequently and objectively assessed to improve healthcare delivery and outcomes for their vulnerable newborn patients. Currently, HCPs use the neonatal resuscitation textbook to answer an at-home online multiple-choice questionnaire about neonatal resuscitation knowledge. This approach is insufficient. Our objective is to evaluate the simulation-based board game RETAIN as an alternative summative assessment method of HCPs' neonatal resuscitation competence.

## Methods

HCPs from the Royal Alexandra Hospital Neonatal Intensive Care Unit (Edmonton, Canada) were recruited to complete i) a pre-test (written open-answer neonatal resuscitation scenario), ii) a short tutorial, and iii) one round of the RETAIN board game. Sessions were audio and video recorded using a GoPro Camera (GoPro Inc., San Mateo, California, USA).

In the RETAIN board game (RETAIN Labs Medical Inc., Edmonton, Canada), players are presented with an evidence-based neonatal resuscitation scenario, and use simulated equipment, supplies, action cards, and adjustable monitors to perform appropriate interventions. Players' decision-making is guided throughout the game by continuous updates about changes in the infant's heart rate, oxygen saturation, work of breathing, and visual appearance.

Performance on the pre-test and RETAIN game was scored using Neonatal Resuscitation Program guidelines (2015) and compared using Spearman Pearson correlation. Data is reported as mean (Standard Deviation (SD)).

## Results

20 neonatal HCPs participated (19 female; Nurse n=8, Respiratory Therapist n=4, Nurse Practitioner n=4, Fellow n=4; mean(SD) 11.3 (9.1) years of clinical neonatal experience). The mean(SD) pre-test score was 7.25(1.29) out of 11 (66%), and the mean game performance score was 8.8(1.39) out of 11 (80%). The mean(SD) pre-test score was 8.35 (1.81) out of 16 (52%), while the game performance score was 18 (5.27) out of 40 (45%). Participants' pre-test and game performance scores were moderately correlated ( $r=0.45$ ,  $p=0.05$ ).

## Conclusion

HCPs' performance on the RETAIN board game was moderately associated with their score on a traditional summative assessment (i.e., open-answer resuscitation scenario). With further refinements to the game and comparable-difficulty scenarios for the pre-test and the game scenario, RETAIN could be used as an alternative summative assessment method to frequently and objectively evaluate HCPs' neonatal resuscitation competence. Potential applications include implementing RETAIN during neonatal resuscitation provider certification, or for ongoing quality measurement of neonatal healthcare delivery.

Funded by WCHRI Trainee Travel award, Heart & Stroke Foundation, and the MatCH scholarship program

The Power of Partnership

Abstract # 203  
Presenter: Nie, Chunpeng  
Supervisor: Graf, Daniel  
Title: Metabolic dysregulation underlies early-onset osteoarthritis in the TMJ  
  
Authors: Chunpeng Nie, Pranidhi Baddam, Arleen Schmidt, Daniel Young, Antoine Dufour, Daniel Graf

### Introduction

Osteoarthritis (OA) of the temporomandibular joint (TMJ) is characterized by loss of articular cartilage, causing jaw pain and immobility. Currently, treatment options are limited partly because disease etiology is poorly understood. Loss of Bone Morphogenetic Protein 7 (BMP7) leads to early-onset OA in the knee and the TMJ. Here, we investigated what type of changes to the TMJ precede OA development. We hypothesize that loss of BMP7 in the TMJ leads to cellular changes in the chondrocytes prior to the onset of OA.

### Methods

To confirm expression of BMP7 in the TMJ, Bmp7LacZ reporter mice were sectioned and counterstained with Safranin O. To delete Bmp7 in neural crest cells, we created Bmp7 fl/fl:Wnt1-Cre (mutant) mice. Micro-computed tomography ( $\mu$ CT) was performed to identify gross morphological changes. Sections of mutant and control mice at 2 and 4 weeks of age were stained with Hematoxylin and Eosin for general morphology and Safranin O for cartilage glycosaminoglycans. To investigate cellular changes preceding histological changes, quantitative shotgun proteomics was performed on dissected condyles at 2 and 4 weeks and analyzed with STRING. Immunofluorescence was done to confirm deregulation and find localization of some proteins identified in proteomics.

### Results

BMP7 is expressed in the subchondral region and lateral articular surface of the condyle. Bmp7 mutant mice showed no gross morphological changes to the mandible, but a smaller synovial space between the mandible and temporal bone was noted. Histological changes were noted at 4 weeks, but not 2 weeks. The hypertrophic zone was increased and the glycosaminoglycan content was decreased. Shotgun proteomics and STRING analysis revealed altered cellular processes both at 2 and 4 weeks. Differences included cell-intrinsic processes such as reduction-oxidation metabolism and control of proteasome function in addition to extracellular changes. Altered expression of several of the changed proteins were validated using immunofluorescence.

### Conclusion

Early OA-like changes in the TMJ are preceded by changes in cellular processes in chondrocytes. Several of these changes are reminiscent to changes seen in BMP7-dependent differentiation of thermogenic brown adipose tissue. Thus, similar to brown adipose tissue, BMP7 appears to control the metabolic state of chondrocytes, which subsequently affects the properties of the formed cartilage. Changes in cartilage properties lead to early joint degeneration manifesting as early onset OA.

Funded by WCHRI, NSERC, Gilbert K Winter Fund

The Power of Partnership



Abstract # 204  
Presenter: Thereza Bussolaro, Claudine  
Supervisor: Flores-Mir, Carlos Flores  
Title: **Nasal structure alterations and high risk of OSA among children: An exploratory study**  
Authors: **Claudine Thereza-Bussolaro, Pranidhi Baddam, Daniel Graf, Carlos Flores-Mir**

### **Introduction**

To investigate structural anomalies in the nasal cavity (nasal septum deviation, hypertrophic turbinates, nasal sinus blockage) in children with/without a high risk of OSA.

### **Methods**

A retrospective cross-sectional clinical study considering Cone Beam Computed Tomography (CBCT) scans of 100 children were conducted. Dolphin software (3D, version 11.95 premium) was used to analyze DICOM images obtained from the CBCT scans. Dataset was assessed by 2 raters. Subjective and objective assessments were conducted. Reliability was calculated using Kappa and ICC. Descriptive statistics, regression and correlation analyses were performed.

### **Results**

Good to excellent intra- and inter-reliability was found for subjective and objective assessments. Of the 99 children included, average age was 10.95 years (39% female, 61% male), and 56% with a positive PSQ for high risk of OSA. In the subjective assessment, 66% presented deviated nasal septum (DNS), and 72% turbinate hypertrophy (TH). In the objective assessment, 26% presented DNS, and 35% TH. Logistic regression analysis of the DNS subjects indicates a strong relationship ( $P < 0.1$ ) between nasal septum deviation and turbinate hypertrophy.

### **Conclusion**

Overall, these results suggest that DNS is present in a significant proportion of children regardless of them being at risk for OSA. Additionally, turbinate hypertrophy is persistent in majority of children with DNS. However, the data suggests that there is no strong correlation between DNS and positive PSQ in children. The presence of DNS in children doesn't significantly influence the risk of sleep-disordered breathing. However, children with DNS were reported as having more behavior problems compared to their normal peers.

Funded by **Support from the Women and Children Health Research Institute Innovation Grant**

The Power of Partnership

Abstract # 205  
Presenter: Leclair, Guillaume  
Supervisor: Attallah, Joseph  
Title: Neurodevelopmental outcomes after neonatal surgical intervention for cyanotic tetralogy of Fallot and other lesions with right ventricular outflow tract obstruction  
Authors: Guillaume Leclair, MDCM, Adil Digankar, MD, Charlene M. T. Robertson, MD, Gwen Y Alton, MSN, Gonzallo Guerra, MD, Joseph Atallah, MD CM.

### **Introduction**

Neonatal cardiac surgery carries a significant risk for adverse neurodevelopmental outcomes. There is little data on right sided obstructive congenital lesions requiring repair in early infancy. We hypothesize that the neurodevelopmental outcomes in cyanotic patients undergoing neonatal repair vs. shunt palliation are comparable.

### **Methods**

A prospective cohort of 85 consecutive cyanotic neonates underwent surgery for right outflow tract obstructive lesion (tetralogy of Fallot, pulmonary atresia with a ventricular septal defect, or double outlet right ventricle with normally related great vessels) at a corrected gestational age of 6 weeks or less, between 2001 and 2017. The Surgeries include complete repair or shunt palliation. They had multisite multidisciplinary health and neurodevelopmental outcomes (Bayley Scales of Infant Development II and III) at 18-24 months of age. Demographic, perioperative and follow-up data was collected including data on cardiac catheterization and repeat surgical interventions. Univariate and multivariable analyses will be performed to identify factors associated with neurodevelopmental outcomes.

### **Results**

Data analysis is ongoing. Seventeen (20%) patients underwent repair by palliative shunt. There were 9 (10%) deaths with 6 (35%) in the palliative shunt group. Seventy seven (90%) patients survived to the 18-24 month mark to assess early infancy neurodevelopmental outcome. Data on disabilities is pending.

### **Conclusion**

We hope this study will yield insightful information on the demographic, anatomical, pre-operative, operative and post-operative variables that may affect the neurodevelopmental outcomes of neonates who undergo full repair or palliative shunt in the first 6 weeks of life for right sided obstructive congenital heart lesions. This information may be particularly useful when counseling pregnant mothers or new parents, as well as potentially identifying modifiable factors to optimize developmental outcomes.

Funded by Western Canadian Complex Pediatric Therapies Follow-up Program, Alberta Health and Wellness.

