Sponges as sensitive animals: sensory systems and energetics of filtration in demosponges

by

Danielle Alexandra Ludeman

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Department of Biological Sciences University of Alberta

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Abstract

Sponges (Porifera) are abundant in most marine and freshwater ecosystems, and as suspension feeders they play a crucial role in filtering the water column. Their active pumping enables them to filter up to 900 times their body volume of water per hour, recycling nutrients and coupling the benthic and pelagic communities. Despite the ecological importance of sponge filter feeding, little is known about how sponges control the water flow through their canal system or how much energy it costs to filter the water. Sponges lack conventional muscles and nervous tissue, yet respond to stimuli through coordinated behaviours. Here, I show the presence of non-motile cilia in the canal system of sponges and study their role as flow sensors. I demonstrate that molecules known to block cationic channels in sensory cilia in other organisms reduce or eliminate sponge behaviour. In addition, removal of the cilia using chloral hydrate eliminates sponge contractions, suggesting the cilia are flow sensors and involved in controlling water flow through the canal system. Sponges have long been considered textbook examples of animals that use current-induced flow. I show evidence that suggests some species of demosponge do not use current-induced flow; rather, they respond behaviourally to increased ambient currents by reducing their pumping volume. Using a morphometric model of the canal system, I also show that filter feeding may be more energetically costly than previously thought. Measurements of pumping volume and oxygen removal in five species of demosponges show that pumping rates are variable within and between species, with more oxygen consumed the greater the pumping volume. Together, these data suggest that sponges have a lot of control over the volume of water pumped, which may be an adaptation to reduce the energetic cost of filtration in times of high stress.

Preface

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Chapter One

A general introduction to behaviour and filter-feeding in sponges

1.1 Ecology of sponges

Sponges (Porifera) are an important structural and functional component of most benthic marine and freshwater environments. Their huge abundance, diversity, and biomass is such that they interact with most other organisms either by providing habitat or acting as competitors, symbionts, hosts of symbionts, consumers, or prey (Diaz and Rützler, 2001; Wulff, 2006). A wide diversity of animals inhabit the interior cavities and canals of sponges (Rützler, 1976; Villamizar and Laughlin, 1991; Ribeiro et al., 2003), with some sponges supporting whole communities of other organisms, such as the glass sponge reefs off the coast of British Columbia spanning hundreds of kilometers in size (Krautter et al., 2001). In addition to animals living in the canal system of sponges, many photosynthetic and chemosynthetic symbionts ranging from bacteria to algae are found in the tissue of sponges, occupying almost 40% of the tissue volume (Vacelet, 1975; Wilkinson, 1978). Sponges also play an important functional role by filtering out particles from the overlying water column, assimilating carbon, and linking the benthic and pelagic environments in a process termed benthic-pelagic coupling (reviewed in Gili and Coma, 1998). By filtering out food from the water column, sponges recycle nutrients and are known to influence levels of primary production (Corredor et al., 1988; Diaz and Ward, 1997; Southwell, 2007; Southwell et al., 2008) and contribute substantially to organic matter cycling in the water column (Reiswig, 1971; Reiswig, 1974; Reiswig, 1981; Pile et al., 1996; Pile et al., 1997; Turon et al., 1997; Yahel et al., 2003). This thesis focuses on the behaviour of pumping water through the sponge body to filter out food particles.

As suspension feeders, the sponge body plan is designed to filter as much water as needed for feeding and respiration (Reiswig, 1975). Their huge range in habitats and their long evolutionary history, however, have led to many adaptations in both body form and pumping rates. A variety of pumping rates have been documented both within individual sponges and between species, with differences in water temperature (Riisgård et al., 1993), suspended sediment concentration (Gerrodette and Flechsig, 1979), sponge body form (Reiswig, 1975), microbial content (Weisz et al., 2008), and tissue density (Turon et al., 1997) all known to influence the volume of water filtered by the sponge. Sponges are a common component of most benthic aquatic environments ranging from the tropics to the poles, including the abyssal deep sea to freshwater rivers and lakes. Substrate type can range from hard rocky bottom, soft sediment, to infaunal, and a wide variety of sponge shapes and sizes exist (Figure 1-1 a-g). Some sponges have even strayed from filter feeding and evolved a carnivorous feeding strategy (Figure 1-1 h), using their spicule skeleton to snag crustaceans in the surrounding water column (Vacelet and Boury-Esnault, 1995). It is unclear exactly what role habitat plays on the filtration and pumping activity of sponges, though sponges have likely adapted their pumping activity to coincide with local food and water dynamics.

Despite their huge abundance, diversity, and ecological importance in most marine and freshwater habitats, there is much about sponge physiology and ecology that is not fully understood (Bergquist, 1978; Wulff, 2006). Sponges lack many of the tissues and systems that define the Metazoa, with a body plan so distinct from other animals that it is often difficult for sponge biologists to communicate results to a broader audience. Historically, it has been challenging to maintain maximal pumping activity in whole sponges in the laboratory, which has led to difficulties in understanding sponge physiology and behaviour in relation to filter feeding (Bergquist, 1978; Hadas et al., 2008; Weisz et al., 2008). Recent advances in technology, however, have led to powerful sensors that can be used *in situ* to measure oxygen removal and pumping rates of sponges such as thermistor flow meters (Reiswig, 1971; Reiswig, 1974; Vogel, 1977), acoustic Doppler velocimeters (ADVs²; Leys et al, 2011), and oxygen optodes (Hadas et al., 2008). In addition, recent improvements in our understanding of water flow and oxygen requirements for sponges has led to the ability to study sponge filter feeding and behaviour in the laboratory



Figure 1-1 The diversity of sponge body forms found in Bocas del Toro, Panama counter-clockwise from top left: (A) barrel sponges (*Xestospongia*) that can grow to a few metres in height, (B) the encrusting sponge *Mycales*, shown here growing on mangrove roots, (C) rope sponges (*Aplysina*), (D) columnar (*Aplysina*) and (E) plate-like sponges (*Ircinia*), (F) vase shaped sponges (*Xestospongia*), and (G) the boring sponge (*Cliona*) that dissolves through coral skeleton [Photos (A-G) taken by N. Lauzon] (H) In addition to suspension feeding sponges, some sponges evolved a carnivorous feeding strategy such as *Asbestopluma* found in British Columbia, Canada, that uses its spicule skeleton to snag small crustaceans in the water column [Photo (H) from Chu and Reiswig (2014)].

(Hadas et al., 2008; Leys et al., 2011). Furthermore, the more widespread use of freshwater sponges as model organisms has led to a greater understanding of some basic anatomy and physiology in relation to the water canal system of sponges (McNair, 1923; Wintermann, 1951; Elliott and Leys, 2007; Adams et al., 2010; Elliott and Leys, 2010). These advances have set the stage to answer some important questions about how sponges control water flow through their bodies and what the energetic cost is for a sponge to pump water. In Chapter Two I use freshwater sponges as model organisms to study how sponges sense their environment to maintain water flow through their canal system. In Chapter Three I describe use of fiber optic oxygen sensors and profiling ADVs to study sponge pumping and oxygen removal *in situ* and *in vitro* to study the energetic cost of filter feeding in sponges.

1.2 Anatomy of sponges

As suspension feeders, sponges pump large volumes of water through a branching canal system to obtain both food and oxygen as well as excrete wastes and release gametes. This water canal system, termed the aquiferous canal system, penetrates all regions of the sponge body (Figure 1-2) leading to an absence in regional specialization. Water flow is unidirectional through the sponge, entering the sponge often through many small holes on the outer surface, termed ostia, and exiting the sponge through one large opening termed the osculum (Figure 1-3). The ostia are formed by porocytes, sphincter-like cells that can control the inflow of water to the canal system. Once water has entered into the canal system it flows through branching incurrent canals that decrease in diameter until they reach the choanocyte chambers through an aperture termed the prosopyle. This branching canal system drastically increases cross-sectional area, decreasing the velocity of water as it enters the choanocyte chambers, just as blood capillaries do. Here, choanocytes act as both a pump and a filter to draw water through the canal system using their flagella and filter out particles using the microvillar collar. Once the water passes through the filter it exits the choanocyte chamber via the apopyle into the excurrent canals. The excurrent canals are similar to a mirror image of the incurrent canals, increasing in diameter and merging together resulting in a jet of filtered water and waste out of the osculum, the terminal opening located at the back-end of the canal system. The entire canal system is lined



Figure 1-2 Major organizational types of Demosponges

Despite many different body forms of sponges, the aquiferous canal system (shown in black) penetrates all regions of the sponge body leading to a reduction in regionalization (taken from Reiswig, 1975).



Figure 1-3 Aquiferous canal system in sponges

(A) Schematic drawing showing water flow through a sponge. Water enters through pores on the sponge surface, into incurrent canals to the choanocyte chambers where the water is filtered, then out through the excurrent canals to the osculum. The branching is such that water is only filtered once in a chamber. (B) Schematic representation showing water flow through a sponge highlighting the huge increase in cross-sectional area as the water enters the choanocyte chambers, which slows the water for filtration. The cross-sectional area then decreases as the water leaves the choanocyte chambers, jetting the water out through the osculum.

with a tight epithelial tissue (Adams et al., 2010) made out of contractile endopinacocytes providing the sponge with a lot of control over the water flow through each region (Nickel, 2004).

1.3 Sponges are sensitive to their environments

Although at first glance sponges may appear to be static animals spending their entire adult life stationary on the sea floor, larvae and adults in all sponge classes have been documented to display responsive behaviour (Leys and Meech, 2006), albeit slower than most other animals. In fact, many of the coordinated responses of sponges are too slow for human eyes to detect, so that we usually rely on time-lapse photography to capture sponge behaviour (Pavans de Ceccatty, 1974). Only then is it easy to see that sponges display coordinated responses to the mechanical touch of other organisms (Nickel, 2004) with some species also undergoing periodic endogenous contractions (Reiswig, 1971; Weissenfels, 1984; Nickel, 2004). Local cellular contractions in the canal system have also been documented and suggested to regulate the flow of water through contractions at myocytes (Bagby, 1966), porocytes (Simpson, 1984), and endopinacocytes lining the canals (Nickel, 2004). In addition, the osculum at the back-end of the canal system is highly contractile in some species (McNair, 1923; Prosser et al., 1962; Emson, 1966; Pavans de Ceccatty, 1969), sometimes taking on a variety of forms. These small adjustments to canal diameters probably occur constantly in sponges allowing them to maintain adequate flow through the aquiferous system.

Much of the early work on sponge behaviour has been limited to laboratory experiments observing how individual structures respond. These studies have demonstrated that sponges respond to mechanical (Parker, 1910; McNair, 1923; Prosser et al., 1962; Emson, 1966), chemical (Parker, 1910; Emson, 1966; Prosser, 1967), and electrical stimulation (Emson, 1966). More complex coordinated behaviours in response to external stimuli have also been demonstrated in a variety of sponges, beginning with the use of sandwich preparations by Wintermann (1951) that provided the first hint that local contractions may be part of a more 'global' behaviour. Since then, sponges have been shown to display endogenous rhythmic or diurnal patterns in behaviour (Pavans de Ceccatty et al., 1960; Reiswig, 1971; Weissenfels, 1984; Nickel, 2004) as well as whole

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body contractions in response to mechanical or chemical stimuli (Nickel, 2004; Elliott and Leys, 2007; Ellwanger et al., 2007; Elliott and Leys, 2010), sometimes causing the whole animal to shrink to one third of its original size. Laboratory studies of this global contractile behaviour have provided insight into the role of ligand-based receptor systems in coordinating signals through the sponge body (Ellwanger et al., 2007; Elliott and Leys, 2010). Such coordinated contractions in sponges have been suggested to help clear debris or eject gametes from the sponge (Pavans de Ceccatty, 1969; Reiswig et al., 1976; Elliott and Leys, 2007), and usually result in periodic cessations or reductions in pumping activity (Reiswig, 1971; Elliott and Leys, 2007).

Although the link between sponge contractions and pumping activity is not always made, the contraction of canals will undoubtedly influence the volume of water that a sponge pumps. Sponges, as suspension feeders, rely on water flow through their bodies for both food and oxygen, and therefore should have a high degree of control over the water flow through their bodies. Sponges have been shown to respond to the flow regime around them and suspended sediment in the water column, altering their pumping rates accordingly (Reiswig, 1971; Gerrodette and Flechsig, 1979; Tompkins-MacDonald and Leys, 2008). Increased suspended sediment in the water column results in periodic cessations of pumping activity (Gerrodette and Flechsig, 1979; Tompkins-MacDonald and Leys, 2008). In addition, pumping volume and behaviour have been linked to wave strength in the sponge Tethya crypta when Reiswig (1971) measured excurrent velocity in 50 individuals of a population over many months while taking images of their oscula. He found that during storms, the increased wave strength and resulting sand scour caused rapid and total oscular closure of all individuals of the population (Figure 1-4), with their effective pumping rate reduced to 51% of their maximum. It is not clear, though, whether the reduced pumping rates were a result of the increased wave action, changes in pressure, or the increased sediment in the water during the storm. Because of the high risk of clogging from sediment, sponges have likely adapted to respond to many different environmental cues that would predict high sediment in the water column.

For an animal to respond to its surroundings requires not only an ability to sense changes in the environment but also a means to relay that information to cells or tissues that

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Figure 1-4| Oscular area of sponges from a population of *Tethya crypta* in relation to wave strength

The relative dilation of 50 oscula were measured and cumulated by Reiswig (1971) each day and plotted as either percent fully dilated (dark), percent fully closed (white), or percent partially dilated (grey). Relative wave strength is shown at the bottom of each graph. High wave strength corresponds to most of the population having fully closed oscula.

can effect a response. For most animals this involves both nerves and muscles; however, sponges lack conventional nerve and muscle tissue yet still respond to their surroundings. The contractile ability of some types of sponge cells is now fairly well known, and recent studies have begun to provide an understanding of some of the paracrine signaling mechanisms in sponges that are involved in coordinating such behaviours (Ellwanger et al., 2007; Elliott and Leys, 2010). It is still unknown, however, what cells are used to sense environmental changes to trigger a response. Recently, short non-motile cilia have been found in the excurrent canal system and osculum of freshwater sponges (Leys et al., 2009) and it has been suggested that these are sensory cilia that may play a role in controlling water flow through the sponge (Elliott, 2009).

1.4 Filter feeding and its energetic cost in sponges

Sponges, as suspension feeders, pump large volumes of water through their aquiferous canal system to remove bacteria and other small plankton from the water column. Although pumping rates can vary greatly both within and between individuals and species, a single sponge has been shown to pump up to 900 times its body volume in one hour (Reiswig, 1974). This high rate of filtration exerts a major impact on the ecosystems in which sponges reside, shaping planktonic communities and coupling energy between the benthos and plankton (reviewed in Maldonado et al., 2012). Scaling up, it has been estimated that a population of the sponge *Halichondria panicea* in the western Baltic Sea can filter $3.7 \text{ m}^3 \text{ m}^{-2} \text{ d}^{-1}$, which is equivalent to 37 % of the overlying water column each day (Riisgård et al., 1993). Another example is a single 20-hectare glass sponge reef off the coast of British Columbia, which has been estimated to filter 80,000 L of water a second (Chu and Leys, 2010) and consume up to 180,000 g of carbon a day (Kahn et al., 2015). This high rate of filtration could filter an Olympic sized swimming pool in just over 30 seconds. Sponge populations, therefore, can have a pronounced effect on nutrient cycling in the overlying water column.

Pumping large volumes of water to extract food is an active process, requiring energy to bring water through the canals to be filtered in chambers. A balance is needed between the amount of energy used to pump a volume of water per unit time and the amount of food and oxygen gained. For all suspension feeders, energy is allocated to a variety of needs such as feeding, growth, reproduction, and basal metabolism. This resource allocation can shift depending on environmental factors such as temperature, food availability, photoperiod, and stress (Brown and Howard, 1985; Coma et al., 1998; Weber et al., 2006). For example, in temperate waters seasonality can result in more energy allocated to feeding and growth during times of high food availability (Coma et al., 1998).

On the other hand environmental stresses can increase an animal's energetic expenditure to deal with the stress, leaving less energy available for important processes such as growth and reproduction. During increased sediment exposure corals will produce mucus to help clear the sediment from the coral surface, an energetically costly process that can further lead to bleaching and necrosis (Weber et al., 2006). Sedimentation has also been shown to decrease sponge growth rates and reproduction (Roberts et al., 2006) and reduce their survival (Maldonado et al., 2008). Sessile suspension feeders obtain their energy by bulk feeding on minute prey, and cannot move to regions of high food abundance to increase the amount of food, and thus energy, they consume. If suspension feeding is a costly process, then environmental stresses that reduce the amount of energy sponges can allocate to feeding would further impact the amount of food energy they can consume and allocate to growth and reproduction. It is therefore important to understand the energetic cost of filter feeding in sponges to determine how sensitive they may be to environmental stresses.

In sponges, the energetic cost of filter feeding is directly proportional to the resistance of water flow through the various regions of the aquiferous canal system (Riisgård et al., 1993); the greater the resistance through the filter and canals, the more energetically expensive it is to pump water. Sponges also feed on bacteria that can be smaller than 1 µm in size (Yahel et al., 2007), requiring very small dimensions at the filter. The cost of filter feeding in sponges has previously been estimated by calculating the resistance, or head loss, across each region of the canal system (Riisgård et al., 1993; Leys et al., 2011). Riisgård and colleagues (1993; 1995) suggest that the cost of pumping is quite low at less than 1% of their total metabolism (Riisgård et al., 1993; Riisgård and Larsen, 1995), which is in line with the hypothesis of Jørgensen (1975) which suggests that filter feeders evolved a low cost of pumping to allow continuous feeding at low rates. However, sponges do not

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pump continuously, and it has been suggested that the lower pumping rates at night in *Tethya crypta* are due to lower abundances of food availability (Reiswig, 1971). This would agree with the hypothesis by Taghon (1981) which suggests that for suspension feeders to maximize their energy intake, they must vary their ingestion rate (or pumping rate) as a function of food quantity and quality. In addition, recent experimental measurements have shown that 25% of oxygen consumed in the sponge *Negombata magnifica* is used for pumping water (Hadas et al., 2008), suggesting that filter feeding is more energetically expensive than previously thought.

1.5 Use of current-induced flow

If the cost of pumping is energetically expensive, then sponges could reduce the metabolic cost of pumping by supplementing active pumping with ambient water velocities in a process termed current-induced flow (Vogel, 1974; Vogel, 1977). There are three different mechanisms in which flow in a large pipe can be induced through a smaller one (Figure 1-5), and it is thought that sponges are designed to allow water to flow passively through them, thus reducing their metabolic cost of pumping (Vogel, 1974). It is not yet clear, though, exactly how flow could be induced through a sponge. Using thermistor flow meters, Vogel (1974, 1977) measured excurrent water velocities from multiple species of marine demosponges (class Demospongaie) both in the laboratory and in situ, while experimentally changing the velocity of water around the sponge. He found that the excurrent water velocity from the sponge osculum increased when ambient velocity increased, suggesting that sponges do take advantage of ambient currents to increase the amount of water they process. However, Vogel did not measure oxygen during these recordings and so it is not known if there was an increase in the amount of energy used when excurrent velocity increased. An alternative hypothesis has been posed suggesting that the increase in excurrent water velocity from sponges may be a result of indirect effects of the ambient currents, such as higher concentrations of food particles available (Harrison and Cowden, 1976). One difficulty, therefore, in interpreting Vogel's results is distinguishing between passive flow moving through the sponge versus increased active

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Figure 1-5| Current-induced flow through pipes

Three mechanisms in which Vogel proposes fluid can flow passively from a large pipe into a smaller pipe based on a) Bernouilli's Principle, b) viscous entrainment, and c) dynamic pressure (taken from Vogel, 1974).

pumping behaviour when there is higher food availability. A second difficulty with his results is his method used to increase ambient currents. Thermistor flow meters cannot distinguish the direction of water velocity. During experiments, Vogel increased ambient velocity using a scuba fin, which would have resulted in turbulent flow in multiple directions. Therefore, the thermistor flow meters inside the osculum of the sponge may have been reading the increased turbulence from the finning method rather than increased excurrent velocity. A further look at the use of current-induced flow in sponges is required.

Recently, Leys et al. (2011) looked at the use of current-induced flow in glass sponges (class Hexactinellida). Glass sponges are distinct from the demosponges that Vogel used in that they have wider canals and larger choanocyte chambers and oscula, and thus are considered good candidates in which to expect current-induced flow. Leys et al. (2011) found that at ambient velocities greater than 15cm s⁻¹, the excurrent velocity of *Aphrocallistes vastus* did increase. Interestingly, however, they found that *A. vastus* could still arrest pumping during high ambient velocities, suggesting they still have a lot of control over the water flow through their canal system. In addition, using a morphometric model, Leys et al. (2011) measured the resistance through the filter and canal system to predict the ability to induce flow through the glass sponge. When comparing glass sponges to demosponges, Leys et al. (2011) suggested that the resistance through the filter and canal system in demosponges may be too high to allow passive flow. The use of current-induced flow, therefore, may not be adaptive for all sponges.

There are many sponge species that inhabit relatively quiet water habitats and are thus unlikely to ever experience ambient flows that could result in passive flow (Reiswig, 1975). Rather, the ability to cease pumping under unfavourable conditions is a more likely adaptation for sponges inhabiting these quiet waters. Other sponges inhabit areas that are prone to storms and high currents that bring in high suspended sediment loads. Here, increased ambient flows would be indicative of high sediment in the water column, and passive flow would not be adaptive as it would likely lead to damage of the filter and canals. Reiswig (1971) found that high ambient currents during storms in Jamaica result in cessation of pumping in *Tethya crypta* during high wave strength (Figure 1-4). Savarese et al. (1997) also found that sponges in Lake Baikal exhibit negative correlations between

ambient current and excurrent flow. It therefore remains unclear what the contribution and importance of passive flow is in sponges.

