Interaction of Immature Red Blood Cells with Gut Bacteria

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Introduction

- CD71⁺ cells are immature erythrocytes, nucleated red blood cells.[1,2] Previously, our group has provided evidence that these cells are enriched in newborn mice, human cord blood, and human placenta.[1,2]
- Furthermore, CD71⁺ cells possess distinct immunosuppressive and immunomodulatory properties.[1,2,3] Their mechanisms of suppression include the production of cytokines (proteins that can affect the behaviour of other cells)[2] and the depletion of arginine (an amino acid that plays a role in protein production).[3,4]
- Additionally, CD71⁺ cells play a role in one's digestive health by preventing gut inflammation following the sudden transition from a sterile *in utero* environment to the initial bacterial exposure in the external environment.[1]
- Although, distinct roles of these cells have been observed and determined, the interaction between CD71+ cells and gut bacteria is still unknown. By defining the function of these cells, it can lead to further application to improve quality of life.

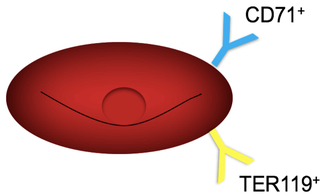

Figure 1: Immature red blood cell expressing both, CD71⁺ and TER119⁺, markers on its surface.

Objective

The purpose of this study was to investigate the relationship between immature red blood cells and gut bacteria.

Methods

- The duodenum, jejunum, ileum, cecum, colon, and spleen were collected from the gastrointestinal tract of adult mice.
- Gut content was collected and used for the extraction of total bacterial DNA.
- qPCR, quantitative polymerase chain reaction, was then performed on the extracted DNA to quantify total bacteria, lactobacilli, and *Enterobacteriaceae* family.
- The tissues of the collected compartments were broken down in a number of processes in order to isolate gut immune cells from the lamina propria.
- These isolated cells were then stained with aqua dye to distinguish if the cells were alive or dead. The cells were then further stained with CD71⁺ and TER119⁺ antibodies and visualized through flow cytometry.

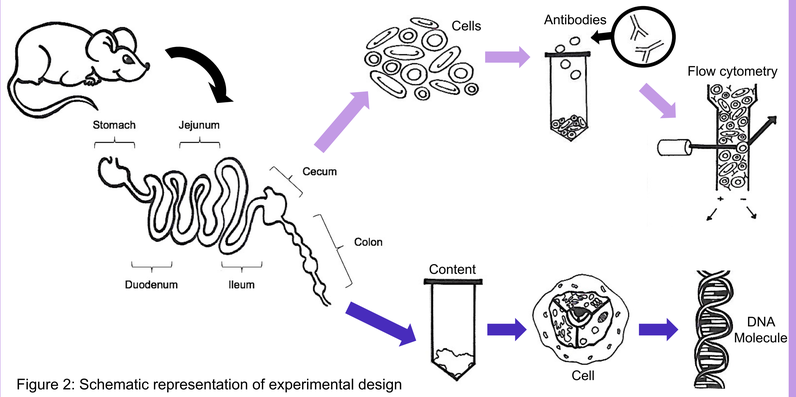

Figure 2: Schematic representation of experimental design

Results

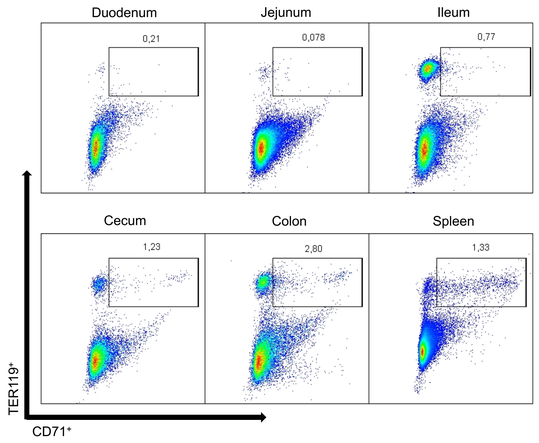

Figure 3: Flow cytometric analysis showing the percentage of CD71⁺ immature red blood cells in different gastrointestinal tract compartments. The numbers indicate the percentage of CD71⁺ immature red blood cells in the adjacent boxed areas.