The Power of Partnership

Abstract # 206  
Presenter: Chan, Jackie  
Supervisor: Chiu, Brian  
Title: Pediatric sarcoidosis: A clinicopathological review with emphasis on early-onset and high-risk sarcoidosis and diagnostic challenges  
Authors: Brian Chiu, Jackie Chan, Sumit Das, Zainab Alshamma, Consolato Sergi

### Introduction

Sarcoidosis is a non-necrotizing granulomatous inflammatory syndrome with a highly variable clinical course and diverse multi-systemic manifestations. The diagnosis relies on the pathologic findings of non-necrotizing granulomas in absence of infective etiology, as well as clinico-radiological correlation. High-risk sarcoidosis--namely cardiac or neural sarcoidosis, or treatment-resistant sarcoidosis--is associated with worsened quality of life and high mortality. Sarcoidosis is uncommon in children, and high-risk sarcoidosis may present differently in this population. The rarity and variable manifestation of the disease present a diagnostic challenge.

This study examines the English literature from the past 20 years on the epidemiology, clinical phenotypes, clinical features, and pathogenetic mechanisms of pediatric sarcoidosis. We aim to review the clinical investigations and laboratory diagnostics of sarcoidosis in this population, and clarify the pathogenesis behind the disease.

### Methods

We performed a systematic narrative review on sarcoidosis, with particular emphases on early-onset sarcoid, high risk sarcoidosis, and newly reported or unusual sarcoid-related diseases in the pediatric population. PubMed, Scopus, Google Scholar, and Cochrane Database of Systematic Reviews were searched. Local case files and references from relevant reviews were also examined.

### Results

Blau Syndrome and early-onset sarcoidosis/ BS-EOS are seen in children younger than 5 years old. The presentation primarily involves extra-thoracic manifestations, which differs from adult sarcoidosis, where there usually is lymphadenopathy and/or pulmonary involvement. The prevalence of high-risk sarcoidosis is very low in children, and is further limited by the difficulty of diagnosis in symptomatic children, and underdiagnosis in subclinical or asymptomatic patients. Reports of sarcoidal syndromes in users of E-cigarette/ marijuana/ other flavorings are of interests and may be challenging to differentiate from metastatic malignancy.

### Conclusion

Despite a wide spectrum of clinical manifestations, the triad of uveitis, arthritis, and skin rash in a pediatric patient should raise suspicion for Blau Syndrome/Early-onset sarcoidosis. The diagnostic considerations in pediatric sarcoidosis are to support a compatible clinoradiographic presentation and the pathologic findings of non-necrotizing granulomas by ruling out granulomas of infective etiology. There is no reliable diagnostic test for sarcoidosis at present, although the diagnostic techniques and imaging modalities are improving. The use of endoscopic bronchial ultrasound (EBUS) and transbronchial fine needle aspiration (TBNA) sampling of intrathoracic lymph nodes and lung provide fair diagnostic yield and excellent patient safety profile in children.

Funded by Not currently funded

The Power of Partnership

Abstract # 207  
Presenter: Young, Kennedy  
Supervisor: Alexander, R. Todd  
Title: **The loss of claudin-2 results in upregulation of the transcellular pathway of calcium reabsorption from the kidney and of absorption from the intestines in pre-weaned mice**  
Authors: **Kennedi Young, Megan R. Beggs, R. Todd Alexander**

### **Introduction**

Infants and children require a net positive calcium (Ca<sup>2+</sup>) balance to achieve optimal bone mineral density by early adulthood. In the intestine, Ca<sup>2+</sup> is absorbed both paracellularly, through claudin proteins that make up the tight junction, and transcellularly. However, these pathways are not well delineated in early life. Previous research from the lab demonstrates that claudin-2 mediates increased intestinal Ca<sup>2+</sup> permeability at P14, i.e. prior to weaning. We hypothesized that loss of this pathway would result in compensatory increases of intestinal absorption and renal reabsorption of Ca<sup>2+</sup> in P14 mice.

### **Methods**

Alterations in Ca<sup>2+</sup> absorption and reabsorption pathways were determined by RT-PCR. To assess Ca<sup>2+</sup> homeostasis, a urinary Ca<sup>2+</sup> to creatinine ratio was measured using ion chromatography and HPLC.

### **Results**

These mice showed increased expression of genes mediating transcellular intestinal Ca<sup>2+</sup> absorption. In particular, KO mice had a 25-fold increase in S100g expression in the jejunum (p=0.001) and 1.7-fold in the ileum (p=0.007) and Atp2b1 (p=0.0379) expression increased 1.7-fold in the ileum. In the proximal colon, KO mice had a 2.7-fold increase in expression of Cacna1d (p=0.003), 2.3-fold increase in S100g (p=0.017), 1.7-fold increase in Atp2b1 (p=0.004) and 1.6-fold increase in Slc8a1 (p=0.026). Similarly, the renal transcellular reabsorption pathway was upregulated in KO mice, with 1.6-fold increase in Trpv5 (p=0.002), 2-fold increase in Atp2b1 (p=0.026) and 1.6-fold increase in Calb1 (p=0.026) gene expression. In global claudin-2 KO mice, we observed decreased urinary calcium excretion (0.86±0.18 WT vs 0.37±0.04 KO; p=0.03) compared to WT.

### **Conclusion**

These results suggest that claudin-2 contributes to maintaining a positive Ca<sup>2+</sup> balance early in life and that loss of this pathway leads to increases in transcellular intestinal Ca<sup>2+</sup> absorption and renal reabsorption in compensation.

Funded by **Alexander Lab**

The Power of Partnership

Abstract # 208  
Presenter: Nguyen, Kim-Cuong  
Supervisor: Le, Lawrence  
Title: **Registration of ultrasound and CBCT images for enhancing periodontal tissues visualization**  
Authors: Kim-Cuong T Nguyen, Kumaradevan Punithakumar, Neelambar R Kaipatur, Edmond HM Lou, Paul W Major, and Lawrence H Le

### **Introduction**

Periodontitis or inflammation of the gingiva affects the periodontal tissues, leading to alveolar bone loss and subsequent loss of teeth. Aggressive periodontitis, characterized by an early onset rapid progression of destruction, is more common in children and adolescents, especially for orthodontic patients. Diagnosis of periodontal diseases in the case of bone destruction mainly depends on clinical examination and radiographs. The two-dimensional (2D) radiographs can provide information regarding alveolar bone level on the mesial and distal aspects of tooth root, but not on the buccal and lingual surfaces of the teeth. This limitation of 2D radiographs can be eliminated by using 3D imaging techniques such as cone-beam computed tomography (CBCT). Although CBCT images provide an excellent visualization of the alveolar bone, the image of gingiva is inferior. Ultrasound has mainly been used to image soft tissues in medical for decades. Recent studies have shown that the gingiva thickness could be measured accurately using ultrasound imaging. Accurate registration of the CBCT and ultrasound images of the tooth-periodontium will help oral clinicians visualize the gingiva and alveolar bone for periodontal disease diagnosis and treatment planning.

### **Methods**

The data was made up of eight pairs of CBCT and US images from eight incisors from two adult volunteers. The center incisors of the upper and lower jaws were scanned at the labial side using high resolution CBCT with a voxel resolution of 0.075-mm and ultrasound imaging with a 40 MHz array transducer. The images at the center of the incisors were extracted from CBCT sagittal projections of the jaws and ultrasound videos. In the next step, an equalized region of interest was determined in both CBCT and ultrasound images containing the manually chosen cementum-enamel junction landmark and a predetermined length. A region-growing segmentation technique and probability-based point set registration using coherent point drift algorithm were then used to fuse the images. The accuracy of the registration was evaluated by measuring the alignment/distances between the three pairs of landmarks in CBCT and the ultrasound images. The measurements were performed by two raters twice to examine the inter-rater and intra-rater agreement.

### **Results**

The mean error of the mismatch between CBCT and ultrasound image registration was around 0.3 mm. The intra-rater and inter-rater limits of agreements for the alignment between CBCT and ultrasound images were [-0.22 mm, 0.26 mm] and [-0.19 mm, 0.21 mm], respectively.

### **Conclusion**

The proposed method has successfully registered CBCT and ultrasound images, which will assist oral clinicians to extract useful underlying information of both soft and hard tissues. More data will be required to validate the accuracy and efficacy of this registration method.

Funded by Alberta Innovates

The Power of Partnership

Abstract # 209  
Presenter: Linda Truong  
Supervisor: Dr. Jackie Whittaker  
Title: Growth is in the struggle: Exploring the perspectives of youth 1-2 years following a sport-related anterior cruciate ligament injury - an interpretive description study  
Authors: Linda K. Truong, Amber D. Mosewich, Maxi Miciak, Andrea Pajkic, Linda Li, Jackie L. Whitaker

## Introduction

Youth who experience an anterior cruciate ligament (ACL) tear will have an increased long-term risk for inactivity, obesity, and osteoarthritis (OA). Exercise-based rehabilitation, physical activity, and sport may mitigate these risks. Currently, little is known about exercise-based activities in youth who have suffered an ACL tear beyond the typical recovery period. This study explores the attitudes towards, priorities for, and experiences of, rehabilitation, physical activity, and sport participation in youth who have suffered a sport-related ACL tear at least 12-months previously.

## Methods

This interpretative description study recruited participants from an on-going prospective cohort study describing health-related outcomes over the first 2-years following a youth sport-related knee injury. We used purposive sampling to identify participants (aged 15-19 years) who had an ACL tear or ACL reconstruction (ACLR) in the past 12-24 months. Efforts were made to ensure a balance of adolescent women and men with variation in age, return to sport status, sport participation level, and weekly minutes in moderate to vigorous physical activity (tri-axial accelerometer) at a scheduled cohort study follow-up visit. One-on-one semi-structured interviews were conducted to explore participants' current attitudes, priorities, and experiences of rehabilitation activities, physical activity endeavors, and/or organized sport participation. Audio recordings were transcribed. Thematic analysis followed an inductive approach guided by Thorne's (2016) analytic process for interpretative description. A patient partner (AP) was involved to test the interview guide and assist in analyzing and interpreting the data. To promote trustworthiness and credibility of the findings, reflexive journaling, memoing, a detailed audit trail, and regular meetings with team members was used throughout data generation and analysis.