1.6 Thesis objectives and outlines

Broadly, this thesis aims to understand the behavioural control and energetic cost of filter feeding in sponges. I aimed to determine the function of the non-motile cilia previously found in the aquiferous system of sponges and study their role as flow sensors. In addition, I aimed to investigate the energetic cost of filtration through the use of morphometric models, as well as assess the use of passive flow in sponges.

In Chapter Two, I show the presence of short, non-motile cilia lining the inner epithelium of the sponge osculum in seven species of demosponges. 'Primary' non-motile cilia are involved in sensation in animals ranging from invertebrates to humans. Here, I show that drugs known to inhibit primary cilia sensation in other organisms reduce or eliminate sponge contractions. In addition, both chemical removal of the cilia and physical removal of the whole osculum in sponges reversibly eliminate sponge contractile behaviour. These findings suggest the cilia in sponges are sensory and involved in the coordination of simple behaviour, and may represent the first step in the evolution of sensory systems.

In Chapter Three I studied the ability of sponges to control water flow through the aquiferous system indirectly by examining oxygen consumption and filtration rates, as well as by modelling resistance through the sponge aquiferous system. First I re-evaluated the cost of pumping in sponges and three other groups of filter feeders using a morphometric model. I show that new measurements for both filter dimensions and pumping rates increase the cost of pumping up to five times that of previous estimates, suggesting that filter size and pumping rates contribute most to the energetic cost of pumping and that this cost may be higher than previously thought. I then compare the design of the aquiferous canal system and the cost of pumping in five species of demosponges from both temperate and tropical waters using measured canal and filter dimensions, pumping rates, and oxygen consumption. Although each species has broad differences in its overall aquiferous canal system, the design of the choanocyte chamber, and specifically of the collar apparatus, is

strikingly similar among the five species. In all species but one, oxygen consumption increased with increased pumping volume. To assess whether the two tropical species use current-induced flow to reduce the cost of pumping I looked at excurrent flow rates and oxygen consumption under different ambient velocities. Interestingly, high ambient currents resulted in a behavioural response by the sponge to change excurrent velocity, suggesting demosponges respond to ambient currents to control the water flow through their aquiferous canal system.

In Chapter Four, I reflect on the above findings and their implications with our current understanding of sponge behaviour and ecology.

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Chapter Two

Evolutionary origins of sensation in metazoans: functional evidence for a new sensory organ in sponges

2.1 Introduction

Sensory systems use specialized cells or organelles to receive signals that are conducted through the body electrically or chemically (Ryan and Grant, 2009). Signal transduction in many unicellular eukaryotes occurs via cilia, which often have both motile and sensory roles (Dunlap, 1977; Singla and Reiter, 2006; Fujiu et al., 2011). The evolution of multicellularity necessarily involved the ability to transduce signals over longer distances, which in animals is now done by nerves (Meech, 2008) to allow rapid coordinated movements of the whole organism (Mackie, 1970). Although cilia play an important role in sensing the environment in both unicellular and multicellular animals, the evolutionary relationship of sensory cilia in unicellular eukaryotes, fungi and metazoans is unclear. Studies of sensory systems in the earliest evolving metazoans could shed light on shared common mechanisms of sensation.

Sponges lack a nervous system and while they are usually considered representatives of the first multicellular animals (Philippe et al., 2009; Sperling et al., 2009; Nosenko et al., 2013; Roure et al., 2013), some recent phylogenomic analyses place ctenophores more basally (Dunn et al., 2008; Nosenko et al., 2013) calling into question our understanding of the evolution of nerves and the ancestral metazoan state. Analysis of sponge genomes and transcriptomes has revealed a complex assortment of signaling molecules and proteins necessary for a post-synaptic scaffold (Sakarya et al., 2007; Conaco et al., 2012). Together with physiological evidence that glutamatergic signaling occurs in sponges (Elliott and Leys, 2007; Ellwanger et al., 2007; Elliott and Leys, 2010) this suggests that a signaling system similar to that seen in other metazoans may be used to

coordinate sponge behavior. Whereas sensory organs are well-known from ctenophores, in sponges the mechanism for transducing sensory information from the environment has as yet remained unknown.

Here we provide experimental data which suggest that an array of non-motile cilia in the sponge osculum-the chimney-like structure through which water exits from the sponge-functions as a sensory system to detect changes in flow and control whole animal responses. We used an emergent model system, the freshwater sponge, to investigate the ultrastructure and physiology of the cilia. We also studied the molecular evolution of sensory channels of the Transient Receptor Potential (TRP) family in Porifera. Regardless of whether sponges as we know them today were or were not the earliest multicellular animals to evolve, it is intriguing to consider that an array of sensory cilia like this in sponge oscula could have given rise to more complex signalling cells, such as nerves and sensory sensilla, in the early evolution of animals.

2.2 Methods

2.2.1 Summary of experimental design

The presence of short, non-motile cilia lining the osculum of sponges led us to hypothesize that the cilia are flow sensors and involved in behaviours that maintain water flow in the sponge canal system. To test this, we conducted pharmacological experiments on freshwater sponges in the laboratory to determine whether the cilia play a role in sponge behaviour. The drugs used in experiments are known to either inhibit ciliary signalling through TRP channels in other animals or remove cilia completely. As a negative control, a calcium channel blocker was used which does not have an effect on ciliary signaling in other animals. We also looked in the transcriptomes of sponges for the presence of TRP channel sequences.

2.2.2 Collecting and culturing of sponges

Gemmules of the freshwater sponges *Ephydatia muelleri* and *Spongilla lacustris* were collected from Frederick Lake, BC and Rousseau Lake, BC, respectively, at a depth of 0-3 m and stored at 4°C in unfiltered lake water, aerated monthly, until use. These species were selected because of their transparent canal system and their ability to gemmulate over the winter, allowing us to culture them in the laboratory to conduct experiments. The spicule skeleton was removed from the gemmules by gently rubbing between two pieces of corduroy, and the gemmules were then sorted, sterilized (using 1% H₂O₂ for 5 min), and rinsed in cold distilled water. Single gemmules placed onto ethanol sterilized glass coverslips in Petri dishes containing M-medium (Rasmont, 1961), hatched in 2-3 days; culture medium was changed every 2d post hatching (dph). Only 5-10dph sponges with fully developed aquiferous canal systems were used in experiments.

2.2.3 Fixation for fluorescence microscopy

Sponges on coverslips were fixed in 3.7% paraformaldehyde and 0.3% glutaraldehyde in 100 mM phosphate-buffered saline (PBS) for 12-24 h at 4°C. Preparations were rinsed three times in cold PBS, permeabilized with PBS + 0.1% Triton X-100 (PBTX) for two minutes and rinsed in PBS. Either whole juvenile sponges or individual oscula (pulled off of the sponge by pinching the base of the osculum with fine forceps) were labeled with mouse anti-acetylated alpha tubulin (Sigma-Aldrich, Oakville, ON) in 10% goat serum (GS) and PBS at 1:1000 at RT overnight. Preparations were rinsed in PBS and incubated in goat anti-mouse 488 (Molecular Probes, Burlington, ON) at 1:100 in 10% GS and PBS for 10 min. Some preparations were stained for actin using Alexa 594 phalloidin (Molecular Probes) in BSA-PBS. Labelled oscula were sliced open using a microscalpel and mounted on a slide in 100% glycerol, which was sealed with nail polish. Whole sponges on coverslips were inverted onto a slide in 100% glycerol and viewed with

a Zeiss Axioskop2 Plus. Confocal images were taken using a Zeiss LSM 710, and surface rendering was done using Imaris v7.2 (Bitplane, Zurich, Switzerland).

2.2.4 Fixation for scanning and transmission electron microscopy (SEM, TEM)

Hatched sponges were fixed and prepared for electron microscopy as described previously (Elliott and Leys, 2007). For SEM oscula were removed from the sponges, dehydrated to 100% ethanol and critical point dried. Dried oscula were mounted on aluminum stubs using adhesive tabs and gold-coated prior to viewing using a scanning electron microscope (JEOL 6301 F field emission or a Zeiss EVO MA 15). For TEM oscula were dehydrated through 100% ethanol and embedded in epoxy (TAAB 812). Ultrathin sections (60 nm) were stained with uranyl acetate and lead citrate and viewed in a Hitatchi H-7000 or Phillips Morgagni (FEI) TEM and images captured with an AMT or Gatan digital camera respectively.

2.2.5 Orientation analysis

To assess orientation of each cilia pair with respect to the direction of water flow along the osculum, a line was drawn between the base of the two cilia and the angle between that line and a line defining the long axis of the cell was calculated using ImageJ (v1.43r; NIH, Bethesda, MD). Circular statistics calculated with Oriana v. 3.13 (KCS, Wales, UK) gave the mean angle of the orientation of cilia pairs and a V-test was performed to determine difference from the long axis of the cell.

2.2.6 Assessment of the possible sensory role

Stock solutions of 10 mM neomycin sulfate (Fisher BioReagents, New Jersey), 1 g/L (178.5 M) FM 1-43FX (Fixable analog; Molecular probes, Invitrogen), 10 mM of GdCl₃ (Sigma-Aldrich), 20 mM Verapamil (Sigma-Aldrich), and 1 M Chloral hydrate (Sigma-Aldrich) were kept covered at 4°C and used at 300 μ M, 35 μ M, 5 μ M, 10 μ M, and

4 mM respectively. Neomycin sulfate and FM1-43FX were added to the Petri dish and the sponge was stimulated using agitation (vigorous shaking of the Petri dish for 30 s) 10 min later for *E. muelleri* or 2 hr later for *S. lacustris*. Gd³⁺ and Verapamil were added to the Petri dish 2 hr prior to stimulation with 75-90 µM L-Glutamate. Treatment in chloral hydrate was for 20 hr prior to stimulation with 75-90 µM L-Glutamate; during washout the M-medium was changed every 2d and the sponge was then stimulated with 75-90 µM L-Glutamate. Oscula were removed by pinching the base of the osculum with fine-tipped forceps, and the sponge was stimulated at 2 hr and then again at 24 hr using agitation. Care was taken to add each treatment to the side of the Petri dish away from the sponge, and the solution was mixed by pipetting gently 5-6 times. Images were captured every 10 s for 50 min, or until the sponge had completed an inflation/contraction cycle. Still images were captured in Northern Eclipse v.7 (Empix Imaging Inc., Mississauga, ON, Canada). Changes in canal diameter were measured every tenth image for the first 60 images, and then every 20th image, using ImageJ (v1.43r; NIH). The neomycin and FM1-43 study had three treatment groups of neomycin, FM1-43, and control (n=8). Due to high variation in changes in canal diameters within a single sponge, three canals in each sponge were measured for the neomycin and FM test and a nested ANOVA was run in R (v.2.4.1). Variance between groups was expected to be greater than either the variance between canals or the variance within a treatment group. The variance between canals within a single individual did not account for any of the variance in the dataset, therefore only one canal was measured per sponge in the remaining experiments and tested via a one-way ANOVA in R (v.2.4.1). For the Gadolinium study there were three treatment groups of control, gadolinium, and gadolinium with 1d washout (n=3). For the verapamil study there were also three treatment groups of control, verapamil, and neomycin (n=5). For the choral hydrate study there were five treatment groups of control, chloral hydrate, 24hr washout, 72hr washout, and 120hr washout (n=5). All data were tested for normality using a Shapiro-Wilks test, with Gd^{3+} data log(x) transformed and chloral hydrate data square root transformed.

Cilia length of sponges treated with neomycin sulfate, FM1-43FX and Gd³⁺, for one hour each, were measured from fluorescence images with ImageJ (v1.43r). Untreated sponges were used as controls. Reversibility of Gd³⁺ treatment was demonstrated by

washing out the blocker for 1 hr in culture medium prior to fixation. Cilia and flagella length of Gd^{3+} -treated sponges were measured from SEM images. The measurements were log(x) transformed and analyzed using a nested ANOVA in R (v.2.4.1), with the number of cilia nested in individual sponge nested in treatment group.

Texas-Red conjugated neomycin (TR-Neo) was made by shaking neomycin sulfate (50 mg/ml in K₂CO₃) and Texas Red (Molecular Probes, Invitrogen; 2 mg/ml in dimethylformamide) overnight (Steyger et al., 2003), and added to M-medium to a final concentration of 300 μ M neomycin sulfate. *S. lacustris* was treated for 2 min in TR-Neo followed by three rinses in M-medium, 5 min in 1 μ M YO-PRO1 (Invitrogen) (Santos et al., 2006; Ou et al., 2009), and three more rinses in M-medium prior to viewing live using a 40X Zeiss water immersion objective.

Both whole *S. lacustris* and oscula removed from the sponge were treated in 4 mM chloral hydrate for 20 hr or 70 hr (medium changed daily to maintain concentration), and fixed for fluorescence microscopy with anti-tubulin and for SEM as described above. Click-iT EdU imaging kit (Invitrogen) was used to label newly synthesized cells post osculum removal. *E. muelleri* was incubated in 50 μ M EdU in M-medium for 8 hr or 24 hr after the osculum was removed, fixed for fluorescence, and labeled using the click copper-catalyzed covalent reaction. Sponges were labelled with acetylated alpha tubulin and Hoechst as described above.

2.2.7 BioInformatics

The transcriptomes of 8 sponge species (*Ephydatia muelleri, Spongilla lacustris, Petrosia ficiformis, Chondrilla nucula, Ircinia fasciculata, Corticium candelabrum, Sycon coactum, Aphrocallistes vastus)* were sequenced using Illumina and assembled *de novo* in either Trinity or CLCGenomics Workbench 5.1 (Riesgo et al., 2012). TRP sequences in these transcriptomes and also in the *Amphimedon queenslandica* genome (Srivastava et al., 2010) were detected using HMMer (Janelia.org) using HMM profiles formed with *pkd1* and *pkd2* sequences collected from NCBI or by blasting NCBI sequences against the transcriptome datasets using the tblastn suite in CLC Genomics Workbench. Sequence
identity and domain conservation was confirmed by BLAST and NCBI's conserved domain search as well as EMBL's InterPro Scan; domain illustrations were conceived using DOG2.0 and 3D models projected using Phyre2 (Kelley and Sternberg, 2009). TRP channel and PKD channel sequences from bilaterians were downloaded from SwissProt following the (vertebrates) taxon sampling for TRP and PKD domains in Pfam (Punta et al., 2012); SwissProts accession numbers are indicated in the sequence labels. Chlamydomonas reinhardti PKD2 ABR14113.1 was downloaded from NCBI. For phylogenetic analysis sequences were aligned in MAFFT (Katoh et al., 2002) using the E-INSI algorithm, and positions shared by 85% of the taxa were selected using MEGA5.1 (Tamura et al., 2011) for further phylogenetic analyses. Evolutionary relationships were inferred by ML using the evolutionary model LG [41] + GAMMA + Invariants as implemented in RAxML (Stamatakis, 2006). The statistical support of the branches was obtained by generating 1000 bootstrap pseudoreplicates. (The full alignment of 344aa and tree are shown in Additional file 1: Figures S2, S3.) The same dataset was analyzed under the Bayesian Inference framework /Phylobayes-MPI (Lartillot et al., 2013) under the CAT-GTR (Lartillot and Philippe, 2004) model (Additional file 1: Figure S4). The tree search was conducted during 7,500 cycles, and a burning of 1000 trees (sub-sampling every 10 trees) was used to discard the trees before the search reached the likelihood optima.

2.3 Results and Discussion

2.3.1 Sponge oscula are ciliated

Sponges are unusual in possessing both cilia and flagella (named for their differing beat patterns (Linck, 1973) on somatic cells. These include ciliated epithelial cells of sponge larvae which are involved in locomotion and also photoresponses (Leys and Degnan, 2002; Rivera et al., 2012), ciliated cells at the exit of the feeding choanocyte chambers (de Vos et al., 1990; Leys and Hill, 2012) and flagellated choanocytes involved in pumping water through the canal system (reviewed in Leys and Hill, 2012). In contrast, the epithelia of adult sponges are usually naked. We were therefore surprised to find cilia on all cells forming the epithelial lining of the osculum in the freshwater sponge *Ephydatia*

muelleri, a demosponge that can be cultured in the laboratory (Figure 2-1a). The osculum is the most prominent feature of a sponge, and is the final exit of water filtered through the sponge body for food and oxygen.

In *E. muelleri* a pair of cilia, each 4-6 microns long, emerges above the nucleus of every epithelial cell (Figure 2-1 b-f). A survey of 6 other demosponges showed that in each, the oscula are also lined by ciliated cells; in some species the cells have a single cilium, and others up to 4 cilia, all arising centrally above the cell nucleus (Appendix 1: A1.1). Even glass sponges (class Hexactinellida), which are syncytial, have cilia at the lip of their large oscula. There is no data available so far for the other two taxa, Calcarea and Homoscleromorpha, although the latter is known to have cilia throughout the canals, and therefore presumably also up to the oscula lip.

Serial sections through the base of the cilium in *E. muelleri* show basal bodies are simple, with no structures linking pairs of cilia in a cell (Figure 2-2a). In contrast to the flagella of choanocyte chambers, which have a central pair of microtubules, in cross section the oscula cilia have a 9 + 0 axonemal skeleton (Figure 2-2b), which is characteristic of sensory cilia in other organisms (Singla and Reiter, 2006). Both fluorescence and scanning electron microscopy show pairs of cilia in *E. muelleri* are oriented perpendicular to the water flow (Figure 2-2c), which may be important for sensing changes in flow. In live animals the cilia label with the vital dye FM 1-43, and high frequency time-lapse microscopy showed that they are non-motile and only vibrate in the flow that passes out of the osculum (Figure 2-2d, and Appendix 1: Movie A1.6).

2.3.2 Cationic channel blockers inhibit sponge behaviour

In the last decade it has been recognized that most cells in the vertebrate body, and many in invertebrates, possess specialized sensory structures called 'primary' cilia, which function as sensory organelles as in kidney epithelial cells, chondrocytes, odontoblasts, embryonic endocardial cells, and 'Kupffer's vesicle' (Praetorius and Spring, 2005). Primary cilia, although similar to motile cilia in their basic structure, lack the radial spokes and dynein arms that enable motility. Instead they possess stretch-activated cationic channels that are part of the transient receptor potential (TRP) channel superfamily (Nauli





a. The sponge *Ephydatia muelleri* in the lake, and grown in the lab viewed from the side (upper inset) and from above (lower inset). The oscula (white dashed circles) extend upwards from the body. **b**,**c**, Scanning electron micrographs show cilia arise from the middle of each cell along the entire length of the inside of the osculum; **b** the lining of the osculum with cilia on each cell (inset shows an osculum removed from the sponge and sliced in half longitudinally); **c**, two cilia arise from each cell. **d**,**e**, Cilia in the oscula labeled with antibodies to acetylated α -tubulin (green), nuclei with Hoechst (blue, n), actin with phalloidin (red). **f**, A 3D surface rendering illustrates how the cilia arise just above the nucleus of the cell. Scale bars **a** 5 mm; inset 1 mm; **b** 20 µm; inset 100 µm **c**, 1 µm **d**, 20 µm **e**,**f** 5 µm.



Figure 2- 2| Cilia are non-motile and are oriented perpendicular to the direction of water flow in the osculum

a. Serial longitudinal sections (86 nm apart) show each cilium arises just above the cell nucleus (n) from simple basal bodies (bb); no links between the bases of the ciliary pair were found. **b**. In cross-section the cilium lacks a central microtubule pair in contrast to the cross section of a flagellum from a choanocyte chamber. **c**. Cilia pairs are aligned parallel to the long axis of the cells in the osculum, and both the cilia pairs and the cells' long axes lie perpendicular to the direction of water flow (shown by the blue arrow) at $345.12 \pm 4.72^{\circ}$ (mean \pm SE) (rose diagram: H_A:0°; V = 0.841; p < 0.001; n = 49). **d**. Still images from high-frequency time-lapse imaging of live cilia (arrows) labeled with FM1-43 (see Additional file 2: Movie S1). Scale bars: **a**, 500 nm **b**, 100 nm **c**, 10 µm **d**, 20 µm.

et al., 2003) including polycystin-1 (PC1) and polycystin-2 (PC2) (Nauli et al., 2003) or their homologs, which allow them to function as sensory organelles (Nauli et al., 2003; (Nauli et al., 2003; Praetorius and Spring, 2003; Praetorius and Spring, 2005; Singla and Reiter, 2006). Remarkably, TRP channels are responsible for almost all forms of sensation experienced by eukaryotic cells, including movement, taste, smell, temperature, vision and osmolarity.