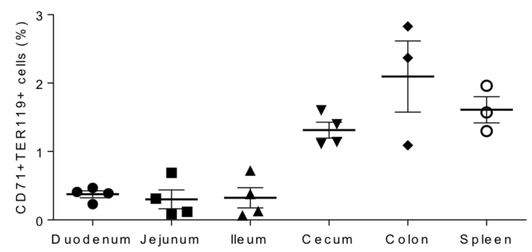

Figure 4: Frequency of CD71⁺ immature red blood cells in gastrointestinal tract compartments of adult mice.

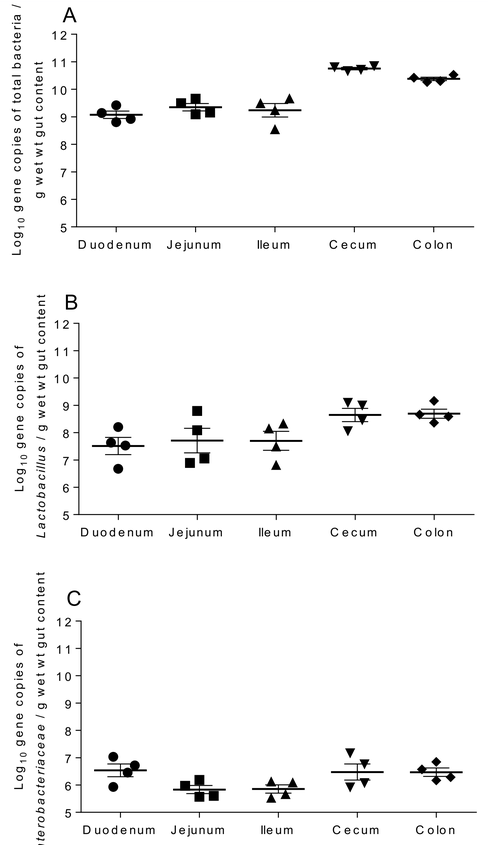

Figure 5: Quantification of dominant bacterial groups in gastrointestinal tract compartments of adult mice. A) total bacteria; B) *Lactobacillus* group ; C) *Enterobacteriaceae* family

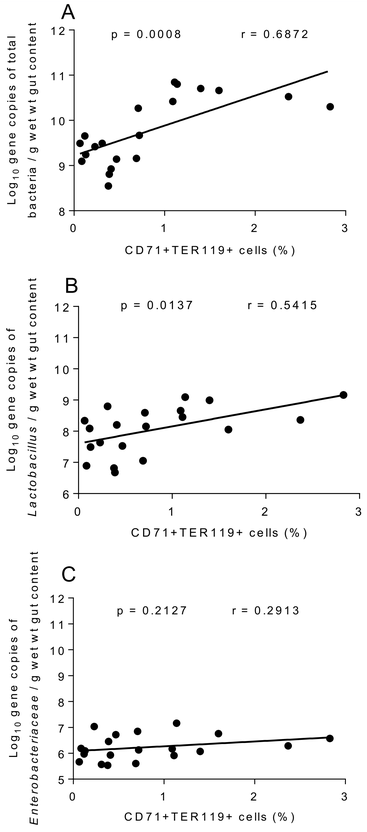

Figure 6: Correlation analysis between CD71⁺ immature red blood cells and dominant bacterial groups quantified in adult mice gut. A) total bacteria; B) *Lactobacillus* group ; C) *Enterobacteriaceae* family

Key Findings

- The percentage of immature red blood cells varies in the different gut compartments, with the highest percentage observed in the cecum and colon.
- As previously demonstrated, a greater abundance of bacteria (total bacteria, lactobacilli, and members belonging to the *Enterobacteriaceae* group) is revealed in the cecum and colon compared to the small intestine.
- A positive correlation is detected between immature red blood cells and the studied bacterial groups.

Conclusion

A higher frequency of immature red blood cells were observed in the gut compartments with the highest number of bacteria, providing pilot evidence for the interaction of these immune cells with gut bacteria.

Relevance

- These results provide preliminary information about the interaction of immature red blood cells with gut bacteria.
- Furthermore, the findings from this study can generate new research questions to better understand the role of immature red blood cells in order to implement these cells in future immune therapies.

Acknowledgements

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Cited Literature

[1] Elahi S, *et al.* 2013, Nature, 504:158; [2] Elahi S, 2014, Front Immunol, 5:376; [3] Dunsmore G *et al.* 2017, J Immunol, 199:2081; [4] Delyea C *et al.* 2018, J Immunol, 200:4044