## Results

Ten youth [6 women, 4 men; median age 17.5 (15-18) years at the time of injury; median of 19.25 (15.5-26) months from injury onset] participated in the study. Seven had ACLR and three managed their ACL tear conservatively. At the time of interview, only 6 of 10 participants had returned to their pre-injury sport. Three themes (and associated subthemes) highlighted rehabilitation participation: attitudes towards exercise therapy (engagement in care), challenges of recovery (managing on-going symptoms; navigating unforeseen roadblocks), and the need for social support (meeting injured peers). Additionally, three themes highlighted sport or physical activity involvement after injury: valuing sport/physical activity (beliefs of benefits of physical activity), adjustments in perspectives (renewed purpose for sport/physical activity) and negotiating return to sport (initial priority to return to sport).

## Conclusion

The preliminary findings from this study highlight current attitudes and priorities of exercise-based activities may shape how youth approach these activities after the typical recovery period following an ACL tear. Further analysis is expected to illuminate the underlying factors that drive physical activity and sport participation so that clinical recommendations may be provided to reduce the risk of inactivity and obesity in youth with ACL tears.

Funded by Faculty of Rehabilitation Medicine, University of Alberta

The Power of Partnership

Abstract # 210  
Presenter: Firouzeh, Pegah  
Supervisor: Pritchard, Lesley  
Title: Evaluation of the effects of ankle foot orthoses on gross motor function, physical activity and participation of young children with cerebral palsy: A mixed-methods study protocol  
Authors: Pegah Firouzeh MSc, Lyn Sonnenberg MD FRCPC, Lesley Pritchard PT, PhD

### Introduction

Ankle Foot Orthoses (AFOs) are often prescribed for children with cerebral palsy before the age of six years to prevent tendo-achilles contracture and improve walking. However, early AFO use may negatively affect joint motions necessary for functional movement, and limit the ability of young children to move up and down from the floor easily. Further assessment of the effects of AFOs on functional outcomes is required to inform clinical practice. In addition, prescription practices would also be informed by a more in-depth understanding of parent experiences with AFO use. Activity and participation outcomes are often most important to parents, and yet they are often ignored in pediatric orthotics research. The objectives of this study are to: 1) evaluate the effects of AFOs on gross motor function, physical activity, and participation of children with cerebral palsy and, 2) explore parents' experiences with children's AFO use.

### Methods

A sequential mixed-methods study will be conducted. The quantitative part (objective 1) will be a randomized cross over design with AFO-on and AFO-off conditions, both two weeks in duration. Children (n=40) with cerebral palsy, Gross Motor Function Classification System levels I & II, aged two to five years, who use AFOs will be assigned to either initial condition of AFO-on or AFO-off and then will alternate to the other condition. Mean gross motor function (GMFM-Dimensions C, D & E) and participation scores (Young Children's Participation and Environment Measure), and physical activity (accelerometer), for both conditions will be compared. Interpretive Description will be the methodological framework for the qualitative part (objective 2). Semi-structured individual interviews will be conducted with parents of children (n=15) who participated in part one. Interviews will be transcribed verbatim and analyzed using inductive thematic analysis.

### Results

This is a study protocol.

### Conclusion

The findings of the cross over trial will provide information about the effects of AFOs on gross motor skills, physical activity, and participation of young children with cerebral palsy. This information will inform clinicians about the effects of AFOs on a broad range of outcomes which will guide prescription practices and discussions with families. In addition, conducting interviews with parents of children with cerebral palsy and giving voice to parents (objective 2), will enable us to identify advantages and disadvantages of AFOs, which may not be apparent to clinicians in the clinical context. This information is particularly clinically relevant since parents' perceptions likely affect their children's AFO use. Findings of this study will create opportunities for considering and embedding parents goals and meaningful expectations in the orthotic prescription practices.

Funded by Faculty of Rehabilitation Medicine, University of Alberta

The Power of Partnership

Abstract # 211  
Presenter: Johnson, Sarah  
Supervisor: Ladha, Tehseen  
Title: Identification of health needs in pediatric immigrants and refugees presenting for screening

Authors: Dr. Sarah Johnson, MD  
Dr. Tehseen Ladha, MD, MPH Candidate

## Introduction

There has been a significant influx of newcomers to Edmonton over the past 10 years. As Edmonton continues to grow and receive more immigrants and refugees, it is important to look at how the health of these newcomers can be optimized. The health status of newcomers to Canada depends on a variety of migration process factors including country of origin, experience of migration, and presence of a supportive community on arrival. For medical professionals, facing the diverse health needs that aren't seen in the typical Canadian population can be a time and effort intensive process, especially as many refugees do not have English (or French) as their native tongue. Despite the described need for a medical home, and the established benefits that are associated with specialized refugee clinics, there have been few studies that systematically approach this topic. Our study aimed to discover the health needs of immigrant and refugee children in Edmonton, to determine what supports are needed, and to utilize this information to see how care can be optimized for this group of children.

## Methods

This was an observational study aimed at quality improvement. A survey using RedCap was distributed to all paediatricians and nurse practitioners at the Northeast Edmonton Health Centre Pediatric Clinic (NEHC PC), and the East Edmonton Health Centre (EEHC). All immigrant and refugee children who have been in Canada for the past five years or less presenting to these sites were included in the study. As well, we later expanded the inclusion criteria to those children whose parents are immigrants and refugees who have lived in Canada for less than 5 years. Survey information included patient demographics, information on the immigration experience, diagnoses made during the appointment, resources needed and referrals made.

Redcap, SAS version 9.4 and SPSS version .24 or later will be utilized to delineate descriptive statistics and summarize continuous and categorical data.

## Results

We are currently in the process of collecting the final patient surveys to achieve our goal of an N of 50. We anticipate this process will be complete prior to the WCHRI research day, and we will then be able to better define the health needs of immigrant and refugee pediatric patients in Edmonton.

## Conclusion

Based on other studies of this nature, we will expect to find a high prevalence of infectious diseases, anemia and dental health issues in the immigrant and refugee population. We also anticipate a high need for interpreter services. However, each community is unique, and so we will likely find unanticipated areas of need with this study. We hope that with our study we can not only identify the medical needs of the pediatric patients in Edmonton but also the social needs of this population. With this information we hope to guide future care, policy making and resource allocation for this important issue.

Funded by WCHRI Operating Grant

The Power of Partnership



Abstract # 212  
Presenter: Hai, Tasmia  
Supervisor: Mrazik, Martin  
Title: **Executive functions in children with ADHD: A follow-up study using both performance-based task and rating scales**  
Authors: Hanna Kubas, Frank P. MacMaster, Jean-Francois Lemay

### **Introduction**

Children with Attention-Deficit/Hyperactivity Disorder often exhibit Executive Functions (EF) challenges. Use of psychostimulant medications (Methylphenidate [MPH]) can improve their EF abilities. However, limited studies have investigated the long-term impact.

### **Methods**

Twenty-one children with ADHD (M=12.33 years, SD=1.55 years, Males=62%) were assessed at 3 time points: 1) baseline (BL: no medication), 2) best dose (BD: following 4-week MPH treatment), and 3) long-term follow-up (FU; up to 2 years duration). Parental ratings of EF were done with the Behavior Rating Inventory of Executive Functioning (BRIEF) questionnaire. EF testing included the Continuous Performance Test (CPT) and Colour-Word Interference Task (Inhibition).

### **Results**

Significant differences were obtained in EF ratings: BRIEF Behavioral Regulation Index,  $F(2,36) = 20.71$ ,  $p < 0.001$  and Metacognition Index,  $F(2,36) = 26.83$ ,  $p < 0.001$ , with pairwise comparison indicating improvement in EF performance at the best dose condition compared to baseline, and decrease in performance at the follow up condition. EF tests showed similar effect: Inhibition,  $F(2,40) = 23.21$ ,  $p < .001$  and CPT Omissions,  $F(2,40) = 6.71$ ,  $p < .01$  with pairwise comparison indicating improved EF at best dose condition and no difference at the follow-up.

### **Conclusion**

The MPH effect was observed in both EF tasks and parent ratings after the medication trial. However, the MPH impact was inconsistent between tests measures and parent ratings at the long-term follow-up. Thus, the results indicate the importance of assessing EF using both parent ratings and performance tasks to evaluate impact of medications.

Funded by Alberta Children's Hospital Foundation

The Power of Partnership

Abstract # 213  
Presenter: Sayed, Tehzeeb  
Supervisor: Lou, Edmond  
Title: **Intra- and inter-rater reliabilities and accuracy of kyphotic angle measurements on ultrasound images for children with adolescent idiopathic scoliosis - a pilot study**  
Authors: **Tehzeeb Sayed, Mahdieh Khodaei, Edmond Lou**

### **Introduction**

Adolescent idiopathic scoliosis (AIS) is a three-dimensional (3D) spinal deformity characterized by lateral curvature and vertebral rotation, primarily affecting girls aged 10 to 18. AIS is diagnosed using the Cobb angle measured on standing posteroanterior (PA) radiographs. However, treatment decisions based solely on PA radiographs may underestimate the 3D nature of AIS. Sagittal parameters such as kyphotic angle (KA) have been identified as important factors in the treatment of AIS. To measure KA, a lateral radiograph is required, which exposes children to higher ionizing radiation. Ultrasound (US) imaging is a radiation-free alternative that has been used to successfully measure the Cobb angle on standing PA images. An efficient method to measure sagittal spinal deformity directly from 3D US images has yet to be developed. Therefore, the objectives of this study were 1) to develop a new method to measure KA on 3D US images, 2) to determine the intra-rater and inter-rater reliabilities of this measurement method and 3) to determine the inter-method accuracy in comparison to the Cobb method measured from radiographs.