The function of TRP channel sensation is difficult to assess directly, and is therefore usually done by behavioral assay; for example inhibition of an avoidance reaction by the unicellular alga Chlamydomonas using TRP channel blockers has shown that TRP11 is involved in mechanosensation (Fujiu et al., 2011). In multicellular organisms it is difficult to study the function of primary cilia in living tissues, except in cell culture. In contrast, freshwater sponges are small and transparent, and cilia can be viewed live. Furthermore, both of the freshwater sponges E. muelleri and S. lacustris can be triggered to inflate and then contract their whole body (a behaviour termed a 'sneeze' (Elliott and Leys, 2007; Elliott and Leys, 2010) in response to mechanical or chemical stimuli (Figure 2-3a). Because the osculum is the final channel through which water exits the sponge, we hypothesized that the cilia have a sensory role in controlling the canal diameter to optimize normal flow through the sponge filter, and in particular during the sneeze behaviour. Three commonly used chemicals-the antibiotic neomycin sulfate, styryl dye FM1-43, and cationic channel blocker Gadolinium (Gd^{3+})-have been shown to inhibit sensory ability of primary cilia in other organisms (Gale et al., 2001; Praetorius and Spring, 2001). These drugs are all thought to block TRPP2 (PC2) channels on the ciliary membrane. In sponges natural stimuli (sediment, vigorous mechanical agitation) as well as bath treatments of 75-90 µM L-glutamate trigger the inflation and contraction of the excurrent canals (Elliott and Leys, 2007; Elliott and Leys, 2010). Treatment of sponges with neomycin sulfate (300 µM) and FM 1-43 (35 μ M) reduced the maximum amplitude of the inflation response by 60% (Figure 2-3b) in both cases, and treatment with Gd^{3+} (5 μ M) eliminated the response; the effects were reversible (Figure 2-3b). After recovery, the Gd³⁺-treated sponges showed an enhanced response to L-Glu (Figure 2-3b). This knock-down and knockout of the sponge behaviour by drugs that are known to affect channels on ciliary membranes implicates the



Figure 2-3 | Cationic channel blockers reduce the 'sneeze' response

a. The sponge 'sneeze' behaviour involves contraction of the osculum (white arrows), inflation, then contraction of canals (black arrows) and recovery (bar shows canal diameter). **b**. Neomycin sulfate (red) and FM1-43 (blue) reduce the peak amplitude of the behaviour in *Ephydatia muelleri* (n = 8; p < 0.001). Gd3+ (solid green) eliminated all response (n = 3; p = 0.015), but after recovery for 24 h the sponge response was even greater than before (dotted green). **c,d** All three compounds caused lengthening of cilia relative to controls (left), but had no effect on choanocyte flagella (bottom right) in *E. muelleri* (*significance at p < 0.001; error bars show \pm SE). Scale bars: **a**, 1,000 µm **c**, 10 µm.

cilia in sensing stimuli and transducing them into behaviour. Further support for this idea comes from the direct effect the drugs had on ciliary length.

Lengthening of primary cilia in other organisms has been proposed to increase their sensitivity (Besschetnova et al., 2010; Miyoshi et al., 2011). Ciliary (and flagellar) length is determined by a dynamic process of intraflagellar transport (IFT) which continuously brings molecules, including tubulin, up and down the cilium (Rosenbaum and Witman, 2002). Chemical or mechanical stimuli that interfere with Ca^{2+} influx have been shown to alter IFT, thereby changing cilium length (Besschetnova et al., 2010; Miyoshi et al., 2011). In *E. muelleri* cilia length increased 1.2-fold after only one hour of treatment in all three drugs (Figure 2-3c,d), and Gd³⁺ treated sponges recovered partially after a one-hour washout. These data suggest that the drugs interfere with IFT in the oscula cilia. Unlike cilia, the flagella in choanocyte chambers of *E. muelleri* did not change length (Figure 2-3d), implying that the effects of the drugs reported here are only on ciliated cells.

Although pharmacology is almost universally used to study the sensory roles of cilia and flagella in other organisms (Gale et al., 2001; Praetorius and Spring, 2001; Harris et al., 2003; Besschetnova et al., 2010; Fujiu et al., 2011), neomycin sulfate, FM 1-43, and Gadolinium can also affect other calcium transport processes in tissues including smooth muscle contractility. We therefore tested whether another calcium channel blocker could equally affect the sponges. In contrast to neomycin sulfate which eliminates all response in the sponge, the L-type calcium channel blocker Verapamil (10 µM) had no effect on the amplitude of the sneeze reflex (Figure 2-4a). This finding is consistent with experiments on vertebrate primary cilia (Gale et al., 2001; Praetorius and Spring, 2001). We found that longer incubation in neomycin sulfate (2 hr in S. lacustris compared to 10 min for E. muelleri) repressed the sneeze reflex for longer. FM 1-43 is fluorescent and was clearly localized primarily to the cilia (Appendix 1: Movie A1-S1), but to determine where neomycin sulfate localized we incubated sponges in Texas Red-conjugates of neomycin sulfate. Cells in the sponge osculum labeled within 2 minutes of incubation in the dye, and the same cells co-labelled with YO-PRO1, which selectively labels hair cells in the lateral line of zebrafish (Danio rerio) (Santos et al., 2006; Ou et al., 2009) (Figure 2-4b). Taken together, the effect of these treatments suggests that stretch-activated, nonselective cation channels are involved in the sponge behaviour.

While we cannot rule out the possibility that any of these drugs have other effects on the sponge in addition to working on the cilia, in our experience very few molecules cause the sponge to relax–most trigger contractions (Ellwanger et al., 2007; Elliott and Leys, 2010). However, to confirm that the cilia in the osculum, and the osculum itself, are indeed required for the sponge sneeze reflex we used both chloral hydrate to deciliate the sponge and removed the osculum, and tested the responsiveness of the sponge in each instance. Chloral hydrate is known to remove cilia from cells, causing a loss of behaviour in both metazoans (Praetorius and Spring, 2003) and unicellular eukaryotes (Dunlap, 1977; Fujiu et al., 2011) after 20 hr exposure. It is thought to act by weakening the attachment of the cilium to the basal body, with full loss of cilia occurring after 68 hr in kidney epithelial cells (Praetorius and Spring, 2003). We found that 20 hr exposure to 4 mM chloral hydrate eliminated the sneeze reflex and it took 120 hr for recovery of sensitivity (Figure 2-4c-e). As in kidney cells (Praetorius and Spring, 2003), it took 70 hr to remove all cilia from the epithelium of the osculum (Figure 2-4f).

We have found that when removed, a new osculum forms after 8 hours. Deosculated sponges could not be triggered to sneeze (Figure 2-4g), and although the sponge continued to filter water at all times during repair of the osculum, it was only after the osculum had fully formed that the sneeze response returned. Together these results suggest that both the osculum and the cilia lining it are necessary for the sneeze reflex. To determine when ciliated cells first appear on newly formed oscula, we labeled sponges from which the osculum had been removed with the cell proliferation marker EdU and detected incorporation of uridine into new cells using Click-iT (Molecular Probes, Invitrogen). At 8 hr after the osculum was removed, cilia were found on cells in a few discrete places on the surface of the sponge (Figure 2-4h). Pinacocytes in the sponge surface are not usually ciliated, therefore we interpreted the differentiation of cilia on pinacocytes as an early marker of the location of a new osculum. Furthermore, although mesohyl cells were labeled within 6 hrs of incubation in EdU, cells of the new osculum were not labeled with EdU, and it was only 24 hr after the new osculum was formed that a few new ciliated cells labeled (Figure 2-4i). Although we were unable to trace the migration of cells in live animals, we interpret these data to suggest that cilia differentiate on cells in the surface of the sponge, thereby identifying the region as a potential osculum; then as the osculum grows to full

Figure 2-4| Cilia are specifically involved in the sponge behaviour. a. In contrast to Neomycin sulfate (solid red) which eliminates the 'sneeze' response (n = 3, p = 0.035), the calcium channel blocker Verapamil (dotted red) does not affect amplitude of the sneeze behaviour in *Spongilla lacustris* (n = 5, p = 0.573). **b**. Texas-Red Neomycin sulfate conjugate (red) and YO-PRO1 (green) selectively label cells in the osculum. c. A 20 hr treatment in chloral hydrate eliminates the sneeze behaviour in S. lacustris (solid green; n = 5, p = 0.004), which does not return until more than 3 days after recovery (dotted green; n = 5, 24 hr washout p = 0.003, 72 hr washout p = 0.018, 120 hr washout p = 0.864; error bars show \pm SE). **d-f(SEM) d'-f'(fluorescence).** Cilia are removed by chloral hydrate treatment; S. lacustris 0 hr (d,d'), 20 hr (e,e'), and 70 hr (f,f') treatment in chloral hydrate. g. The sneeze behaviour in S. lacustris cannot be triggered when the osculum is removed (solid blue; n = 3, p = 0.010) until it has fully regrown (dotted blue; n = 3, p = 0.275). **h**. Ciliated cells on the surface of *Ephydatia muelleri* 8 hr post osculum removal and (i) in the newly formed osculum 24 hr post osculum removal. Ciliated cells do not become labeled with EdU until after the osculum has regrown suggesting they arise by migration of newly formed mesohyl cells which differentiate into ciliated pinacocytes. Cilia are labeled with acetylated a-tubulin (red), nuclei with Hoechst (blue), and newly synthesized DNA with EdU (green). Scale bars: b, 50 µm inset 10 µm d.e, 5 µm d',e',f,f',h,i 10 µm



Figure 2- 4| Cilia are specifically involved in the sponge behaviour

height using cells already present in the sponge, new ciliated epithelial cells differentiate from newly formed mesohyl cells.

2.3.3 Sponges possess a repertoire of transient receptor potential channels

Considering the conserved role of TRP channels, and in particular PKD in sensory behaviour across eukaryotes (Fujiu et al., 2011), we searched the transcriptomes of 8 sponge species for homologs of both *pkd1* and *pkd2* and other TRP channels. A 700aa homolog of *pkd2* (Type II TRP) was identified in *Corticium candelabrum* (Homoscleromorpha) and a 178aa sequence of a *pkd2* (Type II TRP) gene was found in the freshwater *Spongilla lacustris* (Demospongiae) (Figure 2-5a, Appendix 1: A1.2, A1.3). We found a 978aa sequence of a Type II TRP (ML) in *Sycon coactum* (Calcarea), and several sequences with similarity to various Type I TRP channels were found in all 4 Porifera classes (Figure 2-5a-c, Appendix 1: A1.5). These candidates were included in an alignment containing more than 100 representatives for all the TRP families across bilaterians (Figure 2-5a; Appendix 1: A1.2 and A1.3). The ability to retrieve protein sequences depends on the quality of the transcriptome and the divergence of sequences in transcriptomes.

Negative results do not imply conclusive absence. Our phylogenetic analysis grouped sponge *pkd* sequences with Type II TRP and specifically *pkd2* channels genes from bilaterians with high support (91% bootstrap). Sponge *pkd* channel sequences showed similar domain architecture and proposed 3D protein folding to both mouse and *Chlamydomonas* sequences (Figure 2-5b), and other sponge sequences showed amino acids indicative of the TRP domain (Figure 2-5c; Appendix 1: A1.5). Although the pharmacology of the sponge cilia is similar to that of cilia known to have *pkd2* channels, several TRP channels from *Chlamydomonas* have also been found to transduce mechanical signals so we cannot rule out the possibility that other TRP channels are involved in flow sensing in sponges.

Figure 2-5| Phylogenetic analysis of sponge TRP genes

a. Evolutionary relationships of sponge TRP Type I and II genes, values in the nodes indicate Boostrap Support and Posterior Probabilities (see methods); sponge sequences are in bold. **b**. Domain diagrams showing the PKD channel domain, transmembrane domain (TM), EF hand domain, and ion transport domains for the *pkd2* genes from mouse, *Mus musculus*; Cca, *Corticium candelabrum* (Homoscleromorpha); Cel, *Caenorhabditis elegans;* Sla, *Spongilla lacustris* (Demospongiae; Sco; *Sycon coactum* (Calcarea); Ava, *Aphrocallistes vastus* (Hexactinellida); Cre, *Chlamydomonas reinhardtii*, and 3D models of the proteins from mouse, *Corticium, Sycon*, and *Chlamydomonas*. **c**. Alignment of bilaterian, cnidarian and sponge TRP sequences showing the TRP domain and TRPbox (Hsap, *Homo sapiens;* Mmus, *Mus musculus;*Spur, *Strongylocentrotus purpuratus;* Cint, *Ciona intestinalis,* Sko, *Saccoglossus kowaleskii,* Lforb, *Loligo forbesi,* Bflo, *Branchiostoma floridae,* Sman, *Schistosoma mansoni,* Nvec, *Nematostella vectensis*). For the full tree and alignment see Appendix 1: A1.2 and A1.4.



2.4 Conclusions

Obstruction of the canals by particulates in the feeding current would cause changes in pressure across the system; the osculum is the single exit of the entire system and is expected to be sensitive to this change, so it is plausible that the cilia detect changes in water flow or pressure. The absence of motility of the cilia, and their specific localization to the inner lining of the sponge osculum strongly suggest a sensory role for the osculum; the pharmacology and ablation experiments also support the hypothesis that the cilia have a sensory function. The primary cilium, which extends out from the cell and has a high surface-area to volume ratio, is an ideal organelle for both sensing and transducing signals (Singla and Reiter, 2006). These cilia in the sponge osculum have all the characteristics of primary cilia.

While the role of cilia in sensing information may have evolved many times within eukaryotes, the sponge sensory system described here is certainly very similar to signalling via primary cilia in other metazoans (Praetorius and Spring, 2005). The role of cilia in the sponge osculum suggests either a convergent role in sensing and transducing flow information into behaviour across all metazoa, or implies that primary cilia had an ancient evolutionary role in transducing sensory information, and in particular flow, in early multicellular animals. Given the unique position of Porifera as extant representatives of one of the first groups of multicellular animals (Roure et al., 2013), and in particular their lack of conventional nervous and coordination systems, the finding of such an organized array of sensory cells in sponges provides new insight into possible mechanisms of evolution of early sensory systems.

2.5 References

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Chapter Three

It costs more to pump more: energetic cost of filtration and behavioural response to ambient currents in demosponges

3.1 Introduction

Benthic suspension feeders can have a major impact on marine ecosystems by ingesting suspended particulates and dissolved nutrients from the overlying water column and releasing them for use by other organisms (Gili and Coma, 1998). Recycling of nutrients in this way provides an important link between the benthic and pelagic communities, known as benthic-pelagic coupling (Gili and Coma, 1998). Water quality is declining in most coastal marine ecosystems by processes including increased suspended sediment from fishing trawls (Puig et al., 2012), increased eutrophication resulting in harmful algal blooms (Hallegraeff, 1993), oxygen dead zones (Diaz and Rosenberg, 2008), and increased pollutants especially near ports and coastal communities. Suspended sediment in particular is known to impact the efficiency and ability of filter feeders to process water, leading to reduced pumping activity and increased metabolic demand (Gerrodette and Flechsig, 1979; Ellis et al., 2002; Bannister et al., 2012). Knowing the energetic constraints that might affect suspension feeders is therefore important to understand the impacts these additional stresses may have on benthic communities, yet the energetic cost of this type of feeding in invertebrates is still debated.

Many suspension feeders are sessile and use ciliary or muscular pumps to draw water with food towards themselves. Invertebrates such as bivalves, ascidians, polychaetes, and sponges use filters to strain out particles from the water that are too small to be captured individually (Jørgensen, 1966). Where suspended particulates are dilute, this approach can be highly efficient if huge volumes of water are processed (Jørgensen, 1955). It has been suggested that filter feeders evolved a low energetic cost of filtration to allow continuous feeding rates (Jørgensen, 1975). Yet, food availability varies hugely on a temporal basis, with fluctuations occurring seasonally, daily, and with the ebb and flow of the tide. It would therefore be adaptive to sense the variations in food availability and feed when concentrations are high. Although few studies have focused on this question, two examples suggest this hypothesis is correct. Bivalves respond to food availability by reducing filtration and respiration rates when food is scarce (Thompson and Bayne, 1972; Griffiths and King, 1979), and the demosponge *Tethya crypta* reduces pumping activity at night when ambient currents are lower (Reiswig, 1971) which would therefore bring reduced food availability (Newell and Branch, 1980). As all filter feeders demonstrate some fluctuations in pumping rates in response to various environmental cues, filtration may be more costly than previously thought and the animals may be finely adapted to habitats that support the energetic cost to obtain food.

Previous work modeling the filter and pump system for a number of invertebrates has suggested that filter feeding is inexpensive, at less than 4% of total metabolism (Riisgård and Larsen, 1995). In contrast, direct measurements of the uptake of oxygen going from non-feeding to feeding has shown that filter feeding in bivalves accounts for up to 50% of total metabolism (Thompson and Bayne, 1972; Newell and Branch, 1980) and in sponges 25% of total respiration (Hadas et al., 2008). In addition, the resistance through the filter of sponges may be much higher than previously thought due to a difficult to preserve fine glycocalyx (mucus) mesh on the collar (Leys et al., 2011).

In support of the idea that cost of filtration may be high, some animals seem to reduce energy expended to feed by using ambient currents in the water column to enhance flow by dynamic pressure, the Bernoulli effect or viscous entrainment. For example, in high current speeds barnacles will switch from active to passive feeding and orient their bodies toward the current (Trager et al., 1990). Cnidarians (Best, 1988), ascidians (Young and Braithwaite, 1980; Knott et al., 2004), and brachiopods (Labarbera, 1977) also orient their bodies with the current, while other invertebrates may take advantage of current-induced flow through tubes (Vogel, 1977; Murdock and Vogel, 1978; von Dassow, 2005; Shiino, 2009). Sponges are often considered 'textbook' examples of the use of current-induced flow in nature (Bidder, 1923; Vogel, 1974; Vogel, 1977) but experiments to confirm this have been equivocal (Leys et al. 2011).

Even if models are correct and cost of filtration is not great, a universal cost for all sponges is difficult to accept since structural differences in the sponge canal system in relation to body form (Reiswig, 1975a), microbial content (Weisz et al., 2008), and tissue density (Turon et al., 1997) can cause wide differences in pumping rates between species. Temperature and food availability vary across habitats causing differences in seawater viscosity and enzyme function and potentially leading to differences in the metabolic cost of filtering in different habitats. Estimates of the cost of pumping for a range of sponge species and habitats are therefore required to better understand sponge energy budgets.

Do differences in sponge shape, size, pumping volume, and habitat affect the energetic cost of pumping in sponges? I have studied energetics of filtration in five species of demosponge from tropical and temperate habitats using *in situ* measurements of oxygen consumption and pumping rate, experimental tests of pumping at different ambient flow rates, and by morphometric analysis of the canal and filter structures. To evaluate the importance of accurate measures of filter dimensions and volume of water processed, I first examined the effect of changes in these values on cost of filtration calculated in previous work. The results from that analysis focused our attention on these aspects in our own experimental analyses.

3.2 The importance of mesh size and volume flow rates

Animals allocate energy to a variety of processes including growth, reproduction, feeding, and digestion. For filter feeders, the energy allocated to feeding is generally considered to be low, at 0.1 - 4% of total metabolism based on theoretical models (Jørgensen, 1955; Jørgensen et al., 1986; Jørgensen et al., 1988; Riisgård, 1988; Riisgård, 1989; Riisgård et al., 1993). In these studies, the cost of filtration is assumed to be equivalent to the energy lost due to frictional resistance as water flows through the filter and canals. Models can be informative about which structures contribute most to energetic costs, however, their accuracy depends on having correct dimensions for each region of the filter and canal system as well as volume flow rates. This same approach used by Riisgård and colleagues was recently used for the filtration system of the glass sponge *Aphrocallistes vastus* (Leys et al., 2011) where the cost of pumping was found to be 28% of

the total metabolism. Here, the resistance through the filter was found to be much higher than previous estimates due to the small spaces of the glycocalyx mesh (Leys et al., 2011), a structure that is often not preserved with common fixation techniques and was not included by Riisgård et al (1993). In addition, the volume flow rate in *A. vastus* was quite high compared to the 'standard sponge' studied by Riisgård and colleagues (1993) where volume flow rate was obtained indirectly using clearance rates of particles (flagellate cells) during incubation in a closed vessel. Closed vessels have been shown to cause reduced pumping behaviour of sponges (Yahel et al., 2005; Hadas et al., 2008), and the sponge may re-filter the water if sampling times are not well adjusted to pumping rates (Yahel et al., 2005).

I carried out a meta-analysis using data from the literature to determine the cost of pumping in four filter feeding invertebrate group used by Riisgård and colleagues (summarized in Riisgård and Larsen, 1995). I calculated dimensions from electron micrographs of mucus filters (Figure 3-1), where available, and volume flow rates that were obtained using 'direct' methods. By changing filter size and volume flow rate, the estimate for the cost of filtration increased to more than 5 times previous values (Table 3 -1). This suggests that both filter dimensions and volume flow rates contribute substantially to the cost of pumping in filter feeding invertebrates. It also suggests that accurate measurements of filtration and volume flow rates are important when modeling the cost of filtration and forced my attention on these for my own study.

3.3 Methods

3.3.1 Overview

I conducted *in situ* and *in vitro* studies to measure excurrent flow rates and oxygen removal from five species of demosponge, *Neopetrosia problematica, Haliclona mollis, Tethya californiana, Callyspongia vaginalis,* and *Cliona delitrix* (hereafter referred to by genus). These species were selected due to their abundance at each of the study locations as well as the large size of their oscula. Paired flow and oxygen recordings were done on a mimimum of six oscula per species. During paired recordings for *Cliona* and *Callyspongia,*



Figure 3- 1| Feeding filters in four groups of invertebrates used to re-estimate the cost of filtration

(A,B) Scanning electron micrograph (SEM) of the collar of *Spongilla lacustris*, showing the glycocalyx mesh fibrils (arrows) linking adjacent microvilli (Mah et al., 2014) (C) Gill filament of *Mytilus edulis* showing the latero-frontal cirri. (Jones et al., 1992) (D-F) Transmission electron micrographs of the mucus nets in *Chaetopterus variopedatus* (Flood and Fiala-Medioni, 1982) (D), *Ciona intestinales* (Flood and Fiala-Medioni, 1981) (E), and *Styella plicata* (Flood and Fiala-Medioni, 1981) (F) Scale bars (A, D-F) 1 μm (B) 300 nm (C) 100 μm.