### **Methods**

Twenty subjects with AIS were recruited with signed consent. Standing out of brace PA and lateral radiographs, and 3D US scans were obtained from each subject. The KA on both radiographs and US images was measured. On US images, the centres of lamina (COL) of T1, T2, T11, and T12 were identified on the PA view. The midpoints of COL at these 4 vertebral levels were automatically calculated and displayed on the sagittal view. Raters connected the midpoints of the COL of T1 and T2 with a line, and T11 and T12 with a line on the sagittal view. The angle of intersection of these 2 lines formed the proxy KA. Two raters (R1 and R2) measured each radiograph once and each US image twice.

### **Results**

All the intra- and inter-rater ICC [2,1] reliabilities of the KA measurements from both US images and radiographs were ranged from 0.77-0.96 which was indicative of good to excellent reliability. The mean absolute difference of the KA measured on the US images and radiographs ranged from 4.7°-6.3° which are within the clinical acceptance error of 11°.

### **Conclusion**

A new US method was developed to measure KA and this preliminary results showed the proposed US method was as reliable and accurate as the standard radiographic method. A larger clinical study is required to further validate the method prior to clinical application.

Funded by **Scoliosis Research Society and the Edmonton Orthopaedic Research Society**

The Power of Partnership

Abstract # 214  
Presenter: Labban, Wasim  
Supervisor: Whittaker, Jackie  
Title: Physical activity in adolescents with patellofemoral pain: A scoping review  
  
Authors: Wasim Labban, Christopher Holt, Linda Truong, Christina Le, Liz Dennett, Jackie L. Whittaker

### Introduction

Patellofemoral Pain (PFP) is a common musculoskeletal condition amongst active adolescents. In the short-term, it can limit sport participation and in the long-term, increase the risk for patellofemoral osteoarthritis. Given that adolescence is an important life stage for developing physical activity patterns, understanding the relationship between PFP and physical activity in this population is critical. Currently, the evidence related to PFP and physical activity in adolescents is dispersed across various fields of study. This review aims to consolidate the existing evidence pertaining to PFP and physical activity in adolescent populations and identify consistent themes to inform future research and clinical practice.

### Methods

This scoping review was guided by the PRISMA Extension for scoping reviews and Arksey and O'Malley's 5-stage framework. Five electronic databases (i.e., MEDLINE, CINAHL, Embase, SportDiscus, ProQuest) were systematically searched from inception to January 19, 2019, using a strategy designed in consultation with a librarian scientist. English records with original data that reported a physical activity outcome in adolescents (10-19 years) with primary PFP (as defined by an international consensus as pain around or behind the patella during patellofemoral joint loading activities) were included. Two authors independently screened titles and abstracts, performed full-text records review, data charting and methodological quality assessment using the Downs and Black Quality Assessment Tool (DB). A thematic analysis was undertaken.

### Results

Of 2,842 records, 11 studies representing 2,832 participants (80% girls, aged 10-19 years) met the inclusion criteria. Included studies represented a variety of study designs (five prospective cohort; five cross-sectional; one case study) and physical activity outcomes (i.e., hours of practice per week, sports participation (yes/no), weekly frequency of sports participation, percentage of leisure time sports participation per week, metabolic equivalents). The range of DB scores across studies was 4-17. Despite the limited number of studies three overarching themes related to PFP and physical activity were identified; (1) physical activity as a risk factor for PFP; 2) physical inactivity is a consequence of PFP; and 3) physical activity is a treatment modality for PFP.

### Conclusion

There is a limited amount of low-quality evidence suggesting that the relationship between physical activity and PFP is complex and multidimensional. Future high-quality prospective inception cohort studies are required to unravel this complexity prior to developing physical activity guidelines in adolescents at risk of or with PFP.

Funded by W. Labban is partially supported by a Graduate Research Assistantship provided by the Faculty of Graduate Studies and Research, University of Alberta, Edmonton, Canada

The Power of Partnership

Abstract # 215  
Presenter: Bui, An  
Supervisor: Bolduc, Francois  
Title: **Identifying genetic modifiers of Fragile X syndrome in a drosophila model for repetitive behaviors**  
Authors: An Bui, David Lotz, Cory Rosenfelt, Francois Bolduc

### **Introduction**

Fragile X Syndrome (FXS) is an inheritable genetic condition that is linked to many neurodevelopmental disorders (NDDs) such as Intellectual Disability (ID) and Autism Spectrum Disorder (ASD). Fragile X Syndrome occurs in 1 in 4000 males and 1 in 8000 females. One significant trait shown in FXS is repetitive motor behaviors, which can affect one's daily functioning and quality of life. We aim to identify the genes that interact with Fragile X Syndrome's gene (FMR1), called modifiers, which impact repetitive behaviors significantly. These genes will be crucial to developing pharmacological treatment to produce desirable effects, such as decreased repetitive behaviors.

### **Methods**

Our principle methods of study use *Drosophila melanogaster* (fruit flies) as a model, as they have very conserved genetics and a well characterized repetitive behaviour in the form of grooming. We used deficiency lines of multiple gene deletions, and by crossing these lines with *dfmr13* (the fly homolog of FMR1 in human), we looked for a potential modifier of *dfmr13*. The repetitive behaviors were recorded and analyzed.

### **Results**

We observed different deficiency lines in *Drosophila* that drive significant changes in flies' repetitive behaviors when interacting with *dfmr13* mutants.

### **Conclusion**

We aim to utilize Ingenuity Pathway Analysis (IPA) software to identify genes from the deficiency lines that have direct and well-studied interactions with *dfmr13*. Those will then be investigated individually for direct modifications with *dfmr13*. Successful gene candidates could be targeted for pharmacological interventions.

Funded by URI Undergraduate Researcher Stipend

The Power of Partnership

Abstract # 216  
Presenter: Godziuk, Devyn  
Supervisor: Graf, Daniel  
Title: The role of KBG syndrome gene, Ankrd11, in craniofacial development

Authors: Devyn Godziuk, Sarah-Thea De Souza, Pranidhi Baddam, Daniela Roth, Adrienne Watson, Anastassia Voronova, Daniel Graf

### Introduction

KBG syndrome is a rare autosomal dominant disorder caused by loss of function mutations in or deletions of the Ankyrin Repeat Domain 11 (ANKRD11) gene. ANKRD11 is an epigenetic regulator, loss of function in which leads to increased global genomic DNA acetylation. Children with KBG syndrome present with distinct deformities of the head, skeleton, and teeth. Diagnosis of KBG syndrome currently relies on genomic sequencing, and delayed appearance of the characteristic abnormalities prevents early diagnosis. Currently there is a lack of understanding of how these morbidities arise.

### Methods

As complete loss of Ankrd11 is early embryonic lethal, we created mice carrying a neural crest-specific homozygous deletion of Ankrd11 (Ankrd11<sup>fl/fl</sup>;Wnt1-Cre2, Ankrd11<sup>ncko</sup>). Embryos were collected at embryonic day 14 (E14.5) and birth. They were processed for paraffin embedding for analysis by histology and immunohistochemistry. Micro-computed Tomography (uCT) and skeletal preparations were used to characterize skeletal features.

### Results

Ankrd11<sup>ncko</sup> mice live until birth, unlike the complete knockouts which die in the embryonic stage. They present with a cleft palate, a shortened mandible bone, and reduced mineralization of the cranial and midfacial bones. These features were confirmed by skeletal preparations, histological staining, and immunohistochemical analysis. A reduction in proliferation was observed in midfacial bones, explaining the hypoplastic bones. In the shortened mandible phenotype, Collagen X, a marker for hypertrophic chondrocytes, and Sp7, a marker for bone formation, were reduced in the Meckel's cartilage of the mutant, which was associated with decreased hypertrophy and mandibular bone formation. To investigate the cause of the cleft palate, we analyzed E14.5 embryos. Hematoxylin and Eosin staining revealed that palatal shelves had elevated, but were hypoplastic and thus not able to meet for fusion. No changes to proliferation (Ki67) or apoptosis (cleaved Caspase-3) were observed, suggesting that cellular events prior to E14.5 are responsible for the hypoplastic palatal shelves.

### Conclusion

We conclude that loss of Ankrd11 in neural crest cells leads to multiple craniofacial malformations reminiscent of defects reported in KBG patients, such as cleft palate, reduced cranial bone ossification, and underdeveloped lower jaw. Overall, our model will serve to describe malformations associated with loss of Ankrd11, as well as allow investigations into Ankrd11 function. Describing criteria for KBG syndrome could facilitate earlier diagnosis in children and expand our understanding of mutations in chromatin remodeling genes in genetic disorders.

Funded by Gilbert K Winter fund, NSERC

The Power of Partnership

Abstract # 217  
Presenter: Goodkey, Kara  
Supervisor: Voronova, Anastassia  
Title: **Exploring the effect of fractalkine on microglia and oligodendrocyte progenitors in the developing brain**  
Authors: Kara Goodkey, Danny Galleguillos, Afsaneh Lavasanifar, Anastassia Voronova

### **Introduction**

During early development formation of myelin, a fatty substance that coats nerve projections, in the brain is an essential for proper neuronal network formation and function. Pediatric diseases affecting myelin range from leukodystrophies to pediatric multiple sclerosis (MS) and affect formation or protection of myelin, respectively. Myelin is formed exclusively by oligodendrocytes in the central nervous system (CNS). In turn, oligodendrocytes are generated and regenerated by endogenous oligodendrocyte precursor cells (OPCs). The function of OPCs is known to be influenced by microglia, brain immune cells. Moreover, both OPCs and microglia have been proposed to be important pharmacological targets for boosting oligodendrocyte production and myelin for brain repair. Notably, both OPCs and microglia express the fractalkine receptor (CX3CR1), which is activated upon fractalkine (FKN) stimulation. FKN is a naturally occurring chemical in the brain that is released by neurons. Moreover, our lab has shown FKN can increase oligodendrocyte production in the developing brain. To understand whether FKN can be used as a pro-oligodendrogenic therapeutic molecule, we need to understand what cell types FKN targets. As both OPCs and microglia are poised to respond to FKN, I will investigate the role of FKN signalling in these cell types together and alone.