Table 3-1| Estimated cost of pumping (%) for four different groups of filter feeders

Using new measurements from the literature for filter dimensions and volume flow rates (blue). In the absence of volume flow rates for *Spongilla lacustris*, estimates for *Haliclona permollis* (blue) were used instead. Estimates for the cost of pumping (% of metabolism) are based on the morphometric model summarized by Riisgård and Larsen (1995) and outlined in equations 3-8. Original estimates for the cost of pumping are in black and the new estimates are shown in red.

			Volume Flow		Estimate of
Species	Filter dimensions	Filter Dimension Reference	rate	Volume Flow rate Reference	pumping (%)
Sponges					
Haliclona urceolus	d=0.14um, b=0.25um	Riisgard et al (1993)	6 mL/min	Riisgard et al (1993)	0.850
	d=0.14um, b=0.25um	Riisgard et al (1993)	6 mL/min	Riisgard et al (1993)	1.021 *
Haliclona permollis	d=0.14um, b=0.25um	Riisgard et al (1993)	18.84 mL/min	Reiswig (1975)	3.206
Spongilla lacustris	h1=0.048um, h2=0.041um, d=0.04um	Mah et al (2014)	6 mL/min	Riisgard et al (1993)	1.594
	h1=0.048um, h2=0.041um, d=0.04um	Mah et al (2014)	18.84 mL/min	Reiswig (1975)	5.004
Bivalves					
Mytilus edulis	L=200um, l=40um	Jorgensen et al 1986a, 1988	60 mL/min	Jorgensen et al 1986a, 1988	1.562
	L=200um, l=40um	Jorgensen et al 1986a, 1988	67.8 mL/min	Riisgard et al 2011	1.765
	L=200um, l=16um	Jones et al (1992)	60 mL/min	Jorgensen et al 1986a, 1988	4.131
	L=200um, l=16um	Jones et al (1992)	67.8 mL/min	Riisgard et al 2011	4.668
Polychaetes					
Chaetopterus	h1=2.3, h2=1.4, d=0.02	Riisgard (1989)	18 mL/min	Riisgard (1989)	4.032
variopedatus	h1=2.3, h2=1.4, d=0.02	Riisgard (1989)	30 mL/min	Grove et al (2000)	6.719
	h1=0.76 h2=0.46, d=0.02um	Flood and Fiala-Medioni (1982)	18 mL/min	Riisgard (1989)	10.903
	h1=0.76 h2=0.46, d=0.02um	Flood and Fiala-Medioni (1982)	30 mL/min	Grove et al (2000)	18.172
Ascidians					
Styella clava	h1=0.35um, h2=1.35um, d=0.020um	Riisgard and Larsen (1995)	45.6 mL/min	Riisgard and Larsen (1995)	0.191
	h1=0.35um, h2=1.35um, d=0.020um	Riisgard and Larsen (1995)	45.6 mL/min	Riisgard and Larsen (1995)	0.724 **
Mean of three species	h1=0.35um, h2=1.35um, d=0.020um	Riisgard and Larsen (1995)	57.5 mL/min	Fiali-Medioni (1978)	0.913
Mean of six species	h1=1.002, h2=0.366, d = 0.025	Flood and Fiala Medioni (1981)	45.6 mL/min	Riisgard and Larsen (1995)	0.815
Styella plicata	h1=1.959, h2=0.5055, d=0.020	Flood and Fiala Medioni (1981)	83.1 mL/min	Fiali-Medioni (1978)	0.885
Ciona intestinales	h1=0.640, h2=0.405, d=0.020	Flood and Fiala Medioni (1981)	21.5 mL/min	Fiali-Medioni (1978)	0.376

* Cost of pumping re-estimated to use consistent temperatures for kinematic viscosity

** Cost of pumping re-estimated using corrected head loss at the filter

ambient velocity was increased using an underwater pump for one individual to determine use of current-induced flow. Following experiments, pieces of sponge were fixed for both scanning electron microscopy (SEM) and histology to estimate dimensions of the aquiferous canal system. These dimensions along with excurrent flow rates and respiration were used to estimate the resistance through the sponge and cost of filtration for each species, using the models by Riisgård and colleagues (1995) and Leys and colleagues (2011).

3.3.2 Field and lab studies

Work was carried out at two research laboratories: the Bamfield Marine Sciences Centre (BMSC) in Bamfield, British Columbia, Canada, and the Smithsonian Tropical Research Station (STRI) on Isla Colon in Bocas del Toro, Panama (Figure 3-2).

At BMSC the three temperate species of demosponge *Neopetrosia, Haliclona,* and *Tethya* were collected via SCUBA by Amanda Kahn and Sally Leys from Wizard Island and kept in seawater tables with high water flow (up to 3000 L/min) supplied from deep water (30m depth) in Bamfield Inlet. Experiments with acoustic Doppler velocimeters (ADVs) were conducted in a large circular seawater tank approximately 1m in diameter. Samples were collected both in September 2012 and December 2013. Pumping rates, respiration, and passive flow experiments were carried out in December 2013.

At STRI, in July 2013, experiments on *Cliona* and *Callyspongia* were conducted *in situ* by snorkeling at STRI point, GPS coordinates 9°21.169'N 82°15.528'W (Diaz, 2005) at approximately 2 m depth. An aluminum frame made from 80/20 (80/20 Inc., Columbia City, IN) was placed over the sponge and instruments were attached using loc-line (Lockwood Products, OR) and clamps (Figure 3-2). The instruments were tethered via cables to a laptop computer on a boat anchored near the study site to monitor the data collection in real time.

At both STRI and BMSC, photos were taken using a GoPro Hero 2 camera with underwater housing as well as a Panasonic Lumix DMC-TS4 underwater camera.



Figure 3-2 | Experimental set-up and species used.

(A) Haliclona mollis (purple), Neopetrosia problematica (cyan), and Tethya californiana (green) were collected and studied *in vitro* in Bamfield, British Columbia, Canada (top star on the map). Callyspongia vaginalis (blue) and Cliona delitrix (red) were studied *in situ* in Bocas del Toro, Panama (bottom star). (B) Excurrent velocity was measured out of the osculum using a Nortek Vectrino II acoustic Doppler velocity (ADV) and removal of oxygen was measured using a FirestingO₂ bare fiber sensor (O₂) positioned inside of the sponge osculum. (C) Ambient velocity was increased using an underwater pump attached to a PVC tube (shown) positioned at the sponge. (D) Instruments were mounted *in situ* on a frame positioned over the sponge using snorkel.

3.3.2.1 Measurements of excurrent velocity

Maximum excurrent velocity from each sponge species was measured using a Vectrino II profiling acoustic Doppler velocimeter (ADV; Nortek). The profiling ADV is a non-intrusive instrument that measures the velocity of water by sending acoustic waves that reflect off particles moving in three dimensions (X, Y and Z) within a small cylindrical "sampling volume" 45-75 mm from the probe head. The sampling volume is 6 mm in diameter, 30 mm long, and divided into 1 mm intervals or profiles. Because the sampling volume is some distance from the probe head, and because the excurrent flow from a sponge osculum may be small, and may not travel very far from the osculum lip, positioning it over the sponge osculum is challenging. The profiling capabilities of the Vectrino II help because they provide measurements over the full 30 mm profile, and as a result the lip of the sponge osculum itself disrupts the profile, showing exactly where above the sponge the sampling volume is. Using this method it is possible to be sure that the velocity being recorded is just above or inside the sponge osculum, and this becomes important in differentiating between ambient and excurrent water velocities. Fluorescein dye diluted in filtered seawater was used to visualize the excurrent flow, and a plastic cable tie was used to indicate the specific position of the sampling volume by blocking the signal and confirm that the readings were just above or inside the sponge osculum.

The ADV sensor was attached to loc-line to allow fine positioning above the sponge osculum. Movement of the sensor above the sponge while watching the velocity recordings on a computer allowed us to determine the position that gave the maximum excurrent velocity from the sponge osculum. Once the sensor was oriented correctly, excurrent velocity was recorded for 5 minutes at 25 Hz on low power (it was found that high power could push the excurrent flow down, a process termed streaming). Only the Z (vertical – or in line with the excurrent flow and ADV) direction of velocity was used in analysis to differentiate from the ambient velocities. All of the flow exiting the sponge osculum may not be in the exact same direction, and some flow may drift or shear out of the sampling volume; therefore, the Z direction is a conservative estimate of the excurrent velocity. Data were binned using a 5 second median filter in MATLAB (vR2013b). Images of each sponge osculum were taken using a GoPro Hero2 during recording and their diameters

measured in ImageJ (v. 1.43r; NIH) to calculate sponge pumping volume, assuming plug flow in which velocities are equal across the osculum plane.

The ratio of sponge volume to dry weight was calculated by drying three pieces of each species at 100°C to constant weight. This ratio was then used to standardize volume flow rate to dry weight.

3.3.2.2 Measurements of oxygen consumption

Ambient and excurrent oxygen were measured using two 2-channel FireStingO₂ optical oxygen meter (Pyro Science, Germany) with 250 µm diameter bare fiber minisensor probes. Although these sensors are extremely stable, minor differences due to construction of fiber optics meant probes were calibrated separately and can therefore deviate minimally when in the same water volume. Therefore, prior to positioning the excurrent sensor into the sponge osculum, both probes were left in ambient water for at least 5 minutes to obtain the difference in readings between the two sensors (here termed the offset value), and this difference was subtracted from the difference between ambient and excurrent oxygen for all analyses. Oxygen readings were calibrated using an external temperature probe. In addition, the ambient and excurrent sensors were positioned at the same height in the water column, such that any temperature fluctuations were accounted for when offsetting between probes. Data were collected every 1 s and binned using a 5 s median filter using MATLAB (vR2013b). Oxygen removal per hour was calculated using the volume of water filtered per hour, and standardized to per gram dry weight.

3.3.2.3 Test of passive flow

To assess the effect of changes in ambient current velocities on sponge excurrent flow, experiments were conducted on *Cliona* and *Callyspongia* at STRI by manipulating ambient flow with an underwater aquarium pump (Eheim compact + 3000). The pump was anchored near the sponges with a weight and the outflow directed through a 50 cm long, 10 cm diameter PVC pipe at and over the sponges, after Genin and Karp (1994). The aquarium pump had variable speeds that could generate flow at 5 to 40 cm/s through the PVC pipe

when positioned 30 cm from the sponge, as measured in a flow flume. Three flow speeds were used in experiments by setting the pump to low, medium, and high speeds. The ambient velocity was recorded using the Vectrino I point ADV (Nortek) with a sampling volume of 6 mm diameter by 7 mm length, positioned about 10 cm from the sponge perpendicular to the pump outflow (Figure 3-2). The ADV could not be positioned right next to the sponge due to interference between the ADVs. Data were measured with a transmit length of 1.8 mm at 25 Hz on high power and binned using a 5 s median filter using MATLAB (vR2013b).

Paired excurrent velocities and oxygen removal were measured during experiments as described above (sections 3.3.1.1 and 3.3.1.2). The profiling ADV (Nortek) was first positioned to ensure maximum excurrent velocity recordings from the osculum. Then the oxygen sensor was positioned inside the osculum, ensuring that it did not interfere with the ADV sampling volume as determined by a probe check analysis. Paired recordings were measured for 5 minutes at zero flow, 5 minutes with the pump on the 'low' setting, 5 minutes with the pump on the 'medium' setting, and 5 minutes with the pump on the 'high' setting, repeated three times through.

A GoPro Hero2 with underwater dive housing was positioned on the frame above both *Cliona* and *Callyspongia* to record osculum size during the experiment; images were captured every 30 s and a ruler was positioned in one of the images for calibration. Changes in osculum area were measured using a script developed for MATLAB (vR2013b) (Appendix 3). Volume filtered was calculated using excurrent velocity and area of the osculum. The ratio of sponge volume to dry weight was used to standardize volume flow rate and oxygen removal to per gram dry weight.

3.3.2.4 Statistical analyses

If the cost of filtration in sponges was low, as predicted by Jørgensen (1975) and Riisgård and colleagues (1993), then there would be no relationship between the volume of water a sponge pumps and the amount of oxygen it removes. In addition, if all species of sponge used passive flow as predicted by Vogel (1974; 1977), then there would be a positive relationship between ambient velocity and excurrent velocity. All statistical analyses were done using SigmaStat in SigmaPlot v12.5. Data were tested for normality and linearity and subsequently variables were tested for association using a Spearman's rank order correlation test to allow for non-linearity.

3.3.3 Morphometric analysis of sponges

3.3.3.1 Scanning electron microscopy

For scanning electron microscopy (SEM), sponges were cut into 1 mm³ pieces and fixed in a cocktail consisting of 1% OsO_4 , 2% gluteraldehyde in 0.45 mol L⁻¹ sodium acetate buffer with 10% sucrose at 4°C for 6-12 h (Harris and Shaw, 1984). In some preparations 10% ruthenium red was added to the fixative to preserve the fine structure of the glycocalyx mesh on the collar filter. We found that applying 4% OsO₄ directly to the sponge tissue prior to cutting and placing into the cocktail fixative helped to minimize contraction of canals. After 6-12 h, preparations were washed with distilled water and dehydrated to 70% ethanol. Sponges were desilicified in 4% Hydrofluoric Acid (HF) in 70% ethanol at room temperature (RT) for 24-72 h or until the spicules were dissolved. After desilicification, the sponge pieces were dehydrated to 100% ethanol and fractured while still in ethanol, in liquid nitrogen. Fractured pieces were critical point dried and mounted on aluminum stubs with clear nail polish, gold coated, and viewed in a field emission scanning electron microscope (JEOL 6301 F). For some pieces of Cliona and Callyspongia, the pieces were embedded in paraffin wax, sectioned at 12 or 30 µm and mounted on aluminum stubs. Prior to embedding, Cliona was placed in 5% EDTA for 24 hr to remove the coral skeleton. After sectioning the wax was removed by placing the stubs in toluene for 15 minutes. The stubs were then gold coated and viewed in a field emission scanning electron microscope.

3.3.3.2 Histology

For wax embedding, sponges were cut into 1cm³ pieces and fixed in 4% paraformaldehyde in filtered seawater for 24 h. Pieces were rinsed in phosphate buffered

saline (PBS), dehydrated to 70% ethanol and transported back to the laboratory in Edmonton, Alberta where they were processed by Nhu Trieu in the Department of Biological Sciences Microscopy Unit. Preparations were desilicified in 4% HF in 70% ethanol at RT for 24-72 h until the spicules were dissolved. *Cliona* was further placed in Cal-Ex Decalcifier (Fisher Scientific) for 24 h to remove the coral skeleton. Sponges were embedded in paraffin wax and sectioned at 5 µm for *Tethya*, 12 µm for *Haliclona* and *Cliona*, and 30 µm for *Neopetrosia* and *Callyspongia*, with section width dependent on the density of the tissue. Wax was removed with toluene and slides were hydrated and stained using Masson's trichrome stain in Hematoxylin for 1 min 20 sec, Ponceau acid fuchsin for 2 min, and Aniline Blue for 3 min. The slides were then dehydrated to 100% ethanol and cleared in Toluene prior to mounting with Permount. Slides were viewed using a Zeiss Axioskop2 Plus and captured with a QiCam using Northern Eclipse v.7 software (Empix Imaging Inc., Mississauga, ON, Canada).

3.3.3.3 Measurements of the canal system

The approach here was to replicate the methods used by Reiswig (1975a) to compute the dimensions through each portion of the aquiferous system to determine resistance. Dimensions of the aquiferous canal system were measured from both SEM and histological images using ImageJ (v. 1.43r; NIH). Care was taken to select regions of the canal system that were not contracted by looking at the tissue surrounding the canal system. Because pieces imaged by SEM were smaller than one millimeter, SEM images showed the smaller canals but did not capture larger canals; therefore dimensions and path lengths of larger canals were obtained from histological sections. It was not always possible to identify incurrent vs. excurrent canals; in these instances it was assumed that the dimensions and path length were the same between excurrent and incurrent canals following Riisgård et al. (1993). Choanocyte density was also calculated from histological sections. The cross-sectional area of each region of the aquiferous system was calculated for a 100 mm³ (100 μ l) piece after Reiswig (1975a) and Leys et al. (2011). Due to differences in the shape of the sponge body, the dimensions for this 100 μ l piece differed for each species. For *Neopetrosia, Haliclona, Tethya* and *Cliona* inhalant surface was 4.5 x

4.5 mm² and the wall 5 mm thick. The body wall of *Callyspongia*, however, is only 3 mm thick and therefore a larger inhalant surface was used (5.77 x 5.77 mm²) to generate the same 100 μ l volume for the piece.

Sponge volumes and surface area for each of the species were calculated by measuring the dimensions of the sponge from images taken of whole animals *in situ*, and using ImageJ (v. 1.43r; NIH). Most sponges have irregular shapes, therefore volumes and surface areas were estimated by selecting a more regular shape that the sponge resembles: *Callyspongia* most resembles a cylinder, *Cliona* and *Haliclona* an ellipsoid, and *Tethya* a sphere. When there was more than one osculum per sponge, sponge volume was calculated and divided by the number of oscula to get sponge volume/osculum. The ratio of sponge to coral skeleton in *Cliona* was estimated by dissolving the coral skeleton using 5% EDTA for a small piece (~ 2 cm³, or 4.5 g in weight) and scaling up to the whole specimen using the relative immersed volumes. *Neopetrosia* is highly irregular, therefore a combination of triangles was used to estimate volume and surface area.

3.3.3.4 Estimating resistance through the canal system

The velocity of water through each region of the aquiferous canal system, u_i , was calculated using the estimated cross-sectional areas for each part of the sponge and known excurrent velocity from the osculum (Reiswig, 1975a):

$$u_i = \frac{u_{ex}A_{osc}}{A_i} \tag{1}$$

where A_i is the cross sectional area of the region (see section 3.3.3.3), A_{osc} is the cross sectional area of the osculum, and u_{ex} is the measured excurrent velocity from the osculum (see section 3.3.2.1).

Two separate approaches were used to estimate the resistance through the canal system of sponges. The first uses a different equation to model each region of the canal system based on the characteristics of the region (an approach summarized by Riisgård and Larsen, 1995). The different equations in this first approach reflect the estimated different architectures of different regions of the sponge. The second approach uses only one equation for the whole canal system (Leys et al, 2011). This approach assumes that

different equations do not capture the accurate differences between regions and therefore one equation is more straightforward and just as accurate.

Following the approach by Riisgård and colleagues (Jørgensen et al., 1986; 1988; Riisgård, 1988; 1989; Riisgård et al., 1993; Riisgård and Larsen, 1995), the hydraulic head loss through each region of the canal system H_i may be due to apertures, frictional resistance in canals, or pressure drop across lattice nets. Most flows in biological systems occur at low Reynolds numbers $R_e = ud/v$, where d = diameter of tube or aperture, u = is mean velocity, and v = is kinematic viscosity. As water flows from a large diameter canal into a smaller one, the flow becomes fully developed after a length of about $L_d \approx 0.1 dR_e$. Flow in the sponge canals is at low R_e and is fully developed. Head loss for ostia, prosopyles, and apopyles was calculated using equation 15 from Riisgård and Larsen (1995) for creeping flow through a circular aperture with diameter *d* (equation originally from Happel and Brenner, 1983):

$$\Delta H_i = 6\pi v u_{i-l}/gd \tag{2}$$

where v = kinematic viscosity; $u_{i-l} =$ mean velocity of the flow upstream of the structure; g = the acceleration of gravity and d is the diameter of the circular aperture. Head loss at the canals was calculated using a rendition of the Hagen-Poiseuille equation for fully developed laminar flow in a circular tube of length L and radius r, which is equation 19 in Riisgård and Larsen (1995) (originally in Fox et al., 1998):

$$\Delta H_i = 8v u_{i-l} L/gr^2 \tag{3}$$

where *L* is the length of the canal, and r is the radius of the canal. For the subdermal space, which is a region below the dermal membrane, head loss was calculated using equation 21 in Riisgård and Larsen (1995) for flow between parallel plates spaced *l* distance apart (originally in Walshaw and Jobson, 1962):

$$\Delta H_i = 12v u_{i-l} L/g l^2 \tag{4}$$

where *L* is the length of the subdermal space, and *l* is the width of the subdermal space. Head loss across the rectangular lattice mesh, equation 17 in Riisgård and Larsen (1995) and originally described by Silvester (1983), is calculated as:

$$\Delta H = K v u_{i-l} / g h \tag{5}$$

where $K = 8\pi/(1 - 2\ln(\frac{\pi d}{h_0}) + (\frac{\pi d}{h_0})^2/6)$; $h_0 = h_1h_2/\sqrt{(h_1^2 + h_2^2)}$; d = diameter of the cylindrical fiber and h are the dimensions of the mesh where: $h = h_1h_2/(h_1 + h_2)$; $h_1 =$ width of the mesh; and $h_2 =$ length of the mesh. The contribution of head loss from the velocity of water leaving the sponge osculum can be estimated from the kinetic head loss, equation 22 in Riisgård and Larsen (1995), as:

$$\Delta H_i = u_{ex}^2 / 2g \tag{6}$$

where u_{ex} is the velocity of water leaving the osculum. The total head loss through the system is equal to the sum of the head losses at each region of the canal system.

As a comparison to the model by Riisgård and Larsen (1995), we also used the simplified model developed by Leys et al. (2011) which assumes head loss through each region of the aquiferous canal system can be calculated based on the Hagen-Poiseuille equation for fully developed laminar flow in a tube (Equation 3).