### **Methods**

Since conditional FKN receptor (CX3CR1) knockout mice are not available to address this question, we will design nanoparticle delivery of FKN specifically to OPCs or microglia. To do this, we will conjugate OPC and microglia specific antibodies to nanoparticles loaded with FKN. These loaded cell-specific nanoparticles will then be tested in co-cultures and eventually in vivo.

### **Results**

Our first step was to confirm FKN increases oligodendrocyte production. My preliminary data indicate addition of free FKN (without nanoparticles) increases the number of oligodendrocytes in murine postnatal OPC-microglia co-cultures, as expected. My next step was to determine OPC and microglia specific antibodies that work in both single and co-cultures. PDGFR $\alpha$  was found to be the best candidate of an OPC specific antibody. Tmem119 was found to be the best candidate for for microglia specific antibody. Moving forward, the FKN-loaded nanoparticles conjugated to PDGFR $\alpha$  or Tmem119 antibodies will be applied to OPC-microglia co-cultures and the increase in oligodendrocytes will be evaluated.

### **Conclusion**

We have established an OPC-microglia co-culture method to evaluate the role of FKN signalling in both cell types during oligodendrocyte and formation. My preliminary data suggest freely available FKN leads to increase in oligodendrocyte formation in OPC-microglia cu-cultures. In the future, our OPC- and microglia-specific nanoparticle delivery of FKN will determine which cell type is responsible for FKN-mediated enhancement in oligodendrocyte genesis. The optimized delivery method will eventually be used to target fractalkine to cells of interest in vivo. The results will shed light on the fundamental role of FKN-CX3CR1 signalling axis in glial cells and will explore the exciting possibility of using FKN in a novel nanoparticle therapeutic delivery.

Funded by URI Undergraduate Researcher Stipend

The Power of Partnership

Abstract # 218  
Presenter: Chen, Lu Kun  
Supervisor: Lehmann, Ordan  
Title: Role of FOXC1 in pediatric disease and planar cell polarity

Authors: Lu Kun Chen, Serhiy Havrylov, Paul Chrystal, and Ordan Lehmann

### **Introduction**

The Forkhead transcription factor FOXC1 plays an important role in development. The disorders caused by alterations to FOXC1 include Axenfeld-Rieger Syndrome (a pediatric ocular disorder), congenital heart disease, and breast cancer. However, the mechanism remains unclear. There is evidence that alteration to the primary cilium, an organelle that functions as a satellite antenna, is linked between these seemingly different disorders. In addition, FOXC1 mutation appears to disrupt planar cell polarity (PCP), a form of spatial organization along a plane of tissue. Simplistically, each cell receives a GPS signal that ensures it is correctly orientated relative to its neighbours. We hypothesize that FOXC1 may influence PCP and alter the position of the primary cilium, leading to impaired function in a range of organs.

### **Methods**

To investigate this, we assessed changes to PCP by immunostaining against Prickle1, a PCP marker. In addition, we used the microtome to section model organisms to examine the ependyma, a ciliated epithelial lining in the brain ventricles. Ciliary structures were imaged using scanning electron microscopy.

### **Results**

There was significantly higher expression of Prickle1 in the wild type meninges as opposed to FOXC1 knockouts. Secondly, there was an absence of cilia in the ependyma in the FOXC1 mutants.

### **Conclusion**

There is promising evidence that FOXC1 does play role in PCP by affecting the expression levels of its core protein markers. Further, the lack of cilia in FOXC1 mutants may correspond to their hydrocephalus phenotype, as the absence of ciliary beating leads to accumulation of cerebrospinal fluid in the brain. Moving forward, we hope to examine cilia in wild type ependyma for comparison. Elucidating FOXC1's role in PCP may potentially confirm mechanisms for multiple pediatric disorders and identify targets for therapeutic intervention.

Funded by WCHRI Summer Studentship

The Power of Partnership

Abstract # 219  
Presenter: Aslesh, Tejal  
Supervisor: Yokota, Toshifumi  
Title: Systemic delivery of a novel peptide-conjugated morpholino oligomer DG9-PMO improves symptoms in a mouse model of spinal muscular atrophy  
Authors: Tejal Aslesh, Rika Maruyama, Hong Moulton, Toshifumi Yokota.

## Introduction

Spinal muscular atrophy (SMA), an autosomal recessive disorder, is the most frequent genetic cause of infant mortality caused by a mutation in the survival of motor neuron 1 (SMN1) gene. SMN2 is an SMN1 paralogue, but cannot produce enough SMN protein to compensate for loss of SMN1 in SMA. Antisense therapy is a promising strategy to treat SMA. Splice-switching oligonucleotides (SSOs) that bind to SMN2 intron 7 splicing silencer number 1 (ISS-N1) induce exon 7 inclusion and restore the production of proper full-length SMN2 mRNA. Nusinersen (brand name Spinraza), the first approved drug for the treatment of SMA, is an 18-mer SSO. Although there is much hope for this drug, it still has significant problems including injection site adverse effects, cost of the treatment, and a requirement for highly invasive intrathecal injections. More importantly, recent studies revealed that SMA is a multi-organ disorder affecting the heart, liver, thymus, and spleen; however, nusinersen needs to be injected intrathecally due to renal toxicity and therefore can treat only motor neurons. As such, a compound providing effective yet safe delivery of SSO to the central nervous system and bodywide organs is needed to prevent SMA-related morbidity and death.

## Methods

To improve the in vivo efficacy of SSOs through better cellular uptake, we have developed a cell-penetrating peptide called DG9. This novel peptide was derived and modified from a T-cell peptide that is at least 10- to 100-fold more efficient for cellular uptake than previously used peptides. We identified this peptide through in vivo screening in zebrafish. We used DG9 conjugated to an SSO called phosphorodiamidate morpholino oligomer (PMO) targeting SMN2. We injected DG9-PMO into SMA mice to determine the in vivo efficacy. We evaluated the SMN2 expression using quantitative PCR and quantified the SMN expression using Western blots. We also assessed the functional improvement and biodistribution of SSO in various tissues.

## Results

We found that DG9-PMO induced efficient full-length SMN2 expression in the brain and bodywide tissues following a single peripheral administration. qPCR data revealed that DG9-PMO-treated SMA mice exhibited a higher expression of the full-length SMN2 gene compared to PMO-treated, nusinersen-treated and non-treated mice. In addition, these mice showed significantly increased body weight, improved motor function, and extended survival over time compared to nusinersen-treated and non-treated mice. No apparent toxicity was observed.

## Conclusion

DG9-PMO is a promising therapeutic option to treat SMA, which can overcome the necessity for invasive injections with a single peripheral administration and treat bodywide tissues without apparent toxicity. We are currently evaluating the long-term effectiveness of treatments.

Funded by WCHRI Innovation Grant, Slipchuk SMA Research Foundation Research Grant, the Canadian Institutes of Health Research and the Canada Foundation for Innovation

The Power of Partnership



Abstract # 220  
Presenter: Kibalnyk, Yana  
Supervisor: Voronova, Anastassia  
Title: Studying cardiovascular defects in KBG syndrome during development

Authors: Yana Kibalnyk, Pranidhi Baddam, Daniela Roth, Daniel Graf, Anastassia Voronova

### **Introduction**

KBG syndrome is a rare neurodevelopmental disorder characterized by distinctive facial features, short stature, heart and brain defects, global developmental delay, and intellectual disability. The disorder is caused by the haploinsufficiency of the chromatin regulator ANKRD11 (Ankyrin Repeat Domain 11). I am modelling KBG Syndrome in a mouse model, where Ankrd11 has been knocked out specifically in the neural crest cells, which contributes to the development of tissues like the cardiovascular system, peripheral nervous system, and craniofacial tissues. This project explores if ablation of Ankrd11 in the murine neural crest disrupts development of the heart or brain blood vessels, and if either of these defects leads to aberrant brain development.

### **Methods**

I am studying the embryonic mouse heart through histology to determine if the mutant mice have heart defects and I am fluorescently labeling brain vasculature through heart injection and using CLARITY to image the 3D brain vasculature network to search for brain blood vessel defects. I am also using immunohistochemistry on embryonic brains to detect anomalies in the numbers and spatial positioning of different cell types within the developing brain tissue.

### **Results**

My initial results show that neural crest conditional knockouts of Ankrd11 have several heart defects, including truncus arteriosus, ventricular septal defects and aortic valve stenosis, which may impede the blood flow to the body. These defects are consistent with neural crest deficiency.

### **Conclusion**

The results show that Ankrd11 contributes to the development of cardiac neural crest-derived tissues. This project will show how mutations in ANKRD11 lead to vasculature-dependent symptoms in KBG syndrome patients and provide better genetic counseling for affected families.

Funded by Alberta Innovates and WCHRI Summer Research Studentships as well as University Hospital Foundation (Gilbert Winter K. Fund)

The Power of Partnership

Abstract # 221  
Presenter: Huang, Yiqing  
Supervisor: Yokota, Toshifumi  
Title: Developing a minimized antisense oligonucleotide cocktail from RNA and protein perspectives to skip exons 45-55 in Duchenne muscular dystrophy  
Authors: Yiqing Isabella Huang, Kenji Rowel Q. Lim, and Toshifumi Yokota

### Introduction

Duchenne muscular dystrophy (DMD) is an X-linked recessive muscular disease that affects 1 in 3500-5000 males. Progressive muscle degradation can begin as early as age 3 and result in premature death because of cardiopulmonary failure. DMD is caused by out-of-frame mutations in the dystrophin (DMD) gene, leading to a lack of dystrophin protein. Around 40-50% of patients carry mutations in the region from exon 45 to 55. Exon skipping can restore the reading frame and enable partially functional dystrophin production for patients with DMD. We aim to use minimized antisense oligonucleotide cocktails composed of phosphorodiamidate morpholino oligomers (PMO) to skip exons 45 to 55, which can treat 47% of patients. Besides, the exons 45-55 deletion is associated with a remarkably mild phenotype compared to shorter in-frame deletions within the region. Minimized PMO cocktails are not only economically feasible, but also avoid the use of redundant exon skipping PMOs.