As the values used for both the density of seawater, ρ , and kinematic viscosity, v, depend on the temperature of seawater, a temperature of 12°C was used for the temperate demosponges and a temperature of 30°C was used for the tropical demosponges. To estimate the overall pump efficiency (η), and therefore the cost of pumping, we used equation 25 from Riisgård and Larsen (1995):

$$\eta = \frac{P_p}{R_{tot}},\tag{7}$$

Where R_{tot} is the total metabolic power expenditure (total measured respiration) and P_p is the pumping power expressed by the linear energy equation for steady, incompressible flow through a controlled volume, equation 24 in Riisgård and Larsen (1995):

$$\rho g \Delta H Q = P_p. \tag{8}$$

Here ρ is the density of seawater, g the acceleration of gravity, Q the volume flow rate through the system, and ΔH the total pressure drop, or head loss, through the system.

3.4 Results

3.4.1 Experimental work

3.4.1.1 Volume flow rates and oxygen removal

Mean excurrent velocity, volume flow rate, and oxygen removal for each species are provided in Table 3-2. *Cliona* had the fastest excurrent velocity; however, *Callyspongia* had the highest volume flow rate and oxygen removal due to its large osculum size. *Tethya* filtered the least volume of water per unit time and removed the least oxygen of all five species.

All sponges, irrespective of temperature, habitat or species, removed more oxygen when more water was filtered. (Figure 3-3; and see Appendix 2: Figure A2.1). Mean oxygen removal for one osculum from each species was positively correlated with the amount of water filtered (Spearman r = 0.843, p < 0.0001; Figure 3-3 A). For one individual of each species measured over a five minute period, oxygen removal also increased with volume filtered for all species except *Cliona* (*Neopetrosia* Spearman r = 0.813, p<0.0001, *Haliclona* Spearman r = 0.869, p<0.0001; *Tethya* Spearman r = 0.905, p<0.0001; *Cliona* Spearman r = -0.180, p = 0.169; and *Callyspongia* Spearman r = 0.734, p<0.0001; Figure 3-3B).
Species	n	Excurrent Velocity (cm s ⁻¹)	Volume Flow Rate (L h ⁻¹)	Volume Flow Rate (L h ⁻¹ mL ⁻¹ sponge)	Volume Flow Rate (L h ⁻¹ gDW ⁻¹ sponge)	Oxygen removal (μmol L ⁻¹)	Oxygen removal (µmol h ⁻¹ mL ⁻¹ sponge)	Oxygen removal (µmol h ⁻¹ gDW ⁻¹ sponge)		
Cliona delitrix	8	11.04 ± 0.54	175.04 ± 38.83	$0.39\ \pm 0.02$	4.33 ± 0.21	2.20 ± 1.04	0.83 ± 0.38	9.32 ± 4.29		
Callyspongia vaginalis	10	5.93 ± 0.67	44.49 ± 7.29	1.13 ± 0.18	18.02 ± 2.95	2.63 ± 0.53	3.12 ± 0.99	49.72 ± 15.87		
Tethya californiana	9	1.95 ± 0.30	5.16 ± 0.73	0.09 ± 0.007	0.28 ± 0.02	2.71 ± 0.60	0.23 ± 0.04	0.71 ± 0.12		
Haliclona mollis	10	3.04 ± 0.30	2.92 ± 0.47	$0.13\ \pm 0.01$	1.08 ± 0.11	2.32 ± 0.53	0.31 ± 0.08	2.53 ± 0.63		
Neopetrosia problematica	6	1.37 ± 0.25	0.53 ± 0.11	0.28 ± 0.05	2.26 ± 0.41	1.35 ± 0.14	0.38 ± 0.07	3.08 ± 0.63		

Table 3- 2| Mean excurrent velocity, volume flow rate, and oxygen removal from five species of demosponges. Both volume flow rate and oxygen removal are standardised by sponge volume (per mL sponge) and sponge weight (per gram dry weight, gDW).



Figure 3-3 Volume flow rates and oxygen removal

a) Sponge pumping volume (L hr⁻¹ g DW sponge⁻¹) and oxygen removal (μ mol hr⁻¹ g DW sponge⁻¹) were recorded over a five-minute period and plotted for one individual of each of five species of demosponges. Oxygen removal increased as the pumping volume increased both within an individual and between species, with the exception of *Cliona* (red). This same trend can be seen in b) when the mean oxygen removal and pumping volume over a 5 minute period is plotted for multiple individuals of each species (*Callyspongia* n=11; *Cliona* n=8; *Haliclona* n=10; *Neopetrosia* n=7; *Tethya* n=8).

3.4.1.2 Effect of ambient flow on pumping rates

Tests to determine the effect of increased ambient flow showed that the excurrent velocity of *Callyspongia* did increase slightly with increasing ambient flow (Spearman r = 0.141, p<0.001, Figure 3-4 a,b), although over the course of the experiment the excurrent velocity decreased from about 9 cm/s to below 8 cm/s (Figure 3-4 a). When the ambient velocity went above 20 cm/s, the excurrent velocity decreased in the first and third run, but not in the second, and when the pump was turned off, the excurrent velocity slowly increased. Images of the osculum showed the diameter did not change during the experiment, therefore pumping volume would show the same relationship. Interestingly, oxygen removal (µmol hr⁻¹) was negatively correlated with ambient flow (Spearman r = -0.221, p<0.0001, Figure 3-4 a,c); however, oxygen removal at the beginning and end of the experiment was the same despite a decreased excurrent velocity.

The excurrent velocity of *Cliona* was positively correlated with ambient flow (Spearman r = 0.485, p<0.0001, Figure 3-5). However, the osculum constricted during the experiment with the area reducing from 4 cm³ to less than 2 cm³ with increasing ambient flow (Figure 3-5). As such, less water was filtered; therefore, while excurrent velocity increased with increasing ambient flow, the total volume filtered was less (Spearman r = -0.407, p<0.0001). Oxygen removal (μ mol hr⁻¹) also decreased with increasing ambient flow (Spearman r = -0.456, p<0.0001).

3.4.2 Estimating the cost of filtration

Dimensions of each region of the aquiferous canal system for the five species of demosponges studied are given in Table 3-3. The path of water is illustrated in Figure 3-6. Briefly, water flows in through minute holes (ostia) in the dermal membrane (a three layered tissue) into a large subdermal space in four of the five species (except possibly for *Cliona*). From there, water enters into the largest incurrent canals which branch into smaller and smaller canals leading to the choanocyte chambers (Figure 3-7). *Callyspongia* is distinct from the other species in having water flow from the smallest incurrent canals into a lacunar space that holds all of the choanocyte chambers (Johnston and Hildemann, 1982).

Figure 3-4 | **Effect of ambient currents on** *Callyspongia vaginalis.* (A) Top graph: Ambient (black) and excurrent (blue) velocity (cm/s) over time. Ambient velocity was increased every 300 s (5 min) using an underwater aquarium pump. Excurrent velocity remains at around 9 cm/s until about 1500 s when it decreases to below 8 cm/s as the ambient velocity increases above 20 cm/s. Bottom graph: Oxygen removal (µmol/L) over time. Oxygen is stable at about 4 µmol/L for the first 300s until the pump is turned on, when it decreases to around 2 µmol/L. (B) There is a slight positive correlation between ambient and excurrent velocity (Spearman r = 0.141, p <0.001) (C) and a negative correlation between ambient velocity and oxygen removal (Spearman r = -0.221, p<0.0001).



Figure 3- 4| Effect of ambient currents on *Callyspongia vaginalis*

Figure 3-5 | Effect of ambient currents on *Cliona delitrix.* (A) Top graph: Ambient (black) and excurrent (grey dashed) velocity (cm/s) over time. Ambient velocity was increased every 300 s using an underwater aquarium pump. Excurrent velocity increases with increasing ambient velocity, although pumping volume (L/hr; red) calculated using osculum area (top images) does not increase. Middle graph: Oxygen removal (μ mol/L) over time. Oxygen is highly variable when the pump is off, and then slowly decreases once the pump is turned on. Bottom graph: osculum area over time until the camera battery died after about one hour. (B) There is a positive correlation between ambient and excurrent velocity (Spearman r = 0.485, p<0.0001), (C) although a negative correlation between ambient velocity and pumping volume (Spearman r = -0.407, p<0.0001). (D) as well as ambient velocity and oxygen removal (Spearman r = -456, p<0.0001).



Table 3-3 Dimensions of the aquiferous canal system in sponges

Numbers represent means of 3-75 measurements taken from 1-6 images from either scanning electron microscopy (SEM) or histology and light micrographs. Dimensions of collar slit, including the glycocalyx mesh on the collar, are in bold representing the filtration apparatus.

	Halic permo	lona ollis*	Aphroo vast	callistes us**	Neopetrosia problematica		Haliclon	a mollis	Tetl califor	'iya niana	Callys vagi	pongia nalis	Cliona delitrix		
Region of the aquiferous canal system	Diameter (µm)	Path length (µm)	Diameter (µm)	Path length (µm)	Diameter (µm)	Path length (µm)	Diameter (µm)	Path length (µm)	Diameter (µm)	Path length (µm)	Diameter (µm)	Path length (µm)	Diameter (µm)	Path length (µm)	
Ostia	20.6		3.89	0.50	24.5	0.5	14.3	0.5	40.6	0.5	31.2	0.5	37.3	0.5	
Subdermal space			90	82	242	86.1	95.0	50.6	177	105	168	131			
Large incurrent canal	50-340	3000	366	2000	383	2944	333	930	678	1118	407	923	294	1130	
Medium incurrent canal				529	156	648	140	834	170	1118	195	725	144	969	
Small incurrent canal				237	33	250	51.3	151.9	34.7	68.9	43.8	1	60.1	251	
Prosopyles	1 to 5		2.15	2.15		0.5	2.37	0.5	4.52	0.5	1.61	0.5	2.59	0.5	
Pre-collar space		2		2	1.3	2.6	5.7	3.6	1.6	2.2	0.5	2.6	0.69	2.19	
Glycocalyx mesh			0.045	0.010	0.095		0.166		0.059		0.052		0.118		
Collar slit	0.120	0.140	0.119	0.070	0.074	0.118	0.110	0.100	0.066	0.086	0.069	0.109	0.070	0.099	
Glycocalyx mesh			0.045	0.010											
Post-collar space			2	2	2.6	2.1	3.3	3.3	2.2	3.4	2.6	1.6	2.2	2.65	
Chamber	30		56	56	23.3	23.3	28.5	28.5	21.1	21.1	19.7	19.7	16.0	16.0	
Apopyle	14	1	26.4	2	16.0	0.5	14.1	0.5	0.90	0.5	5.97	0.5	4.23	0.5	
Small excurrent canal				118	45.2	173	51.9	189	34.9	74	52.9	0.5	60.1	251	
Medium excurrent canal					130	648	155	546	170	994	179	1096	144	969	
Large excurrent canal	102-235	3000	405	2840	282	2944	411	930	678	994	339	1342	294	1130	
Osculum	2300		44734	279000	3464	6676	5527	7420	8666	2184	16209	198410	22666	9983	
Chambers per mm ³ Collars per chamber Microvilli per collar	12,000 95 28		1,876 260 38		9,792 80 40		2,684 139 40		14,403 99 39		14,358 93 33		35,175 50 33		

* Haliclona permollis measurements taken from Reiswig (1975), with path lengths from Riisgard et al. (1993)

** Aphrocallistes vastus measurements taken from Leys et al. (2011)





Schematic drawings showing water flow through the aquiferous canal system of sponges. (A) Water enters through pores (ostia) on the sponge surface, into incurrent canals to the choanocyte chambers where the water is filtered, then out through the excurrent canals to the osculum. (B) There is a huge increase in cross-sectional area of the aquiferous system as the water enters the choanocyte chambers, which slows the water for filtration. The cross-sectional area then decreases as the water leaves the choanocyte chambers, jetting the water out through the osculum. (C) Water enters the choanocyte chamber through prosopyles and exits via the apopyle. (D) Glycocalyx (yellow) forms a gasket that connects all of the collars of choanocyte cells together, forcing the water through the microvilli of the choanocyte chambers. (E) Each microvillus is connected by a glycocalyx mesh (yellow), forcing the water through narrow rectangular openings.

In *Callyspongia*, water flows freely through the lacunar space before entering the choanocyte chambers through openings between choanocytes (Figure 3-8a). As there are no prosopyles in *Callyspongia*, openings between the choanocytes were considered to be prosopyles when estimating resistance through the canal system (Figure 3-8b). In the other four species, water enters the choanocyte chambers from the smallest incurrent canal through one or more prosopyles. At choanocyte chambers water moves through the collar microvilli. In Haliclona a set of cells forms a flat layer that, like a gasket, connects all collars in the chamber (Figure 3-8 c). In both *Neopetrosia* and *Callyspongia* a mucus glycocalyx mesh connected to each of the collars also serves as a gasket (Figure 3-8 b,d). Although a gasket has not been found yet in *Tethya* and *Cliona* (Figure 3-8 e,f), this sort of structure may be more common in demosponges than has previously been appreciated since those made from mucus glycocalyx are difficult to preserve. A glycocalyx mesh was found between the microvilli of the choanocyte cells in each species studied (Figure 3-8 b), but in the case of Tethya and Cliona it was only found in a few well-preserved choanocytes within a chamber. After passing through the glycocalyx mesh filter on the collar, the water flows into the chamber and from there, out of the apopyle (exit of the sponge choanocyte chamber). In *Tethya*, the apopyle consists of a sieve-plate (Figure 3-8 e); in others it is a circular aperture. From the apopyle the water enters small excurrent canals that merge into increasingly larger canals before flowing out of the osculum.

Cross-sectional area, velocity of water flow, and head loss for each region of the canal system based on Riisgård and colleagues (1995) model are given in Table 3-3. In each species, the cross-sectional area increases as the water enters the choanocyte chambers (Figure 3-9). Velocity through each region (u_i) was calculated from total cross-sectional area of each region (i), A_{i_i} and excurrent (ex) velocity out of the sponge osculum, u_{ex} , using equation (1). The effective velocity u_i through the collar slit of the two warm-water species, *Callyspongia* and *Cliona*, was 0.011 mm/s and 0.010 mm/s respectively, which is 2-10 times higher than the effective velocity in the temperate species (*Neopetrosia* = 0.005 mm/s, *Haliclona* = 0.004 mm/s, and *Tethya* = 0.0011 mm/s), a difference resulting from the higher excurrent pumping rates of those species. The total head loss through the canal system – the sum of head loss through each region calculated using equations (1-6) – is also 5-38 times higher for the tropical species (Table 3-4).

Figure 3-7 | **Histological sections in five species of demosponges.** Incurrent (ic) and excurrent (ec) canals in (**A**) *Neopetrosia* (**B**) *Haliclona* (**C**) *Tethya* (**D**) *Cliona* (**E**) and *Callyspongia.* Insets show choanocyte chambers. Scale bars: 1 mm; insets: 100 μm.



Figure 3- 7| Histological sections in five species of demosponges

Figure 3-8| Scanning electron micrographs of choanocyte chambers in five species of demosponges. (A,B) Choanocyte chambers (cc) of *Callyspongia* within the lacunar spaces (ls). Each choanocyte cell (cho) has a collar of microvilli (mv) that are connected by glycocalyx mesh (gly). (C) Large choanocyte chamber in *Haliclona* showing the cellular gasket (g) that connects each choanocyte cell. Water exits the chamber via the large apopyle (apo). (D) A glycocalyx gasket (gly) connects the collars in *Neopetrosia*. (E) The apopyle in *Tethya* consists of a sieve plate (sp). (F) Smaller choanocyte chamber in *Cliona* with the flagella protruding from the apopyle. Scale bars A,C,E 10 μ m B, 2 μ m inset, 1 μ m D, 1 μ m F, 5 μ m.



Figure 3- 8| Scanning electron micrographs of choanocyte chambers in five species of demosponges

Figure 3-9 Morphometric model of five species of demosponges. (A) Total cross-

sectional area of the aquiferous canal systems from the inhalant surface to the osculum for five species of demosponges: *Haliclona mollis* (purple), *Neopetrosia problematica* (cyan), *Tethya californiana* (green), *Callyspongia vaginalis* (blue) and *Cliona delitrix* (red). **(B)** Estimated water velocity (solid lines) and relative head loss (dotted lines) through the aquiferous canal system as water travels from the inhalant surface to the osculum for the same five species of demosponges.



Figure 3-9| Morphometric model of five species of demosponges

To determine the cost of filtration, the power required to pump water across the sponge, P_p , was calculated using the total head loss, ΔH , and volume flow rate, Q, and divided by the total measured oxygen removal R_{tot} using the conversion 1 µL O₂ hr⁻¹ = 5.333 µW and the mean oxygen removal and volume flow rates reported in Table 3-2. Using the model by Riisgård and Larsen (1995) the estimates of the cost of filtration were quite variable, ranging from 0.97% for *Tethya* and 40.27% for *Cliona*. The simplified model developed by Leys et al (2011) gives the same relationship for cost of filtration between the five species of demosponge, although the range is slightly lower at 0.89% for *Tethya* and 31.9% for *Cliona*. It also estimates a higher cost of pumping for *Callyspongia* at 16.97% total respiration. Both of the warm-water species *Callyspongia* and *Cliona* had the highest cost of filtration regardless of the model used (Table 3-4).

3.5 Discussion

Our study aimed to assess the energetic cost of filtration in demosponges and to determine whether sponges reduce their cost of filtration by taking advantage of ambient currents. Using a suite of different approaches we have shown that the cost of pumping in demosponges is quite variable and depends on the volume of water pumped. Of the five species of demosponges studied, the tropical species *Cliona* and *Callyspongia* filtered the most water and extracted the most oxygen per gram of tissue, leading to higher estimates for the energetic cost of filtration than the three temperate demosponges *Neopetrosia*, *Haliclona*, and *Tethya*. This suggests that the cost of filtration for demosponges is higher than previously estimated and that reducing the volume of water filtered would reduce the cost of filtration in times of low food availability. Interestingly, we found that demosponges in ambient flow. Both *Cliona* and *Callyspongia* reduce the amount of water filtered at very high ambient velocities, which may be a mechanism to protect themselves from damage during storms.

Table 3-4| Morphometric model of the aquiferous system in five species of

demosponges. Estimated total cross-sectional area for each region was measured from the dimensions listed in Table 4-3 as well the density of the structures as found in SEM and histological images. The velocity of water flow through each area u_{∞} was calculated from cross-sectional area A_i and measured excurrent velocity u_{ex} out of the osculum using equation (4). Head loss H in each region was calculated using equations (3-6) from dimensions and velocity u_{∞} of each region. Riisgård and Larson's (1995) model used a different equation of head loss for each region of the aquiferous canal system, whereas Leys et al's (2011) model used only equation (3). The sum of the head loss ΔH and measured volume flow rate are used to calculated the pumping power P_p using equation (2). The cost of pumping η (%) is then estimated using equation (1) from the pumping power P_p and the measured respiration rate R_{tot} . The collar slit is in bold, representing the filtration apparatus.

Table 3- 4| Morphometric model of the aquiferous canal system in five species of demosponges

	Neo	petrosia _l	problema	tica	Haliclona mollis				Tethya californiana				Ca	llyspongi	ia vagina	lis	Cliona delitrix			
	Head loss, H (μm H ₂ 0)			Head loss, H (µm H ₂ 0)				Head loss, H (µm H ₂ 0)					Head loss, H (µm H ₂ 0)				Head loss, H (µm H ₂ 0)			
Region of the aquiferous canal system	Cross- sectional area, A_i (mm ²)	Velocity, <i>u_i</i> (mm/s)	Riisgard and Larson (1995)	Leys <i>et al</i> (2011)	Cross- sectional area, A_i (mm ²)	Velocity, <i>u_i</i> (mm/s)	Riisgard and Larson (1995)	Leys <i>et al</i> (2011)	Cross- sectional area, A_i (mm ²)	Velocity, <i>u_i</i> (mm/s)	Riisgard and Larson (1995)	l Leys <i>et al</i> (2011)	Cross- sectional area, A_i (mm ²)	Velocity, <i>u_i</i> (mm/s)	Riisgard and Larson (1995)	1 Leys <i>et al</i> (2011)	Cross- sectional area, A_i (mm ²)	Velocity, <i>u_i</i> (mm/s)	Riisgard and Larson (1995)	Leys <i>et al</i> (2011)
Ostia	3.37	1.04	111	4	0.90	3.90	709	42	1.38	1.76	113	2	12.8	0.68	51	1	2.82	6.57	409	9
Subdermal space	19.7	0.18	56	7	22.2	0.16	239	96	16.7	0.14	46	26	21.8	0.40	10	12				
Large incurrent canal	15.9	0.22	16	16	14.4	0.24	6	6	21.7	0.11	2	2	14.1	0.62	9	9	3.31	5.60	338	338
Medium incurrent canal	7.21	0.49	26	26	3.21	1.09	45	45	24.8	0.10	19	19	2.70	3.25	47	47	2.57	7.22	1026	1026
Small incurrent canal	5.79	0.61	491	491	4.16	0.84	278	278	3.66	0.66	25	25	3.67	2.39	3	3	1.71	10.84	1969	1969
Prosopyles	494	0.007	438	103	346	0.010	922	330	172	0.014	380	71	55.2	0.159	3434	1806	17.7	1.04	9714	3186
Pre-collar space	255	0.014	49	49	775	0.005	5	5	504	0.005	55	55	170	0.051	6768	6768	264	0.070	19158	19158
Collar slit	376	0.009	288	797	546	0.006	471	73	1237	0.0020	147	521	492	0.018	668	8202	1095	0.017	2300	1969
Post-collar space	412	0.009	13	13	405	0.009	9	9	1077	0.0022	6	6	566	0.015	17	17	1019	0.018	37	37
Chamber	408	0.009	2	2	171	0.020	1	1	488	0.005	0	0	406	0.022	3	3	674	0.027	4	4
Apopyle	208	0.02	1	0	44.6	0.08	4	0	110	0.02	14	13	40.3	0.22	8	1	52.1	0.36	15	3
Small excurrent canal	4.66	0.75	6	6	6.79	0.52	24	24	2.47	0.98	6	6	0.52	16.9	0	0	1.71	10.84	97	97
Medium excurrent canal	3.47	1.01	128	128	6.33	0.55	52	52	24.8	0.10	149	149	2.87	3.05	2288	2288	2.57	7.22	1985	1985
Large excurrent canal	1.21	2.90	165	165	13.1	0.27	13	13	21.7	0.11	1	1	3.04	2.88	140	140	3.31	5.60	371	371
Osculum	0.26	13.66	10	33	0.12	30.44	47	33	0.11	21.95	25	3	0.15	59.33	179	176	0.17	110.41	622	8
Volume flow rate, <i>Q</i> (mL/min) 9.0		48.6					82.1					7	42		2668					
Respiration, R _{tot} (µW) 87		37	790					1396					14218				42102			
Head loss, ΔH ($\mu m H_2 0$)		1799	1840			2825	1008			988	900			13626	19474			38043	30161
Pumping Power	r, P_p (μW)	3	3			23	8			14	12			1688	2412			16955	13442
Cost of pumping	g, η (%)		3.12	3.19			2.91	1.04			0.97	0.89			11.87	16.97			40.27	31.93

3.5.1 The cost of pumping

Cost of filtration was estimated by determining the energy required to overcome the resistance through the aquiferous system. Although there are differences in gross morphology among the five species, we found similar morphology at the filter for each of the species studied. The cost of pumping was variable ranging from 0.97% for Tethya to 40.27% for *Cliona* of the total oxygen consumed (assuming oxygen consumed is used for all metabolism including filtration). Previous estimates on the energetic cost of pumping in demosponges also show a large range, from 0.4% for Haliclona urceolus (Riisgård et al., 1993) to 25% for *Negombata magnifica* (Hadas et al., 2008). Although this variability may indicate inconsistencies between the theoretical models used by Riisgård et al. (1993) and direct measurements done by Hadas et al. (2008), our results suggest that the variability in 'cost' may simply reflect differences in the volume of water pumped. Although our findings in Section 3.2 suggest that filter dimensions contribute a large amount to the cost of filtration (Table 3-1), the dimensions of the glycocalyx mesh are smaller in *Tethya* than Cliona and therefore do not account for the difference in costs. Rather, volume flow rates contribute mostly to differences in the energetic cost of filtration, with the two species found in the tropics having the largest volume flow rates resulting in the largest cost of filtration (Table 3-4). In addition, when individuals of each species filtered more water they also consumed more oxygen (Figure 3-3), suggesting that the energetic cost of pumping is variable within an individual depending on how much water is being pumped at any one time. This implies that sponges could save energy in times of low food availability by lowering the volume of water pumped.