### Methods

Various minimized PMO cocktails were transfected three days post-differentiation and cells were harvested two days later for assessing exon 45-55 skipping efficiency and dystrophin rescue. Different cell lines were used to test the cocktails, mimicking different types of deletions in patients, including KM155 (healthy control), KM571 (exon 52 deletion), 6594 (exons 48-50 deletion) and 6311 (exons 45-52 deletion).

### Results

In KM155, the “block” (targeting exons 45, 49, 50, 52, 53, 55) and “3-PMO” (targeting exons 45, 50, 55) cocktails induced exon 45-55 skipping that was not significantly different from what the full 12-PMO cocktail achieved. The result was similar in KM571; additionally, the “block” cocktail significantly restored dystrophin protein levels in these cells. Interestingly, a 2-PMO derivative of the “3-PMO” cocktail (targeting exons 45 and 55) had an overwhelming performance in 6594 cells, skipping exons 45-55 at levels significantly higher than the full 12-PMO cocktail. However, no cocktail could perform as well as the 12-PMO cocktail in terms of dystrophin rescue. Further minimization may not be achievable in 6311 as the skipping efficiency of other candidate cocktails was significantly lower than the 12-PMO cocktail.

### Conclusion

The “block” and “3-PMO” cocktails are overall promising minimized PMO cocktails for exon 45-55 skipping in most of the cell lines. Further investigations, including more effective assessment in dystrophin rescue levels and toxicity of the cocktails need to be implemented in the future study.

Funded by The Friends of Garrett Cumming Research & Muscular Dystrophy Canada  
HM Toupin Neurological Science Research Chair, Canadian Institutes of Health Research

The Power of Partnership

Abstract # 222  
Presenter: Li, Yutong  
Supervisor: Voronova, Anastassia  
Title: **Regulation of oligodendrocyte genesis in the developing brain by hepatoma derived growth factor (HDGF)**  
Authors: Yutong Li, Adrienne Watson, Anastassia Voronova

### **Introduction**

Oligodendrocytes, the myelinating cells of the central nervous system (CNS), perform vital functions in neural protection, communication and efficient information transmission. Developmental oligodendrocyte formation is regulated by cell-to-cell communication between neural stem cells (NSCs) and inhibitory interneurons (Voronova et al. 2017 Neuron). These interneurons secrete over 50 paracrine ligands, including HDGF that could potentially affect oligodendrocyte formation from NSCs.

### **Methods**

To test whether HDGF could enhance oligodendrocyte genesis from NSCs, I isolated NSCs from murine postnatal day 7 brain subventricular zone (SVZ), an NSC rich area that is known to generate oligodendrocytes throughout life. NSCs were cultured in the presence or absence of HDGF added to minimal media, which allows for oligodendrocyte differentiation and permits the observation of exogenous ligands on this process. Generation of oligodendrocyte precursor cells, the obligate progenitors of oligodendrocytes, and differentiated oligodendrocytes was analyzed using immunocytochemistry.

### **Results**

My results demonstrate that HDGF increases the number of mature oligodendrocytes that express myelin basic protein (MBP), but does not have an effect on the formation of immature oligodendrocytes or oligodendrocyte precursor cells. Future studies will determine whether HDGF acts by increasing precursor proliferation and/or differentiation.

### **Conclusion**

My data suggest HDGF may be a novel pro-oligodendrogenic molecule. This has implications for neurodevelopmental disorders, such as fetal alcohol spectrum disorders (FASD) and Williams syndrome, where patients demonstrate decreased myelination in the brain associated with delayed differentiation and maturation of oligodendrocytes. Thus, my studies may not only uncover a novel role of HDGF in oligodendrocyte formation, but could also be used to inform novel pro-oligodendrogenic therapies in the future.

Funded by Natural Sciences and Engineering Research Council (NSERC)

The Power of Partnership

Abstract #223

## Intestinal epithelial injury is associated with systemic inflammation in vertically HIV-1 infected children

Bipasha Choudhury, Victor Mocanu, Jason Brophy, Fatima Kakkar, Ari Bitnun, Lindy Samson, Stanley Read, Hugo Soudeyns, Michael Hawkes.

**Introduction:** Infection of gut associated lymphatic tissue in human immunodeficiency virus 1 (HIV-1) infection permits microbial translocation (MT) from the GI lumen to the circulation which drives systemic inflammation and endothelial activation (EA). Intestinal fatty acid binding protein (I-FABP) is an epithelial cytosolic protein, abnormally released into the circulation with MT, and elevated in the plasma of HIV-1 infected adults, even with sustained viral suppression (SVS) on combination anti-retroviral therapy (cART). I-FABP has not been extensively studied in HIV-1 infected children. Nonetheless, children face decades of chronic immune activation, which may predispose to cardiovascular disease and/or malignancy.

**Hypothesis:** We hypothesize that quantitative levels of I-FABP will be correlated with markers of inflammation in HIV-1 infected children with suppressed viral load on cART.

**Methods:** Cross-sectional analysis of I-FABP and markers of inflammation: tumour necrosis factor (TNF) and interleukin-6 (IL-6). Plasma samples were collected from vertically HIV infected children who achieved SVS (<40 copies/mL) with cART from the Early Pediatric Initiation – Canadian Child Cure cohort study (EPIC4). Commercial ELISA assays (R&D Systems) were used to quantify biomarker levels.

**Results:** We included 90 vertically HIV-1-infected children from 9 Canadian tertiary pediatric HIV treatment centres. 35/63 (56%) were girls, with median age 13 years (range 4-19). All had a suppressed viral load on cART at the time of testing. Biomarkers of inflammation were correlated with each other: TNF with IL-6 ( $\rho=0.91$ ,  $p<0.001$ ). Given the high degree of correlation between the biomarkers of inflammation, we used principal component analysis to derive an index of systemic inflammation. I-FABP was positively correlated with this index of inflammation ( $\rho=0.70$ ,  $p<0.001$ ).

**Conclusions:** Despite excellent virologic control with cART, intestinal epithelial injury (as reflected by elevated I-FABP) was associated with systemic inflammation in pediatric HIV-1 infection. Future studies should examine long-term outcomes (e.g., cardiovascular events) in children with elevated I-FABP.

The Power of Partnership

Abstract # 224  
Presenter: Anjum, Bushra  
Supervisor: West, Lori  
Title: Differences in ABO antibody production in female vs. male mice

Authors: Bushra Anjum, Ibrahim Adam, Jordana Fersovich, Maurits Sulzer, Jean Pearcey, Kesheng Tao, Bruce Motyka and Lori J. West

### Introduction

ABO histo-blood group incompatibility is a barrier in solid organ transplant due to the presence of 'natural' preformed ABO antibodies. However, ABO-incompatible (ABOi) heart transplantation is successful in infants as ABO antibodies are low/absent. A better understanding of the specificity and the production of natural ABO antibodies may allow for successful ABOi transplantation at older ages. In mice, ABO antibodies develop naturally with age and can be 'induced' following sensitization (eg, with human A/B erythrocytes). Herein, we sought to determine the isotype (IgM/IgG) and subtype (I-VI) specificity of ABO antibodies produced naturally or induced by sensitization in mice as a function of age and sex.

### Methods

BALB/c mice were assessed for natural ABO antibody production over time (n=32/39, female/male; age 1-18 months), or challenged with human A erythrocytes (5 weekly intraperitoneal injection) beginning at 5 weeks of age to measure induced ABO antibody production (n=13/8, female/male; age 1-3 months). Blood samples from each mouse was collected in regular intervals by tail bleed and plasma ABO antibody titre and ABO antibody isotype and subtype specificity was determined by hemagglutination assay and ABH glycan microarray, respectively.

### Results

Female mice produced markedly higher natural anti-A and anti-B ABO antibodies compared with male mice. With age, natural ABO antibodies shifted from an IgM to IgG isotype in females but remained predominantly IgM in males. Most natural ABO antibodies were specific to subtypes III/IV with specificity to subtypes I and II absent or very low. In contrast, following A-antigen sensitization both female and male mice produced IgM and IgG anti-A antibodies with specificities for all subtypes (I-VI).

### Conclusion

Male and female mice show distinct differences in ABO antibody production depending on whether these antibodies are produced naturally or induced by sensitization. Future studies will explore mechanisms for these sex differences and relevance to humans.

Funded by GlycoNet Summer Studentship

The Power of Partnership

Abstract # 225  
Presenter: Morin, Estelle  
Supervisor: Foulds, Jessica  
Title: Management and outcome of febrile neutropenia in admitted presumed immunocompetent patients with suspected viral illness  
Authors: E. Morin, C. Corriveau-Bourque, J. Foulds

## Introduction

Febrile neutropenia (FN) is a medical emergency in hematology and oncology patients due to the risk of serious bacterial infections (SBIs). Empiric FN protocols for these patients are often used for healthy children with incidental neutropenia in the context of viral symptoms. There is currently insufficient evidence to provide guidance in management for non-chemotherapy related neutropenia but the limited studies have shown low rates of SBIs in this population. This study aims to quantify the rates of proven infections in presumed immunocompetent children with suspected viral illnesses who are admitted to the Stollery Children's Hospital (STOL) for FN.

## Methods

This is a retrospective chart review of patients aged 3 months to 18 years admitted to the STOL over a 10 year period. Charts with the diagnostic code for "febrile neutropenia" and without codes for neoplasms were selected. The remaining charts are being reviewed to exclude patients on immunosuppressants, with known immune or hematological disorders, with complex chronic disease or with other medications or diseases associated with neutropenia. Only patients with severe neutropenia ( $ANC < 0.5 \times 10^9/L$ ) will be included. Charts are also being reviewed for documented symptoms consistent with a viral infection. The primary outcomes of this study are the presence of SBIs, defined as positive bacterial cultures from a sterile site, and radiographically-confirmed pneumonia. Secondary outcomes will include the length of stay (LOS), discharge medications, return to the Emergency Department within 72 hours of discharge and subsequent diagnosis of an underlying hematological or immunological disorder.

## Results

This is an interim analysis of 383 patient encounters. Of these, there were 62 admissions for 49 patients meeting criteria, with 87 charts remaining for review. 54 encounters (87%) were treated with Piperacillin-Tazobactam, most with a dose of Tobramycin, prior to or during admission. 47% of patients had viruses on nasopharyngeal aspirate and one had rotavirus in the stool. There were three positive blood cultures with coagulase-negative Staphylococcus, which were interpreted as contaminants. Of 13 positive urine cultures, only one was considered a true urinary tract infection (UTI), with continuation of antibiotics on discharge. An additional seven patients were discharged on antibiotics: two for possible bacterial pneumonia, and the remainder for mucocutaneous infections and otitis media. The mean LOS was 2.34 days. 40 of the 49 patients (82%) had eventual normalization of neutrophil counts while the remaining nine either remained neutropenic or lacked repeat investigations. Follow-up diagnoses included benign neutropenia of childhood and one patient with STING-associated vasculopathy with onset in infancy.

## Conclusion

Of the 62 encounters evaluated to date, there has only been one SBI (1.6%), which was a UTI without bacteremia, and two possible bacterial pneumonias, supporting previous findings of low rates of invasive bacterial infections in healthy patients with FN. Of the patients discharged on antibiotics, most were given for non-serious bacterial infections. Given the low SBI rates and few significant follow up diagnoses, prospective studies would be valuable to evaluate whether a change in practice is needed regarding antibiotic use in low-risk patients with suspected viral-induced neutropenia

Funded by WCHRI

The Power of Partnership

Abstract # 226  
Presenter: Thompson, Alison  
Supervisor: Scott, Shannon  
Title: **A systematic review of parents' experiences and information needs related to pediatric functional constipation**  
Authors: Alison Thompson, Eytan Wine, Shannon MacDonald, Shannon Scott

### **Introduction**

Functional Constipation affects approximately 1 in 5 Canadian children. The condition causes significant physical, emotional, psychosocial, and financial burdens for children, families, and healthcare systems. Clinical practice guidelines suggest that patient and family education is the primary step in successful treatment and yet there is little research exploring what information families need and how to best support them. The primary aim of this study is to map and synthesize current evidence on the experiences of parents caring for a child with functional constipation.

### **Methods**

We undertook a systematic review of published research. Our search was carried out in Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily, Ovid Embase, Ovid PsycINFO, EBSCO CINAHL Plus with Full-text, Wiley Cochrane Library, ProQuest Dissertations & Theses Global, Scopus, Web of Science Core Collection. All databases were searched from inception to current without date, language or format limits applied. First and second level screening with two reviewers determined inclusion. Only full-text articles were considered. We will use a narrative synthesis approach for data analysis which allows for inclusion of both quantitative and qualitative designs. Included studies will undergo quality assessment using the Mixed Methods Appraisal Tool. Reporting will follow the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

### **Results**

14 studies were included for evidence synthesis. Preliminary themes across the research suggest that experiences of caring for a child with functional constipation include increased familial stress and novel parenting challenges. Parents commonly identified feelings of isolation and uncertainty. In addition, parents carried a lasting sense of guilt related to the idea of causing or contributing to their child's condition. Parents were often unclear about the physiology of functional constipation and had a vague understanding of recommended therapies.

### **Conclusion**

A comprehensive understanding of parents' experiences and self-identified needs related to caring for a child with functional constipation is foundational to ensure clinicians can provide relevant support. Results of this review can be used to create resources for and improve clinical interactions with parents caring for a child with functional constipation.

Funded by This research has been funded by the generous support of the Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute.

The Power of Partnership

Abstract # 227  
Presenter: Eaton, Andrea  
Supervisor: Ball, Geoff  
Title: Determining stakeholders' priorities for child and family research – progress to date  
  
Authors: Eaton, A., Dyson, M., Gokiert, R., Rajani, H., Ladha, T., Birken, C., Maguire, J., Ball, G.D.C.

### **Introduction**

Children attend community-based medical appointments with pediatricians and allied health providers for diverse reasons, leading to a range of preventive interventions and therapeutic services. Given this breadth, a pediatric and family healthcare setting is an ideal venue to learn about stakeholders' most pressing health questions. The Northeast Community Health Centre (NECHC) provides health services for a substantial proportion of new Canadians from immigrant and refugee backgrounds as well as lower income families. Given the sociodemographic characteristics of families living in northeast Edmonton, their health needs and priorities are likely to differ from their peers in other communities. Our research is a critical first step to develop a long-term plan to conduct practice-based and patient-oriented research to meet the priorities of families and health care providers in northeast Edmonton. Our objectives are to (1) identify unanswered questions that our stakeholders (parents of 0-17 year olds and their healthcare providers) at the NECHC have regarding child and family health and well-being and (2) prioritize questions that stakeholders perceive to be of greatest importance into a 'Top 10' list.

### **Methods**

Stakeholders' priorities will be generated using an augmented James Lind Alliance methodology. This is a systematic, step-by-step, group-based process, where stakeholders are active and integral partners in the research process. Parents (n~4) and front-line clinicians (n~4) are first invited to join researchers (n~4) on a Steering Committee to oversee the study process. Unanswered questions will be collected through an online REDCap questionnaire from a diverse mix of parents (n~100) of 0-17 year olds and front-line clinicians (n~25) providing child/family health services at the NECHC. Questions will be combined and categorized, then stakeholder input solicited via a second online survey to rank-order the questions considered to be the most important based on stakeholders' perceived value. Results will be collated and taken to a facilitated focus group for parents and clinicians to discuss and select the ten most important unanswered questions for research to address. This mixed method approach will be used to rank the most important topics and will generate a 'Top 10' research priorities list.

### **Results**

Alberta Health Services operational and ethics approvals have been secured. We began working at the NECHC in July 2019. With 8 of ~12 Steering Committee members confirmed, we plan to hold the first steering committee meeting in October 2019. We will produce a 'Top 10' list of child and family research priorities unique to the NECHC community. The study is expected to be complete in the summer of 2020.

### **Conclusion**

Members of our research team range from trainees to well-established academic researchers; we know there is a strong desire to engage in future research with this community, in this setting. As the creation of an authentic, open partnership between researchers and stakeholders is crucial in quality and valued research, this project is foundational for meaningful patient-oriented, community-based future research at the NECHC. These 'Top 10' research priorities can be used by our research team, and others, to have a sound basis for the direction of future research carried out in this pediatric and family health care setting.

Funded by WCHRI CRISP Grant and WCHRI PaCET Award

The Power of Partnership



Abstract # 228  
Presenter: Kebbe, Maryam  
Supervisor: Ball, Geoff  
Title: **Preliminary evaluation of Conversation Cards for Adolescents©: A Pilot randomized controlled trial**  
Authors: Maryam Kebbe, Anna Farmer, Michele P Dyson, Shannon D Scott, Tara-Leigh F McHugh, Scot Lappa, Hasu Rajani, Bonnie Islam, Lynn Jacoby, Tehseen Ladha, Kiran Talwar, Mona Zhang, Geoff DC Ball

### **Introduction**

Providers can benefit from practical tools to encourage healthy lifestyles in adolescents. We created Conversation Cards for Adolescents© (CCAs), a patient-centered communication and behavior change tool for adolescents to identify barriers and enablers for behavior change. Our purpose is to report preliminary results on the (i) feasibility of CCAs in a clinical care setting and (ii) user experiences of CCAs.

### **Methods**

This ongoing study is a mixed-methods, pragmatic, theory-driven, pilot randomized controlled trial that will include 50 adolescents (13–17 years old) and 9 providers at the Northeast Community Health Centre (Edmonton, Canada). Adolescents will collaboratively set one S.M.A.R.T. (Specific, Measurable, Attainable, Realistic, Timely) goal with their provider with (intervention group) or without (control group) using CCAs. User experiences of CCAs will be measured by the User Experience Questionnaire for attractiveness, perspicuity (clarity), efficiency, dependability, stimulation, and novelty.

### **Results**

As of August 2019, we enrolled 5 adolescents with obesity (15.4±1.7 years old; ≥95th percentile at baseline; 60.0% female; 80.0% Caucasian). Randomization interest and accuracy, task and outcome measure completion, and retention were all 100% in the intervention and control groups, and met a priori criteria for feasibility. Except for novelty, CCAs received a positive evaluation for all scales (attractiveness, efficiency, perspicuity, dependability, stimulation) Based on the User Experience Questionnaire.

### **Conclusion**

In our current sample, CCAs were well-received and practical for use in a clinical care setting. With recruitment continuing to the end of 2019, we will complete our assessment of feasibility, user experiences, and preliminary effectiveness of CCAs on behavior change to inform necessary elements and modifications for a full-scale randomized controlled trial on behavior change in adolescents with obesity.

Trial registration: NCT03821896 (clinicaltrials.gov). Registered on 30 January 2019, <https://clinicaltrials.gov/ct2/show/NCT03821896>

Funded by Alberta Health Services

The Power of Partnership

Abstract # 229  
Presenter: Sung, Hyelin  
Supervisor: Scott, Shannon  
Title: Usability of infographics for UTI and bronchiolitis

Authors: Hyelin Sung, Anne Le, Tabatha Plesuk, Hannah Brooks, Tony Ahn, Lisa Hartling, Shannon D. Scott

### Introduction

Urinary tract infections (UTIs) and bronchiolitis are common causes of pediatric acute illness. Parents have expressed a lack of knowledge about these two common childhood illnesses. This may lead to delayed care, mistrust of health care providers, feelings of isolation, and further health consequences, demonstrating the need for more effective information resources. Infographics combine text and images to convey complex health information to parents in a simple, easy to understand, and aesthetically pleasing way. The purpose of this study was to work with parents to test the usability of both a UTI and a bronchiolitis digital infographic.