That pumping more water would cost more energy in sponges is intuitive. How a sponge changes its pumping rate and volume filtered, however, is not known. One mechanism, in demosponges, may be to dilate the canals while maintaining excurrent velocity, increasing the volume of the canal system and therefore the volume filtered. The more water flowing through the canal system at any one time would increase the resistance and therefore also the energetic cost of pumping. Another mechanism could be to increase the rate of flagellar beating in the choanocyte chambers. This would increase the velocity of

water through the canal system and therefore increase the volume of water filtered as well as the energetic cost of pumping. Sponges likely control the rate of flagellar beating to save energy when the sponge contracts. We did not look at the energy spent on the flagellar beat nor the drag on the flagella when estimating the cost of pumping, which is a limitation in the model and probably makes our estimates more conservative in our cost of filtration.

It is important to consider why the two tropical species of demosponge had higher volume flow rates and therefore higher estimates for the cost of filtration in this study. Differences in pumping rates between species can be caused by structural differences in the sponge canal system (Reiswig, 1975a), microbial content (Weisz et al., 2008), and tissue density (Turon et al., 1997). In addition, Riisgård et al. (1993) found that volume flow rate in *Haliclona permollis* increased up to ten times with a change in temperature from 6°C to 15°C. The higher volume flow rate per gram weight in the two tropical species in this study therefore may be a result of the higher temperature of water and lower viscosity. However, due to the high energetic cost to pump more water it would only be adaptive to have such high volume flow rates if there is enough food in the water to support this.

Sponges are found in almost every marine and freshwater habitat and, with the exception of carnivorous sponges, all feed on ultraplankton and dissolved organic carbon. Increasing cross-sectional area through the canal system slows the velocity of water, enabling food capture either in the small incurrent canals or at the filter. Slight differences in filtration ability and size of plankton captured between different species of sponges are known (Reiswig, 1975b; Turon et al., 1997; Yahel et al., 2007). There is little information, however, on the relationship between filtration ability, diet, and microarchitecture of the aquiferous canal system. Among the five species studied here, slight variations in the architecture of the aquiferous canal system were found such as the lacunar space in Callyspongia and the sieve-plate apopyle of Tethya. We also found wide differences in the velocities of water measured out of the osculum, although similar velocities of water at the filter (Table 3-4). This suggests that despite wide differences in volume flow rates and adaptations to a variety of habitats and ecological niches, the canal system of sponges is designed to slow the velocity of water down to a certain speed that enables food capture at the filter. The small differences that were found in velocities at the filter may reflect small differences in preferred plankton size or filtration ability. The model predicted that both

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tropical species *Callyspongia* and *Cliona* had faster velocities of water at the collar filter. In addition, *Callyspongia* lacks the small incurrent canals leading into the choanocyte chambers, suggesting that it does not rely on pinacocyte capture of plankton in the canals. The diet and filtration ability of these two species is unknown, although it would be interesting to determine the relationship between microarchitecture, velocity of water at the filter, and diet of the sponges.

3.5.2 Response to ambient currents

One way to reduce the cost of pumping in sponges would be to take advantage of ambient currents through passive flow. In both *Cliona* and *Callyspongia* excurrent volume flow rates were not correlated to the ambient currents, suggesting they do not use passive flow. Rather, both species decreased their volume flow rate when ambient velocities reached a certain level, which may be to reduce damage caused by high currents or sediments during storms. High velocities through the canal system may cause damage to some of the smaller spaces, including the fine glycocalyx mesh at the filter. In addition, storms can stir up sediment into the water column which has been shown to have a negative impact on sponge filtration and respiration (Gerrodette and Flechsig, 1979; Tompkins-MacDonald and Leys, 2008; Bannister et al., 2012).

Sponges have long been considered textbook examples of animals that can take advantage of current-induced flow (Bidder, 1923; Vogel, 1974; Vogel, 1977). In the 1970's Vogel used thermistor flow meters to record excurrent flow while increasing ambient currents, and found a strong correlation between excurrent and ambient velocities. His method, however, did not take into account changes in dimensions of the osculum. Moreover, Vogel only plotted points in time rather than the full time series. Therefore, the increased excurrent velocity recorded by Vogel (1977) in the species *Amphimedon viridis* (referred to as *Haliclona viridis*), *Ircinia variabilis* (referred to as *Ircinia fasciculata*), and *Aplysina fistularis* (referred to as *Verongia fistularis*), could also have been behavioural responses, as shown here in *Cliona delitrix*. In this study, although excurrent velocity in *Cliona* did increase with increasing ambient currents, this was due to the sponge osculum contracting resulting in a decrease in volume flow rate as ambient currents increased. In addition to positive correlations between ambient velocity and oscular flow, there are reports in the literature of a negative correlation. When studying *in situ* pumping rates for the globose freshwater sponge *Baikalospongia bacillifera* in Lake Baikal, Savarese et al. (1997) noted that two individuals monitored over a diel cycle showed negative correlations between ambient and oscular velocities. In addition, they noted periodic cessation of pumping on the order of minutes to hours that did not correlate with ambient flow. Reiswig (1971) also found periodic oscular closures and therefore cessations of pumping with *Tethya crypta* that were negatively correlated to wave action (Figure 1-4). Here, we found both *Callyspongia* and *Cliona* reduced the volume of water filtered when ambient currents reached a certain threshold. Some demosponges therefore show a large amount of control of their excurrent volume flow rate despite fluctuations in the ambient water velocity.

3.5.3 General conclusions

The over-arching finding of this work is that demosponges control the water flow through their aquiferous systems. The architecture and design of the aquiferous canal system is such that the velocity of water slows at the filter to enable food capture, although each species accomplishes this in slightly different ways. Despite the broad similarity in the canal system architecture among demosponge species, the amount of water filtered by each (volume flow rate) varies considerably, resulting in different costs of pumping. For the three temperate demosponges, our estimates for the cost of pumping are comparable to that found by Riisgård et al. (1993) for what he termed the 'standard sponge'. However, the two tropical demosponges we studied had much higher volume flow rates with much higher cost of pumping; the cost of pumping for *Cliona* was more comparable to the cost of pumping found by both Leys et al. (2011) and Hadas et al. (2008). It is likely that habitat and ecological niche of sponges has led to adaptations in body form and physiology over time and together these play a large role in differences in cost of pumping.

We also found that demosponges respond to ambient currents, reducing the excurrent velocity and volume filtered as ambient flows increase. Previously, we have shown that demosponges have sensory cilia in their osculum, which allow them to sense and respond to changes in their environment (Chapter Two). Here, we show that

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demosponges also respond to changes in ambient currents, possibly to reduce their cost of filtration or to reduce damage caused by high currents or sediment.

3.5 References

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Chapter Four

A general discussion on filter feeding in sponges

4.1 Overview

Sponges (Porifera) are sessile suspension feeders that actively pump water through their canal system bringing in food and oxygen and excreting metabolic wastes. This suspension feeding has a major impact on ecosystems, shaping planktonic communities as well as coupling nutrients between the water column and the benthos (reviewed in Gili and Coma, 1998). Recently, sponges have been rapidly disappearing in some marine habitats (Wulff, 2006). The reason for this decline is still not known, although episodic changes in salinity, temperature, or sedimentation are a possible cause. Increasingly, sedimentation from resource exploitation such as oil exploration or fishing trawls is having severe impacts on benthic suspension feeders including sponges, which are sensitive to materials that can clog their filtration system (Ellis et al., 2002; Bannister et al., 2012; Puig et al., 2012). Before we can understand the impacts of additional stresses in the environment, however, we must first answer some important questions on sponge physiology and behaviour.

Some demosponges have been shown to deal with short pulses of high sediment by carrying out slow rhythmic contractions that help to clear out debris (Nickel, 2004; Elliott and Leys, 2007; Ellwanger et al., 2007). It is still not understood, however, how sponges detect the increased sediment and coordinate a response without the use of nerves. High suspended sediment loads have also been linked to reduced pumping activity (Gerrodette and Flechsig, 1979; Tompkins-MacDonald and Leys, 2008) and increased metabolic demand (Bannister et al., 2012), which is thought to be a result of clogging of the filtration apparatus. Yet, the amount of energy required for a sponge to filter water under normal conditions is still not known. Thus, to further understand the impacts of additional stresses such as sediment, we must first understand the energetic constraints that might affect sponges. In addition, sessile filter feeders depend on water currents to bring in food and

carry wastes away, yet increased water currents during storms usually bring in increased suspended sediment loads. The same stimulus – water velocity – can therefore be either beneficial or damaging to a sponge, and it is not yet understood how sponges detect and respond to a range of ambient current speeds.

This thesis examines how sponges control water flow during filter feeding. Chapter Two reveals the presence of sensory cilia in the water canal system and suggests that the cilia are involved in responding to stimuli and coordinating behaviour in the sponge. This thesis also assesses the amount of energy that it takes the sponge to filter water for food. Chapter Three examines the energetic cost of filter feeding and suggests that the cost of pumping is quite variable both within and between species, depending on the volume of water pumped. In addition, Chapter Three shows that demosponges control the amount of water flow through their canal system by responding behaviourally to increased ambient currents. Here, in Chapter Four, I discuss several new questions and areas for future research on filter feeding and behaviour in demosponges.

4.2 Sponges respond to their environment using sensory cilia

Sponges typically respond to stimuli within minutes to hours, compared to the milliseconds that our nerves and muscles effect a response. Though it has long been known that sponges do not possess nerve cells or nervous tissue (Jones, 1962; Pavans de Ceccatty, 1974), until now it has largely been unknown how sponges detect and respond to their external surroundings. In Chapter Two I showed the presence of short, non-motile sensory cilia in the excurrent canal system of six species of demosponge and one species of glass sponge. These cilia closely resemble the primary cilia that function as sensory organelles found in most cells in the vertebrate body and in many cells in invertebrates (Praetorius and Spring, 2005). I have suggested that these cilia detect changes in water flow or pressure in the aquiferous canal system of the sponge and coordinate a response in the form of whole body contractions.

These sensory cilia have eluded detection by scientists until now, mostly because of the difficulty in preserving them during fixation. In addition, they are very small (4-6 μ m in length) and found in localized regions of the sponge, therefore one must be looking

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specifically at the endopinacocyte cells of the osculum or regions of the excurrent canal system to observe them. Now that these cilia have been observed, it would be important for other researchers to look for the cilia in a range of species to determine just how widespread the cilia are among sponges. It would also be important to understand exactly where the cilia are located in each species of sponge to further understand the role they may play in detecting environmental signals and controlling behaviours.

In Chapter Two I used chemicals commonly used to block channels on the ciliary membrane and which inhibit sensory function in other organisms (Gale et al., 2001; Praetorius and Spring, 2001). These drugs are thought to block TRPP2 (PC2) channels on the ciliary membrane, with TRP channels responsible for almost all forms of sensation in eukaryotic cells (Nauli et al., 2003; Praetorius and Spring, 2003; Praetorius and Spring, 2005; Singla and Reiter, 2006; Fujiu et al., 2011). TRP channels have not previously been known in sponges; here, we showed the presence of *pkd2* sequence in transcriptomes of sponges. Developing a TRP channel antibody for the sponge would be a powerful tool to determine where sensory cells are located in the sponge body, although this would not be an easy task. It has previously been done in Chlamydomonas to determine the location of a variety of TRP channels along the length of the flagella (Fujiu et al., 2011), although a good sequence is necessary to develop a proper antibody. Another important area for further research in the sponge would be to link Ca²⁺ signalling, L-glutamate, and channels on the ciliary membrane in order to further understand the role of these cilia in triggering responses in the sponge. Previously, influential work on Ca²⁺ signalling in kidney cell primary cilia has been done using fluorescent markers for calcium (Praetorius and Spring, 2001), and a similar study in sponges would be very informative.

A common misconception about sponges is their lack of responsiveness, despite many studies showing that sponges have whole body behaviours and respond to stimuli (for example see Reiswig, 1971; Weissenfels, 1984; Nickel, 2004; Elliott and Leys, 2007). While carrying out experiments in both Chapters Two and Three of this thesis I was surprised at how sensitive sponges are – sometimes just the vibrations of the computer would be enough to trigger the sneeze behaviour (described in Ch 2). More research is required to explore this sensitivity and the range of behaviours that sponges exhibit. Underwater time-lapse photography is a powerful tool that can help us to visualize and study these behaviours. Technological advances have allowed underwater cameras to be set up year-round, paired with instruments that measure abiotic factors such as the North East Pacific Time-series Underwater Networked Experiment (NEPTUNE), part of Ocean Networks Canada. This tool enables researchers to study long-term behaviours and phenomena that would previously be missed with SCUBA, snorkelling, or traditional shipbased exploration alone. It also enables sponge behaviours to be observed *in situ*, and by pairing the responses with abiotic factors it will help to understand how factors such as temperature, salinity, pressure, suspended sediment load, or current velocity may play a role in behaviour. Since contractions of the canal system are linked to changes in volume of water pumped (Reiswig, 1971), understanding the factors that may influence behaviour may help to understand the stresses that impact filter feeding in sponges.

4.3 Demosponges control water flow through their bodies

It has long been recognized that sponges show considerable morphological plasticity (Bidder, 1923; Warburton, 1960; Palumbi, 1986) and behaviour (Reiswig, 1971; Vogel, 1974; Vogel, 1977) to different flow conditions. However, it is still not fully understood how different flow conditions affect pumping volume in the sponge. The results in Chapter Three suggest that higher ambient flow rates actually reduce the volume of water pumped, which is contrary to previous studies suggesting sponges use currentinduced flow (Vogel, 1974; Vogel, 1977; Leys et al., 2011). Other studies have also found that higher ambient flow can be correlated with reduced pumping activity in the demosponges Tethya crypta (Reiswig, 1971) and Baikalospongia bacilifera (Savarese et al., 1997). This suggests that sponges are not just passive conduits for water and have a lot more control over the water flow through their bodies than previously thought. The ambient current speeds we used in Chapter Three were higher than the current speeds the sponges would naturally experience, except perhaps during storms. In addition, due to logistics and time, we were only able to study one individual for each species properly. More replicates are therefore required to determine the relationship between ambient velocity and pumping volume.

Sponges do rely on at least some ambient water flow to bring food in and carry wastes away. Yet our results showed that high ambient currents caused sponges to reduce their pumping volume in at least some species, suggesting intermediate ambient flow conditions would result in the maximum amount of water that sponges process. This is in line with studies for other suspension feeders that have found rates of particle capture and growth are highest at an intermediate ambient flow speed (Best, 1988; Shimeta and Jumars, 1991; Eckman and Duggins, 1993). During our in situ experiments on Cliona, it was evident that the sponge responded favourably to a small increase in ambient flow. At the beginning of one experiment, we arrived at the study location to find that the sponge oscula had been eaten by fish and the sponge was fully contracted. We decided to direct flow over the sponge from a pump we had brought while setting up the instruments, and found that over the course of about one hour the sponge relaxed and resumed pumping, though not as strongly as the previous day. We then continued to use this technique on contracted sponges prior to beginning our experiments. While maintaining sponges in the laboratory in Bamfield it was also determined that to obtain maximal pumping volume the inflow to the tanks needed to be on high flow with the hoses directed at the sponges. Not all sponges, however, seem to respond to ambient flow conditions. Reiswig (1971) found that the species *Mycale sp.* did not alter its pumping volume despite changes in wave action, and predicted that species with thin walls and low pumping velocities would show little to no changes in pumping activity over time. Some flow is therefore required to obtain maximal pumping in many demosponges, though there is still much to learn about the effect of ambient currents on sponge pumping volume.

The amount of water that a sponge processes is directly proportional to the amount of food that it obtains. So why do some sponges reduce their pumping volume in high ambient flow conditions? In suspension feeders that use external filters to capture food particles, high ambient flows can cause deformation and damage to the filter (Best, 1988; Shimeta and Jumars, 1991). For sponges, however, the filter is inside the sponge body and thus does not come in direct contact with ambient flow. The morphometric model used in Chapter Three however suggests that increasing the velocity of water out of the osculum without changing the canal dimensions would also increase the velocity at the filter. This suggests that if the sponge increases pumping volume with increasing ambient flow rates to take advantage of higher food concentrations, the velocity at the filter will also increase and may reach a threshold in which damage to the filter might occur. Therefore, to reduce damage, sponges may control the velocity of water at the filter by contracting their canals. More studies are required to understand the mechanisms used to alter pumping volumes under a range of ambient flow conditions.

4.4 It is energetically expensive to filter water

4.4.1 Optimal foraging with respect to habitat

Sessile filter feeders are unable to move to search out food and instead rely on water currents to bring food in as well as carry wastes away. To optimize their net rate of energy gain, sessile suspension feeders may alter their ingestion rates to feed more when food is more abundant (Taghon, 1981). This also suggests that suspension feeders will have evolved optimal levels of filtration that are fine-tuned to their habitat, and that they will alter their filtration rate based on food availability, seasonality, wave action, suspended sediment loads, temperature, and predation. Chapter Three reports on experiments which suggest that for five species of demosponge in both temperate and tropical habitats, pumping volumes do differ within an individual, between individuals of the same species, and between each of the five species. Pumping rates among sponges are therefore quite variable, likely as a mechanism to increase net energy gain.

Why do sponges not continuously pump high volumes of water to obtain more food? Jørgensen (1966) suggested that filter feeding is inexpensive to allow for continuous rates of feeding. However, my results in Chapter Three suggest that there is a trade-off to pumping more water because it costs more energy to do so. There would therefore be an optimal level of filtration that is dependent on the sponge's environment. Although sponges do selectively feed on certain particles within the water column (for example see Yahel et al, 2007), they cannot move to search out more or better food, suggesting that during low food conditions sponges could reduce their pumping rates to save energy.

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4.4.2 Amount of oxygen consumed by sponges

The results of this thesis suggest that it is energetically expensive for sponges to pump large volumes of water and that sponges that pump more water also consume more oxygen. But how do the rates of oxygen consumption found in this thesis compare to those reported for other sponges? Previously, oxygen consumption for sponges has been found to range from 7.42 μ mol O₂ h⁻¹ g_{DW}⁻¹ for *Tethva crypta* to 46.58 μ mol O₂ h⁻¹ g_{DW}⁻¹ for *Mycale* sp (Reiswig, 1974). In Chapter Three, I reported oxygen consumption values that ranged from 0.71 μ mol O₂ h⁻¹ g_{DW}⁻¹ for *Tethya californiana* to 49.72 μ mol O₂ h⁻¹ g_{DW}⁻¹ for Callyspongia vaginalis. In fact, each of the three temperate demosponges Tethya californiana, Haliclona mollis, and Neopetrosia problematica had oxygen consumption values less than 3 μ mol O₂ h⁻¹ g_{DW}⁻¹, which is much lower than the known range of oxygen consumption for other sponges. Although this low oxygen consumption can be attributed to the low pumping volumes recorded for each of the species, the reason for the low pumping volumes is not certain. One reason may be the method of measurement. The small osculum sizes of the temperate species may have led to conservative estimates in excurrent velocity when using an acoustic Doppler velocimeter (ADV). The sampling volume of the ADV used in our experiments measures the velocity of water in a 6mm diameter, which is larger than some of the oscula measured. Another reason for the lower pumping volumes may be seasonality since the measurements were done during the winter months. Further studies need to be done to determine what role seasonality plays in both pumping volumes and oxygen consumption in temperate sponges.

A recent study has suggested that sponges do not require much oxygen, and even goes so far as to say that sponges may have evolved prior to the oxygenation of the oceans (Mills et al., 2014). Mills et al. (2014) reported that *H. panacea* could both respire and feed at oxygen levels 0.5% – 4% present atmospheric levels, and even reported some sponge 'growth' at these levels. This reported 'growth' was the elongation of several of the sponge protrusions, but because the weight of the sponge was not measured it is unknown if this elongation resulted in an increase in tissue. Sponges have been known to relocate under poor environmental conditions by extending fibrils and 'crawling' along the substrate (Maldonado and Uriz, 1999). This elongation of protrusions, therefore, may have been an

escape mechanism to try to find more suitable habitat. In addition, the clearance rates reported by Mills et al. (2014) were 40% clearance rates previously reported for *H. panacea* (Riisgård et al., 1993). Based on the results from this thesis, the reduced clearance rates reported by Mills et al. (2014) may be an indication of reduced pumping rates to save energy under unfavourable conditions. Increased filtration to obtain food comes with increased energy and thus oxygen uptake. Therefore, although some sponges are able to withstand short periods of low oxygen it is unlikely that they would be able to thrive under these conditions.

4.5 Concluding statements

This thesis presents the first evidence of non-motile sensory cilia in the osculum of sponges, which may represent the first steps in the evolution of sensory and coordination systems in metazoans. I show evidence suggesting these sensory cilia provide the sponge with the ability to sense changes in the environment and control the amount of water flow through the aquiferous canal system. Sponges rely on this water flow to filter out particles for food. However, a repeatedly overlooked component of filter feeding is the amount of energy required to pump the large volumes of water needed to meet food requirements. My results suggest that this filter feeding is energetically costly, and that in times of low food availability or other additional stresses sponges may be able to reduce the volume of water filtered to lower the cost of filtration.

4.6 References

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Appendix One

Supplemental material for Chapter Two

A1.1 Cilia in the oscula of various sponges



a. Ephydatia muelleri, b, c. Spongilla lacustris, d. Neopetrosia vanilla, e. Haliclona mollis,
f. Haliclona sp,. g. Neopetrosia problematica, h. Aphrocallistes vastus. Scale bars 1 μm.

A1.2 Uncompressed tree showing the evolutionary relationships of sponge TRPType I and II genes.

Values at nodes indicate Bootstrap support. (Tree has been split into three pages for viewing. For the full scale complete tree see http://www.biomedcentral.com/1471-2148/14/3/additional)







A1.3 Full alignment of TRP sequences for uncompressed tree in Fig 2-5a

TRPC1 Hsap	NP 003295	1 WRP 1 i	LFLLACDK	YYMVKKILEN	LDILOLLLDY	G		I R
TRPC1 Mmus	NP 035773	1 WRP 1LF	LLACDKGDYY	MVKKILESLD	ILOLLLDYGS	ADALLVAIDS	EVVGAVDILL	NHRKRSILAA
TRPC1 Drer	NP 001185	590 1 TRP	LFLLACEK	YYMVKKLLEN	LDILOLLLDH	GATDALLV	DSEVVGAVDI	LLNHRRRSI
TRPC2 Mmus	NP 035774	2 TRP 2 i	TLLRAIQEGQ	LGLVQQLLGH	EVITDVLLAK	FIHEALLVAV	DTNQPAVVRR	LLARLERET
TRPC2 Drer	NP 001025	337 1 TRP	ELLGAIREGN	LNLVSSLLGN	EDTMASLLQK	FIHEALLV.V	DTNQPRVVKR	LLDRLDQET
TRPC2 Drer	XP 688403	2 PREDICT	ELILAIQEGN	MAWVDSLLGS	EDIMTSLLLK	FIHEALLV.V	DTNQPRFVKH	LLDRLDLETL
TRPC3_Hsap	NP 001124	170_1_TRP_	RFLDAAEYGN	IPVVRKMLEH	LEVTELLLKK	EIGDALLLAI	SKGYVRIVEA	ILNHPGFAIL
TRPC3_Mmus	NP 062383	2 IRP 3RF	LDAAEYGNIP	VVRKMLEHLE	VTELLLKKEI	GDALLLAISK	GYVRIVEAIL	GHPGFAILAA
TRPC4_Hsap	NP 003297	1 TRP 4 i	AYLNAVEKGD	YASVKKSLEN	LELIELLLSF	NVGDALLHAI	RKEVVGAVEL	LLNHKKPSI
TRPC4_Mmus	NP_058680	_1 <u>NRP</u> 4 i	AYLNAVEKGD	YASVKKSLEN	LELIELLLSF	NVGDALLHAI	RKEVVGAVEL	LLNHKKPSI
TRPC4_Drer	_xp_001920	781_1_PRED	SYLSAVEKGD	YASVKLALEN	LEIIELLLSF	NVGDALLHAI	RKEVVGAVEL	LLNHKKPSIL
TRPC4_Dmel	NP_609802	_1_trpgamm	KFLLAVERGD	MAGTRRMLEN	LEMVELLINY	NTKDALLHSI	SEEFVEAVEV	LLDHENVTIL
TRPC4_Cele	NP_001022	703 <u>1</u> TRP_	QFLLSCERGD	IGSVRKLLEN	IEMIELLLDH	NTGDAILYAI	GEENVEAVEI	IVEHLKMDVI
TRPC5_Hsap	NP_036603	1 IRP 5AF	LNAVEKGDYA	TVKQALENLE	IMELLLNHSV	GDALLYAIRK	EVVGAVELLL	SYRRPSMLAA
TRPC5_Mmus	NP_033454	_1_NRP_5AF	LSAVEKGDYA	TVKQALENLE	IMELLLNHSV	GDALLYAIRK	EVVGAVELLL	SYRKPSMLAA
TRPC6_Hsap	NP_004612	_2_TRP_6RF	LDAAEYGNIP	VVRKMLEHLE	ITELLLKKEV	GDALLLAISK	GYVRIVEAIL	SHPAFAILAA
TRPC6_Mmus	NP 038866	_2_1050 6RF	LDAAEYGNIP	VVRKMLEHLE	ITELLLKKEV	GDALLLAISK	GYVRIVEAIL	NHPAFAILAA
TRPC6_Drer	NE 001025	453_1_TRP_	RFLDAAEYEN	TPVVRRMLEH	LEVTELLLKK	DIGDALLLAI	SKGYTRIVEA	ILSHRAFAIL
TRPC6_Drer	XP 002665	445_1_PRED	RFLEAAEIGN	IPVIRRMLEH KDELOECLEN	MEMTELLIKK	DICUNIT	DECUVDITEN	ILSHQAFAIL
TRPC0_Cere	NE 065122	1 1 7 i	RF LEARELON	TRADECLEN	MEAAEPPPÄÄ	FUCDALLUT	SKCYURTUEN	TINUDAFATI
TRPC7 Mmus	NE 036165		LDSAFYCNTP	VVPKMLEHLE	VTELLIKKEV	CDALLIATSK	GYVETVEATT.	SHDAFATIAA
TRPC7 Drer	XP 695955	2 PREDICT	RELDAAEY	TPSVRKMLEH	LEVTELLLKK	EVGDALLIAT	SKGYVRT	TLAHPAFET
TRPN Dmel	NP 0012458	91 WERN no	PMHLAAENCH	AHVIEILAGH	MELVNNLLAA	RGRSALHLAA	ERGYLHVCDA	LLTNKFINH
TRPN Cele	NP 493429	TRPN TRP 4	PVHVAAER	TSMVESLIGH	SGVANILLKA	RGRTALHLAA	FNGHLSLVHL	LLOHKFVNH
TRPN Drer	NP 899192	TRPN nompC	PLHIAAERGH	TNVVEILTGH	TEVVKILLQA	RGKAAIHLAA	QRGHQDIVDV	LLSQKFVNHL
TRPM1 Hsap	NP 002411	3 TRP M 1	PLVGLVVEGG	PNVVSIVLVD	IARSQIFVFH	WLEQAMLDAL	VLDRVDFVKL	LIENGNMORI
TRPM1 Mmus	NP 001034	193 2 TRP	PVVGLVVE <mark>G</mark> G	PNVVSIVLVD	IARSQIFVFH	WLEQAMLDAL	VLDRVDFVKL	LIENGNMQR
TRPM2_Hsap	NP 003298	1 TRP M 2	PIVCVVLEGG	PGTLHTIDVD	IARSEIFMDQ	WLHPTMTAAL	ISNKPEFVKL	FLENGQLKT
TRPM2_Mmus	NP 612174	2 11RP M 2	PIVCVVLEGG	PGTLHTIYVD	IARSEIFTDQ	WLHPMMTAAL	ISNKPEFURL	FLENGRLKTL
TRPM3_Hsap	<u>NP</u> 001007	472_2_TRP_	PVVALIVE GG	PNVISIVLVD	IARSQIFIYQ	WLEQAMLDAL	VLDRVDFVKL	LIENGSMHRL
TRPM3_Mmus	<u>NP</u> 001030	317 <u>1</u> TRP_	PVVALIVEGG	PNVISIVLVD	IARSQIFIYQ	WLEQAMLDAL	VLDRVDFVKL	LIENGSMHR
TRPM3_Drer	_XE_694167	_4_PREDICT	PVVALIVEGG	PNVISIVLVD	IARSQIFIYQ	WLEQSMLDAL	VLDRVDFVKL	LIENGSMHRI
TRPM3_Dmel	001097	320_1_trpm	PVVCLVIEGG	TNTIRAVLVD	IARSEIFVYE	WLDEAMMQ	EHDRIDFVKL	LLENGSMKRI
TRPM3_Cele	NP 001122	506_1_GON_	PVVCVVLEGG	SCTIRSVLVD	TARSDVFAME	WLHNAMMEOL	THDRVDEWRL	LLEQGNMQR
TRPM3_Cele	NP 502111	_3_GTL_IPL	VCVVLEGGAF	TIRMVHADIA CINATUMDIA	RIEIFANEWL	HNAMIEALSN	DRIDFVHLLL	ENGSMORLEH
TRPMA Usan	NE 060106	2	DVILLEGGIS	FEMT TO TEVD	TAOSETERCO	WIEASIMDALIW	INDEDEE	TTSUCSTOR
TRPM4_Mmus	NE 780339	2 110P M 4	PVIJIJI	EKMLKRIEVD	TAOSELERGO	WLEASTMDAL	LNDRPEEVRL	LISHGSLGR
TRPM4 Drer	XE 003199	613 1 PRED	PVLNMLIAGD	TSMLEFLEVD	IAKSELFNGD	WLVDSMTDAL	ENNKPOFVRL	LIDNGNILR
TRPM4 Drer	xp 001339	981 4 PRED	PVLNMLIAGD	TSMLEFLEVD	IAKSELFNGD	WLKDSMTDAL	ENNKPOFVRL	LIDNGNISR
TRPM4 Drer	XP 002663	943 2 PRED	PVLNMLIAGD	TSMLEFLEVD	IAKSELFNGD	WLVDSMTDAL	ENNKPQFVRL	LIDSGNILR
TRPM4_Drer	_xp_003198	181_1_PRED	PVLCVLIAGD	ATMLERVDVD	IAKTELFNGH	WLEESMTDAL	VNDKPDFVRL	FVESGNILRL
TRPM5_Hsap	NP 055370	1 10 RP M 5	PVLCLLVNGD	PNTLERISVD	IAKSEIFNGE	WLEEVMVDAL	VSNKPEFVRL	FVDNGDVARL
TRPM5_Mmus	NP_064673	_2_1013PP_M_5	PVLCLLVNGD	PNTLERISVD	IAKSEIFNGE	WLEEVMTDAL	VSNKPDFVRL	FVDSGDMARI
TRPM5_Drer	NP_001121	711_1_TRP_	PVLCLLVHGE	PRILQKMYVD	IAKSEIFSGQ	WLEEVMMEAL	VNDKPDFVRL	FVDNGNIKRI
TRPM6_Hsap	NP 001170	781 1 TRP	PVVGLVVEGG	PNVILSVWVD	IAKKHILIYH	WLEQAMSDAL	VMDRVDFVKL	LIEYGNLHR
TRPM6_MMUS	NP 060143	_1_1000 M 0	PVVGLVMEGG	PNVILWVWMD	TAKKHILTIH	WLEQAMLDAL	VMDRVDFVKL	LIENGNLHRI
TRPM7_HSap	NE 001157	_3_ <u>4444</u> M_/	DUNITEECC	PNVILIVLVD	TAKNHVEVIQ	WIEQAMIDAL	VMDRVAFVKL	LIENGSMHR
TRPM7 Drer	NP 001025	232 1 TRP	PVVALTEEGG	PNVTLTVLVD	TAKDHVEVYO	LLEOAMLDAL	VMDRVEFVKL	LIENGSMHRI
TRPM8 Hsap	NP 076985	4 100 M 8	PTVCFAOGCG	KETLKAINLD	LANDETETNE	WLOEVMETAL	TKDRPKEVRL	FLENGNLEVI
TRPM8 Mmus	NP 599013	1 WRP M 8	PIVCFAOGG	RETLKAINLD	LASDEIFTNR	WLOEVMET	IKDRPKFVRL	FLENGNLOV
TRPA Hsap	NP 015628	2 TRP A 1P	LHIAVQGMNN	EVMKVLLEHG	YSRQLHINNN	KATPLHLAVQ	NGDLEMIKMC	LDNGQIDILA
TRPA_Mmus_	NP_808449_	1_TRP_A_1P	LHIAVHGMYN	EVIKVLTKNG	YSRETHINNH	KASPLHLAVQ	SGDLDMIKMC	LDNGHIDILA
TRPA_Drer_	NP_0010070	66_1_TRP_A	PIHMAVSLCK	NFVLEQLVEA	GLSIDAHIND	KCSSPLHLAV	RGGNLDIIKL	CIGYGKIDL
TRPA_Drer_	NP_0010070	67 <u>1</u> TRP_A	PLHLAVTKQY	NHLAEVLLEL	GVSSTLHIND	KKSTPLHLAV	RGGNIEVIKL	CILKGKVEL
TRPA_Dmel_	NP_648263_	4_iso_A1_i	PVHLATELNK	VKSLRVMGQR	GCTREEMISD	SGNVPLHSAV	HGGDIKAVEL	CLKSGKISL
TRPA_Cele_	NP 502249	3_TRPA 1PL	HYAAMKSNFS	ALHALIHDPV	EAIKALNNNK	KTPLRMAVEG	NHPETLKKIL	QMEKNSMMAV
TRPVI_Hsap	NP 061197	_4_ <u>10505</u> _V_1	SIFEAVAQNN	CODLESLLOT	DSLKELVNAT	DGQTALHIAI	ERRNMALVIL	LVENGDVQSL
TRPVI_Mmus	NP 001001	445_1_TRP_	SIFDAVAQSN	USEMOCI UKM	CDI KNETNAT	DGQTALHIAI	ERRNMALVIL	LVENGDVQSL
TREVI_DIEL	NE 057197	2 11 1 1 KP	RLFEAVSSCD	DEDIACIDES	CNDODIVNAT	DCUSALUTAT	EKRSHAFVOM	LVENCNUUSI
TRPV2_Mmis	NE 035836	2 110P V 2	RLESVVSROV	PEFLUCILDS	CNPOPLVNAT	DCHSALHTAT	FKRSLWCWKL	LVENGNVHSI
TRPV3 Hsap	NE 659505	1 0RP V 3	RIFAAVSEC	VEELVELLEN	DILGREINAT	EGOTALNIAI	ERROGDIAAL	LIAAGDVNAL
TRPV3 Mmus	NP 659567	2 URP V 3	RIFAAVSEC	VEELRELLEN	DILDRFINAT	EGOTALNIAI	ERROGDITAV	LIAAGDVNAL
TRPV4 Hsap	NP 067638	3 TRP V 4	ILFDIVSRCS	TADLDGLLRT	GNMREFINSR	DGQTALHIAI	ERRCKHYVEL	LVAQGDVHSL
TRPV4 Clup	NP 001120	787 1 TRP	ILFDIVSRGS	TTDLDGLLRT	GNMREFINSR	DGQTALHIAI	ERRCKHYVEL	LVAQGDVHSL
TRPV4_Mmus	NP 071300	2 TRP V 4	ILFDIVSRCS	TADLDGLLRT	GNMREFINSR	DGQTSLHIAI	ERRCKHYVEL	LVAQGDVHSL
TRPV4_Drer	NP 001036	195 1 TRP	MLFEAVSRAD	PRALDGLLQT	GNLREFINTR	DGQMALHIAI	ERRCKQYVEL	LVEKGDVHSL
TRPV5_Hsap	<u>NP</u> 062815	_2_11RP_V_5	PLLRASKEND	LSVLRQLLDN	LEAALVLMEP	EGQTALHIAV	VNQNVNLVRA	LLTRRSVSSF
TRPV5_Mmus	NE 001007	573 1 TRP	PLLRAAKEND	MCTLKKLQDN	LDAAIMLMEP	YGQTALHIAV	MNQNVNLVRA	LLARGSASSF
TRPV6_Hsap	061116	_2_0000_V_6	PLLLAAKDND	VQALNKLLDN	LEAAMVLMEP	EGQTALHIOV	VNQNMNLVRA	LLARRSVSSF
TRPV6_Mmus	071858	_2_ <u>14549</u> V_6	PLLLAAKEND	VQALSKLLDN	LEAAMVLMEP	EGQTALHIAV	INQNVNLVRA	MIKECOWAR
TRPMI1 USS	UU1001	4 1 micol ²	F DE SATKENN	WUTVOI II NT	TAPPHTETTO	DADDTE27	THOUSENLINE	AVDOVAT DA
TRPML1 Mmi	s NP 44440	7 1 micoli	KLMLOVVKTT.	VVTVOT.TT.NT	IAFRHI.FT.I.S	DSDDTFMA	YTOLYOATEV	AVDOYTLPAT