### Methods

Usability testing was conducted on iPads at an urban pediatric emergency department and a general urgent care center in Edmonton, Alberta. The usability of each tool was assessed through a 9-question survey on a 5-point Likert scale. Parents were randomly assigned to evaluate either the UTI or bronchiolitis infographic. Statistical analyses were completed using SPSS.

### Results

64 parents participated in usability evaluations of the infographics. Overall, responses to the tools were positive (mean scores ranged from 4.10-4.48). Parents agreed that both infographics (UTI/bronchiolitis) were useful (4.10/4.38), relevant (4.27/4.32), and simple to use (4.48/4.26). When asked if the infographic could be used without additional instructions, the UTI infographic scored 4.40 and the bronchiolitis infographic scored 4.21. Both infographics had an appropriate length (4.37/4.09) and were aesthetically pleasing (4.43/4.42). When asked if the infographics would be used in the future, the UTI infographic scored 4.43 and the bronchiolitis infographic scored 4.24. Parents generally agreed the infographics would help them make decisions about their child's health (4.17/4.22) and they would recommend the infographics to a friend (4.30/4.38).

### Conclusion

Both infographics were well received by parents. The differences in responses for UTI and bronchiolitis infographics were minimal. The positive feedback from parents suggests that infographics are useful mediums of knowledge translation.

Funded by NCE, WCHRI

The Power of Partnership

Abstract # 230  
Presenter: Saini, Jashan  
Supervisor: Pagliardini, Silvia  
Title: Modulation of respiratory rhythms via periaqueductal gray optostimulation

Authors: Jashan Saini, Silvia Pagliardini PhD

## Introduction

Breathing is a seemingly simple behaviour that is essential for life. However, its simple, rhythmic occurrence is vulnerable and breathing disturbances may occur, especially during sleep. Conditions such as apnea of prematurity, SIDS, and hypoventilation syndromes are common in preterm children and newborns. Pharmacological treatments exist although are not always effective. In order to develop new approaches to alternate treatments, we need to gain a deeper understanding of how breathing rhythms are generated and modulated. Respiratory rhythms are controlled by neuronal networks in the ventral medulla, where different neuronal groups are responsible for the rhythm and pattern of respiratory muscle contraction. The Periaqueductal gray (PAG) is a region involved in relaying emotional responses, vocalization, fight/flight responses, pain and has an influence on breathing. Previous work suggests the existence of connectivity between PAG and the respiratory network. Studies have also demonstrated that electrical stimulation and pharmacological excitation of the PAG elicits active expiration and perturbs respiratory rhythm (rhythm reset and tachypnea).

## Methods

We aimed to investigate the functional role of neuronal connections between the PAG and the respiratory network by using optogenetics to stimulate the PAG in a temporally and spatially specific fashion. We unilaterally injected into the DLPAG/VLPAG of adult male rats, a virus expressing photosensitive membrane proteins along with a fluorescent reporter protein for detection of transfected neurons. Following a postoperative period of 2-3 weeks, we photostimulated DLPAG/VLPAG neurons. Electromyography was used to record from respiratory muscles (genioglossus, diaphragm, and abdominal) to assess stimulus-associated respiratory responses. Brain tissue was fixed and processed for detection of viral expression.

## Results

Our results indicate that optogenetic stimulation of the dorsolateral PAG (DLPAG) elicited tachypnea (transient increase in respiratory rhythm), reset respiratory rhythm, however did not promote active expiration. Stimulations at the level of the ventrolateral PAG (VLPAG) did not result in marked changes to respiratory rhythm and pattern, and the onset of active expiration was also not observed.

## Conclusion

We conclude that the PAG is involved in the modulation of central respiratory rhythm generation such that temporally and spatially specific activation of the DLPAG contributes to resetting the phase of breathing and induces tachypnea. Periaqueductal Gray modulation of breathing may be associated with direct stimulus of the inspiratory oscillator known as the PreBötzinger complex (PBC). Further studies will address these potential connections and their relation to modulation of breathing across states.

Funded by Office of the Provost and VP (Academic) Summer Research Award and CIHR Project Scheme Grant (2018-2023)

The Power of Partnership

Abstract # 231  
Presenter: Saini, Jasmeen  
Supervisor: Pagliardini, Silvia  
Title: Ventilatory recovery by etonogestrel in central chemoreflex-impaired female rats  
Authors: Jasmeen K. Saini, Landon A. De Hoog, Silvia Pagliardini

### Introduction

Congenital central hypoventilation syndrome (CCHS) is caused by a genetic mutation of the transcription factor Paired-Like Homeobox2b (PHOX2B), which is essential for neural development of several classes of brainstem neurons. CCHS and other hypoventilation syndromes are associated with sleep-related hypoventilation and impairment of CO<sub>2</sub> chemosensitivity. Respiratory stimulants are ineffective in promoting chemoreflex recovery with the exception of a serendipitous finding indicating a 2-3 fold increase in the hypercapnic ventilatory response following introduction of a daily oral contraceptive containing Desogestrel, a potent progestin. Here we investigated the effect of the active metabolite of Desogestrel (Etonogestrel) in normoxia and during the hypercapnic and hypoxic ventilatory challenges in healthy female rats and in rats with an impaired CO chemoreflex response.

### Methods

Ventilatory responses to hypercapnia and hypoxia were tested within whole-body plethysmographs in adult female Sprague-Dawley rats during chronic (1-4 weeks) delivery of Etonogestrel. Impairment of the CO<sub>2</sub> chemoreflex response was achieved through microinjection of substance-P saporin into the retrotrapezoid nucleus, a key component of the CO<sub>2</sub> chemoreflex in the brainstem.

### Results

Etonogestrel did not affect baseline breathing nor CO<sub>2</sub> chemoreflex in healthy rats. Etonogestrel increased normoxic respiratory frequency, tidal volume and minute ventilation in rats with chemoreflex impairments. Furthermore, Etonogestrel restored respiratory frequency and minute ventilation responses to control levels during the hypercapnic and hypoxic ventilatory responses in rats with lesions of the retrotrapezoid nucleus.

### Conclusion

Etonogestrel supplementation is effective in promoting recovery of the hypercapnic ventilatory response in conditions in which the central chemoreflex is impaired.

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The Power of Partnership

Abstract # 232  
Presenter: Biancardi, Vivian  
Supervisor: Funk, Gregory D.  
Title: Identification of an ion channel in the inspiratory rhythm generator that is potentiated by ATP and counteracts the life-threatening depression of breathing during hypoxia  
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## Introduction

Breathing in premature infants often stops briefly (apnea) because the brainstem network that controls breathing is immature (apnea of prematurity, AOP). During these apneas, oxygen levels fall (hypoxia) triggering the biphasic hypoxic ventilatory response, which comprises an initial increase in ventilation followed by a centrally-mediated secondary depression that can be life-threatening in AOP. Caffeine, is used to stimulate breathing in AOP. However, ~20% of these infants do not respond to caffeine. Thus, alternate therapies are urgently needed. The transmitter ATP is released in the preBötzing Complex (preBötC, brainstem region that generates inspiration), during hypoxia where it attenuates the secondary depression by activating P2Y1 receptors that excite inspiratory neurons and increase breathing. Understanding the mechanism underlying this excitation may provide alternate means for stimulating breathing in AOP. Preliminary data suggest that ATP excites breathing by potentiating an ion channel that underlies the hyperpolarization-activated inward current, Ih. The objectives of this study are to 1) directly test whether P2Y1 receptors excite breathing in vitro by modulating Ih and 2) test whether potentiation of Ih in the preBötC during hypoxia in vivo attenuates the hypoxic respiratory depression.

## Methods

To test hypothesis 1, we applied whole-cell and nerve recording methods to rhythmic neonatal rat, preBötC-containing brain slices and measured the effects of P2Y1 receptor activation on Ih currents in inspiratory neurons and whether blocking Ih (and the second messenger, cAMP) affected the P2Y1-mediated increase in inspiratory frequency. To test hypothesis 2, we compared the hypoxic ventilatory responses (10% O<sub>2</sub>) of intact, anesthetized, vagotomized spontaneously-breathing adult rats in control and after blocking Ih via reverse microdialysis of ZD7288 into the vicinity of the preBötC.

## Results

In vitro, MRS2365 (P2Y1 agonist) potentiated Ih by  $32 \pm 6\%$  at -100 mV (in 18 of 45 neurons). The MRS2365 inward current and its potentiation of Ih were blocked by ZD7288 (open channel blocker of Ih, 100  $\mu$ M), while ZD7288 at 100 and 25  $\mu$ M attenuated the MRS2365-induced frequency increase by  $90 \pm 2\%$  and  $67 \pm 12\%$ , respectively. Similarly, inhibition of cAMP, the second messenger that potentiates Ih, by SQ 22536 (100  $\mu$ M) significantly attenuated the MRS2365 currents ( $60 \pm 4\%$  in 9 of 18 cells) and attenuated the MRS2365-induced frequency increase by  $51 \pm 13\%$ . In vivo, reverse microdialysis of ZD7288 (100  $\mu$ M; n=13) in the preBötC area caused a significant, 20% increase in the hypoxic depression of inspiratory frequency compared to aCSF microdialysis (n=6).

## Conclusion

These data suggest that the P2Y1R-mediated excitation of the preBötC network is produced, at least in part, via a cAMP-dependent modulation of Ih in a subpopulation of inspiratory neurons; and that activation of Ih in the preBötC attenuates the hypoxic ventilatory depression in adult animals. These data identify Ih, and second messengers that modulate Ih, as potential targets for the development of therapies to counteract respiratory depression in premature infants.

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