TRPML1 Dre	r XP 00133	6199 1 PRE	KLALQLLKII	IVTVQLVMNT	DSFKHLFLRV	ESQEPLCL	HTQVHEHIRY	AIDQYILSY
TRPML2_Hsa	p_NP_69499	1_2_mucoli	KLGLQILKIV	MVTTQLVRNT	VAFKHLFLKS	GDEDDYSCSV	YTDAYESIFF	AINQYQLKKV
TRPML2_Mmu	s_NP_08093	2_2_mucoli	KLGLQILKIV	MVTTQLVRNT	VAFKHLFLKS	GDEDDYSCSI	YTNTYESIFF	AIKQYHLKKV
TRPML2_Dre	r_NP_95744	2_1_mucoli	KLAVQIFKIF	MITLQLILNL	MAFKNLFLKS	GDEDEYSISI	YTRVFDSLHY	VLDQYQLQII
TRPML3_Hsa	p_NP_06076	8_8_mucoli	KLAIQILKIA	MVTIQLVLNT	IAFKHLFLKM	DMDDTYAV	YTDVYDQLIF	AVNQYQLYAI
TRPML3_Mmu	s_NP_59892	1_1_mucoli	KLAIQILKIA	MVTIQLVLNT	IAFKHLFLKM	DMDDTYAV	YTEVYDQIIF	AVTQYQLQAI
TRPML3_Dre	r_XP_00134	1182_4_PRE	KLFLQIVKIA	VVTVQLVSNL	LTFRHLFLKS	ENTNTYAI	YTDVYTHITH	IVQQFMLPCI
TRPML3_Dme	1_NP_00116	3472_1_CG4	KFVVQIVKIF	LVTMQLCLNR	FAFSHLFLRD	SAVGPFAL	YLEFFDTVQY	AVNGYNVSK
TRPML3_Dite	1_NP_64914	5_1_1SO_mu	KEVVQIVKIF	EVIMQLCLNR	FAFSHLFLRD	SAVGPFOL	VDCISENISE	AVNGINVSN
TRPMLS_CEI	HOND ND 00	4_3_COP_3_	DMGT AVEO	DIAMENNA	T DATIMIT COA	DEVEDUCHTM	VADNDAA	SUTI SELATO
TRPP PKD1	Mmile NP 03	8658 2 pol	VISPSVEOCA	DMINISASINH	LEATINHLOSA	NEVEDVESLT	T.SDNDA AVAM	SUTLOFIAR
TRPP PKD1	Drer XP 00	3197787 1	MSSAPTEHNT	PTVIRASLVI	LKATNLLGOV	NFLDPVODLV	LEPNPAAVNA	MTNMTSVNRK
TRPP PKD2	Hsap NP 00	0288 1 pol	FLDTPVSKTE	KTNFKTLS		-YENLLLGVP	RIROLRVRNG	SCSIPDLREI
TRPP PKD2	Mmus NP 03	2887 3 pol	FIDTPVSKTE	KTNFKTLS		-YENLLLGVP	RLRQLRVRNG	SCSIPDLREI
TRPP PKD2	Drer NP 00	1002310 1	FLDTPLSSCE	PTNFKSLS		-YENLLLGVP	RLRQLRVRNE	SCSVHDLREV
TRPP_PKD2_	Cele_NP_50	2838_3_PKD	FVASTGASC-	APAFGSCT		-YENRLLGEP	RIRMLKVTND	SCTVMSFQEI
TRPP_PKD2L	1_Hsap_NP	057196_2_P	FLHTPSDTG-	-VSFQAIS		-YENMLLGVP	RLRQLKVRND	SCVVHDFRDI
TRPP_PKD2L	1_Clup_XP_	543967_3_P	FLHTPSDTG-	-VSFQAIS		-YENLLLGVP	RLRQLRVRND	SCVVHDFRDI
TRPP_PKD2L	1_Mmus_NP_	852087_2_P	FLHTPSDSG-	-VSFQTIS		-YENLLLGAP	RLRQLRVRND	SCVVHDFRDI
TRPP_PKD2L	1_Drer_XP_	695404_2_P	FVNLPGSNG-	-MSFSSIG		-YENLLLGVP	RVRQLKVKQN	SCKVPDFKEI
TRPP_PKD2L	2_Hsap_NP_	055201_2_P	FLDTSVPGEE	RTNFKSIR		-YENILLGVP	RVRQLKVRNN	TCKVYSFQLM
TRPP_PKD2L	2_Mmus_NP_	001156476_	FVDTSLPDDE	RSSFRSIR		-YENVLLGIP	RVRQLRVRNN	TCKVYAFQLV
TRPP_PKD2L	2_Dmel_NP_	609561_2_P	NREMVVAPSV	TVGFEKLISD	SIQANMSFHE	GYENLLLGPP	RLRQIRVRKE	SCYVNAFIYF
CCa/050	LFLHACVHGS	KATLQELLLE	LAIAARVDHQ	DGSTPLHYAC	AAENDAVISL	LIEAGDMNNL	SIKSQHIYQD	LYTLFERMAK
Cca21/84	1	KI FOCCOOME	TAIDKGVDHS	DGNTPLHIAA	AADNHEVIEL	LIGDADINCE	AVLSNORIER	CDCDDVWAMC
CCa260897	I KDZFVNV	RLESGSSSTF	ESIT	IEN	KLLGRPRLRL	LRVRSDSCSI	HEFKEITDCI	GDSRDIWATG
Sucon24227	2 6530000	PESNYSBUTE	VSAFFAVMNT	VENSO	FARH	LLDGL TARCD	T.G	FUVVAHDAMP
Sycon24228	3SAOOPRE	SNYSEVTEVS	AFFAVMNTVE	NSO	EARHLL	DGLTARGDLG	FV	YVAHDAMRKM
Sycon 9763	1							
Ava16635 4	PIVRIVIDNT	LHVIEOVGVD	LAEONIFTEV	WLFOHYFAIL	ILNOVDFLEL	MLERNIDHNL	ERLYFVNLFI	WNAAIAGMHH
Ava9904 1	PAVCLLLDNS	IDGLRHTLPS	LALEKIFICK	WVQRIFFSAL	TTNNTGFVHR	MLESKYL	SOLYKROVFI	WTVAIRGMK
Ava7536_5		МА	FVSKYALDQS	TRKQVFHLNL	LETNRDLTR-			
Ava6620 1	-IRYALFYGS	REIVENIFNN	SDIQQRLIKE	ELFQRLMFAL	TKDEEYVEKK	IKGCKEFTSL	EVVKFLYIMV	WNAILYGVEQ
Cca31351	DIGVQEEVGQ	MDTARTFS		VEEKL	TSFDESFVKF	MNGNENVDVF	KEKGGLALEM	FTARLNVISL
Cca30979_3	DIVLKANGGS	GIAFSDVS		-PYLKLVGKP	RLKQFRVEKG	SCTVPILAEV	TRCYNSTWLI	WGTGVVDLDR
Ava26193 2	VLHAKNREGD	TPFELAVN		-KODAMAAYI.	AGPDYEVRRL	FTASGDPS		
				ngonaanna				
Ava26160_2								
Ava26160_2								
Ava26160_2 TRPC1_Hsap	AAHRNNRLDI	YRALLKELSL	VIKYNQKEFV	SQSNCQQF	TVUIHTPFMK	FIIHGASYFT	LLLLNLYRI	DYLLILWIIG
Ava26160_2 TRPC1_Hsap TRPC1_Mmus	AAHRNNRLDI HRNNRLDIYR	YRALLKELSL ALLKELSLVI	VIKYNQKEFV KYNQKEFVSQ	SQSNCQQFUN SNCQQFLNTV	TVMIHTPFMK WIHTPFMKFI	SIIHGASYFT IHGASYFTFL	BLLLLNLYRI LLLNLYRIDY	DYLLILWIIG LLILWIIGMI
Ava26160_2 TRPC1_Hsap TRPC1_Mmus TRPC1_Drer TRPC2_Mmus	AAHRNNRLDI HRNNRLDIYR AAHRNNRLDI ACOKDLBINT	YRALLKELSL ALLKELSLVI YRALLKELSL VAALTPDTAD	VIKYNQKEFV KYNQKEFVSQ VIKYNQKEFV KVNVNOKOFV	SQSNCQQFIN SNCQQFINTV AQSNCQQFIN AHDICOOVIS	TVWIHTPFMK WIHTPFMKFI TVWIHTPFIK SIMIKIPVIK	FIIHGASYFT IHGASYFTFL FIIHSASYFT	FLLLLNLYRI LLLNLYRIDY FLLLLNLYFI	DYLLILWIIG LLILWIIGMI DYLLILWIIG SILMIWYTG
Ava26160_2 TRPC1_Hsap TRPC1_Mmus TRPC1_Drer TRPC2_Mmus TRPC2_Drer	AAHRNNRLDI HRNNRLDIYR AAHRNNRLDI ACQKDLRINT ACQKDLRINT	YRALLKELSL ALLKELSLVI YRALLKELSL YAALLRRLAR YSALLRKLSK	VIKYNQKEFV KYNQKEFVSQ VIKYNQKEFV KVNYNQKQFV KVNYNOKOFV	SQSNCQQFIN SNCQQFINTV AQSNCQQFIN AHPICQQVIS AHPICQQVIS	TVWIHTPFMK WIHTPFMKFI TVWIHTPFIK SIWLKIPVLK SIWLKIPVLK	FIIHGASYFT IHGASYFTFL FIIHSASYFT FLLHSASYLW FILHSASYM	FLLLLNLYRI LLLNLYRIDY FLLLNLYFI FLIFLLGEVW FLIFLLGETL	DYLLILWIIG LLILWIIGMI DYLLILWIG SSLHMIWVTG HSFHMVWVVG
Ava26160_2 TRPC1_Hsap TRPC1_Mmus TRPC1_Drer TRPC2_Mmus TRPC2_Drer TRPC2_Drer	AAHRNNRLDI HRNNRLDIYR AAHRNNRLDI ACQKDLRINT ACQKDLRINT ACOKDLRINT	YRALLKELSL ALLKELSLVI YRALLKELSL YAALLRRLAR YSALLRKLSK YSALLRKLSK	VIKYNQKEFV KYNQKEFVSQ VIKYNQKEFV KVNYNQKQFV KVNYNQKQFV KVNYNOKOFV	SQSNCQQFIN SNCQQFINTV AQSNCQQFIN AHPICQQVIS AHPICQQVIS THPICQQVIS	TVWIHTPFMK WIHTPFMKFI TVWIHTPFIK SIWLKIPVLK SIWLKIPVIK SIWLKVPVIK	FIIHGASYFT IHGASYFTFL FIIHSASYFT FLLHSASYLW FLLHSASYMW FLLHSASYMW	FLLLLNLYRI LLLNLYRIDY FLLLLNLYFI FLIFLLGEVW FLITLLGEIL FLIALITEIL	DYLLILWIIG LLILWIIGMI DYLLILWIG SLHMIWVTG HSFHMVWVVG HSLHMYWVAG
Ava26160_2 TRPC1_Hsap TRPC1_Mmus TRPC1_Drer TRPC2_Mmus TRPC2_Drer TRPC2_Drer TRPC3_Hsap	AAHRNNRLDI HRNNRLDIYR AAHRNNRLDI ACQKDLRINT ACQKDLRINT AACQKDLRINT AAHCQKRINA	YRALLKELSL ALLKELSLVI YRALLKELSL YAALLRRLAR YSALLRKLSK YSALLRKLSK YTALLAKLAN	VIKYNQKEFV KYNQKEFVSQ VIKYNQKEFV KVNYNQKQFV KVNYNQKQFV KVNYNQKQFV IIKYEVKKFV	SQSNCQQFIN SNCQQFINTV AQSNCQQFIN AHPICQQVIS AHPICQQVIS AHPNCQQVIS	TVAIHTPFMK WIHTPFMKFI TVAIHTPFIK SIALKIPVIK SIALKIPVIK SIALKVPVIK TIALRSPFMK	EIIHGASYFT IHGASYFTFL EIIHSASYFT ELLHSASYTW ELLHSASYMW ELLHSASYMW EVAHAASFII	LLLLNLYRI LLLNLYRIDY LLLLNLYFI LIFLLGEVW LIFLLGEIL LIALLTEIL LGLLVFNWT	DYLLILWIIG LLILWIIGMI DYLLILWIIG SSHMNWVTG HSLHMVWVAG BMLIMVWVAG
Ava26160_2 TRPC1_Hsap TRPC1_Mmus TRPC2_Drer TRPC2_Drer TRPC2_Drer TRPC3_Hsap TRPC3_Hsap	AAHRNNRLDI HRNNRLDIYR AAHRNNRLDI ACQKDLRINT ACQKDLRINT AAHCQKRINA HCHKRINAYT	YRALLKELSL ALLKELSLVI YRALLKELSL YAALLRRLAR YSALLRKLSK YSALLRKLSK YTALLAKLANII	VIKYNQKEFV KYNQKEFVSQ VIKYNQKEFV KVNYNQKQFV KVNYNQKQFV KVNYNQKQFV IIKYEVKKFV KYEVKKFVAH	SQSNCQQFLNTV SNCQQFLNTV AQSNCQQFLNTV AHPICQQVIS AHPICQQVIS AHPICQQVIS AHPNCQQQL PNCQQQLTI	TVMIHTPFMK WIHTPFMKFI TVMIHTPFIK SIMLKIPVLK SIMLKIPVIK SIMLKVPVIK TIMLRSPFMK WLRSPFMKFV	JIHGASYFT IHGASYFTFL TIHSASYFT ELLHSASYFW ELLHSASYMW FLLHSASYMW EVAHAASFII AHAASFIIFL	SLLLNLYRI LLLNLYRIDY SLLLLNLYFI LIFLLGEVW SLITLLGEIL SLGLVFNWT GLLVFNWTEM	DYLLILWIIG LLILWIIGMI DYLLILWIIG SLHMIWVTG HSFHMVWVVG HSLHMVWVJG MLIMVWVLGM
Ava26160_2 TRPC1_Hsap TRPC1_Drer TRPC2_Drer TRPC2_Drer TRPC2_Drer TRPC3_Hsap TRPC3_Mmus TRPC4_Hsap	AAHRNNRLDI HRNNRLDIYR AAHRNNRLDI ACQKDLRINT ACQKDLRINT AAHCQKRINA HCHKRINAYT AAHTNNRLNI	YRALLKELSL ALLKELSLVI YRALLKELSL YAALLRRLAR YSALLRKLSK YTALLAKLAN ALLAKLANII YTALLQELSK	VIKYNQKEFV KYNQKEFVSQ VIKYNQKEFV KVNYNQKQFV KVNYNQKQFV KVNYNQKQFV IIKYEVKKFV KYEVKKFVAH VIKYRQKEFV	SQSNCQQFUN SNCQQFUNTV AQSNCQQFUN AHPICQQVIS AHPICQQVIS THPICQQVIS AHPNCQQQIL PNCQQQILTI AQPNCQQQIA	TVÅ IHTPFMK WIHTPFMKFI TVÅ IHTPFIK SI ÅLKIPVLK SI ÅLKIPVIK SI ÅLKVPVIK TI ÅLRSPFMK WLRSPFMKFV SRÅ IRKPFIK	SIIHGASYFT IHGASYFTFL SIIHSASYFT SLLHSASYLW SLLHSASYLW SVAHAASFII AHAASFIIFL SICHTASYLT	SLLLINLYRI LLLNLYRIDY SLIFLLGEVW SLIFLLGEVW SLIFLLGEIL SLIALLTEIL SLIGLVFNWT GLLVFNWTEM SLFILLLAIV	DYLLILWIIG LLILWIIGMI DYLLILWIIG SLHMIWVTG HSFHMVWVVG MLIMVWVLG LIMVWVLG WMILPWVLG
Ava26160_2 TRPC1_Hsap TRPC1_Drer TRPC2_Mmus TRPC2_Drer TRPC2_Drer TRPC3_Hsap TRPC3_Hsap TRPC4_Hsap TRPC4_Mmus	AAHRNNRLDI HENNRLDIYR AAHRNNRLDI ACQKDLRINT ACQKDLRINT ACQKDLRINT AAHCQKRINA HCHKRINAYT AAHTNNRLNI AAHTNNRLNI	YRALLKELSL ALLKELSLVI YRALLKELSL YSALLRKLSK YSALLRKLSK YTALLAKLAN ALLAKLANII YTALLQELSK YTALLQELSK	VIKYNQKEFV KYNQKEFVSQ VIKYNQKEFV KVNYNQKQFV KVNYNQKQFV IIKYEVKKFV IIKYEVKKFV VIKYRQKEFV VIKYRQKEFV	SQSNCQQFINTV AQSNCQQFINTV AQSNCQQFIN AHPICQQVIS AHPICQQVIS AHPNCQQQI PNCQQQIA AQPNCQQIA AQPNCQQIA	TVM IHTPFMK WHTPFMKFI TVM IHTPFIK SINLKIPVIK SINLKIPVIK SINLKVPVIK TINLRSPFMK WLRSPFMKFV SRNIRKPFIK SRNIRKPFIK	EIIHGASYFT HGASYFTFL HIHSASYFT LLHSASYFT SLLHSASYMW SLLHSASYMW VAHAASFII HAASFIIFL SICHTASYLT SICHTASYLT	ELLLNLYRI LLLNLYRIDY LLLLNLYFI LIFLLGEVW LITLLGEIL LGLLVFNWT GLLVFNWTEM LFILLLAIV SLFILLLAIV	DYLLILWIIG LLILWIIGMI DYLLILWIIG SSLHMIWVTG HSFHMVWVTG HSIHMVWVTG LIMVWVLGM WMILPWVTG WMILPWVTG WMILPWVTG
Ava26160_2 TRPC1_Hsap TRPC1_Drer TRPC2_Drer TRPC2_Drer TRPC2_Drer TRPC3_Mmus TRPC4_Hsap TRPC4_Hsap TRPC4_Mmus TRPC4_Drer	AAHRNNRLDI HRNNRLDIYR AAHRNNRLDIYR ACQKDLRINT ACQKDLRINT ACQKDLRINT AAHCQKRINA HCHKRINAYT AAHTNNRLNI AAHTNNRLNI AAHTNNRLNI	YRALLKEISL ALLKEISLVI YRALLKEISL YAALLKEISL YSALLRKISK YTALLAKLAN ALLAKLANII YTALLQEISK YTALLQEISK	VIKYNQKEFV KYNQKEFVSQ VIKYNQKEFV KVNYNQKQFV KVNYNQKQFV IIKYEVKKFV KYEVKKFVAH VIKYRQKEFV VIKYRQKEFV	SQSNCQQFIIN SNCQQFIINTV AQSNCQQFIIN AHPICQQVIS AHPICQQVIS AHPNCQQUII PNCQQUIITI AQPNCQQUIITI AQPNCQQIIIA AQPNCQQIIIA	TVNIHTPFMK WIHTPFMKFI TVNIHTPFIK SITLKIPVIK SITLKIPVIK SITLKVPVIK WIRSPFMKFV SRUIRKPFIK SRUIRKPFIK	EIIHGASYFTEI HIGASYFTFI EIIHSASYFT FLIHSASYIW FLIHSASYIW FVAHAASFII AHAASFIIFI FICHTASYLT FICHTASYLT	SLLLLNLYRI LLINLYRDY SLLFLLGEVW SLIFLLGEVW SLIFLLGEIL SLGLLVFNWT GLLVFNWTEM SLFLLLLAIV SLFLLLAIV	DYLLILWIIG LLILWIIGMI DYLLILWIIG SLHMIWVTG HSFHMVWVG MLIMVWVLG DMLIMVWVLG WMILPWVLG WMILPWVLG WMILPWVLG
Ava26160_2 TRPC1_Hsap TRPC1_Mmus TRPC2_Drer TRPC2_Drer TRPC2_Drer TRPC3_Hsap TRPC3_Hsap TRPC4_Hsap TRPC4_Mmus TRPC4_Drer TRPC4_Dren	AAHRNNRLDI HRNNRLDIYR AAHRNNRLDI ACQKDLRINT ACQKDLRINT ACQKDLRINT AAHCOKRINA HCHRRINAYT AAHTNNRLNI AAHTNNRLNI AAHTNNRLNI	YRALLKELSL ALLKELSLVI YRALLKELSL YSALLRKLSK YSALLRKLSK YTALLAKLAN YTALLQELSK YTALLQELSK YTALLQELSK YTALLQELSK	VIKYNQKEFV KYNQKEFVSQ VIKYNQKEFV KVNYNQKQFV KVNYNQKQFV KVNYNQKQFV IIKYEVKKFV VIKYRQKEFV VIKYRQKEFV VIKYRQKEFV	SQSNCQQFIN SNCQQFINTV AQSNCQQFINTV AHPICQQVIS THPICQQVIS THPICQQVIS AHPNCQQUI TI AQPNCQQUI AQPNCQQUI AQPNCQQUI AQPNCQQUI AAHSNVQQUIA	TVNIHTPFMK WIHTPFMKFI TVNIHTPFIK SITLKIPVIK SITLKIPVIK SITLKIPVIK SITLKIPVIK SRIIKKPFIK SRIIKKPFIK SITMRKPFIK SITMRKPFIK	SIIHGASYFT IHGASYFTFI SIIHSASYFT SILHSASYFT SILHSASYMW SILHSASYMW SULHSASYMW SVAHAASFII SICHTASYLT SICHTASYLT SICHTASYLT SICHTASYLT SICHSASYFT	SLILLNLYRI LLINLYRI SLIFLLGEVL SLIFLLGEVL SLIFLLGEIL SLGUVENWTEM SLFLLLAIV SLFLLLAIV SLFLLLAIV SLFLLLAIV	DYLLILWIG LLILWIGMI DYLLILWIGMI SSLHMIWVG SSLHMIWVVG HSLHWVWVG BMILPWVLG SWMILPWVLG SWMILPWVLG SWMILPWVLG SMMILPWVLG SMMILPWVLG
Ava26160_2 TRPC1_Hsap TRPC1_Mrus TRPC2_Drer TRPC2_Mrus TRPC2_Drer TRPC3_Hsap TRPC3_Hsap TRPC4_Hsap TRPC4_Isap TRPC4_Drer TRPC4_Drel TRPC4_Cele	AAHRNNRLDI HRNNRLDIYR AAHRNNRLDI ACQRDLRINT ACQRDLRINT ACQKDLRINT AAHCQKRINA HCHRRINAYT AAHTNNRLNI AAHTNNRLNI AAHTNNRLNI AAHRNNRINA AAHRNRINA	YRALLKELSL ALLKELSLVI YRALLKELSLVI YSALLRKLSK YSALLRKLSK YTALLAKLAN ALLAKLANI YTALLQELSK YTALLQELSK YTALLQELSK YTALLQELSS YTALLQELSS YTALLXRLSF	VIKYNQKEFV KYNQKEFVSQ VIKYNQKEFVSQ VIKYNQKQFV KVNYNQKQFV KVNYNQKQFV IIKYRQKEFV VIKYRQKEFV VIKYRQKEFV VIKYRQKEFV VIKYRQKEFV	SQSNCQQFLNV SNCQQFLNTV AQSNCQQFLNTV AHPTCQQVIS AHPTCQQVIS AHPCQQQU AHPNCQQUI AQPNCQQII AQPNCQQII AQPNCQQII AHSNCQQII AHSNCQQII	TVOIHTPFMK WIHTPFMKFI TVOIHTPFIK SIDLKIPVIK SIDLKIPVIK SIDLKIPVIK TIDLRSPFMK SRIIKKPFIK SRIIKKPFIK SIDMKKPFIK SIDMKKPFIK	SIIHGASYFT IHGASYFTI SIHSASYTW SLHSASYIW SLHSASYIW SLHSASYMW SVARAASFII AHAASFIITI SICHTASYLT SICHTASYLT SICHTASYLT SICHSASYTT SICHSASYTT	SLLLLNLYRI LLINLYRIDY SLLFLLCEVW SLIFILCEVW SLIFILCEV SLIALLTEIL SLGLUPNWTEM SLFLLLAIV SLFLLLAIV SLFLLLAIV SLFLLLAIV	DYLLILWIG LLILWIGMI DYLLILWIG SSLEMIWVTG HSEHNWVVG HSLHNWVLG MMILPWVLG DMMILPWVLG DMMILPWVLG SWMILPWVLG SWMILPWVLG SWLILAWVG SCAIFLWVLG
Ava26160_2 TRPC1_Hsap TRPC1_Mrus TRPC2_Mrus TRPC2_Mrus TRPC2_Drer TRPC2_Drer TRPC3_Mrus TRPC4_Hsap TRPC4_Mrus TRPC4_Mrus TRPC4_Mrus TRPC4_Mrus TRPC4_Mrus	AAHRNNRLDI HRNNRLDIYR AAHRNNRLDIYR ACQKDLRINT ACQKDLRINT ACQKDLRINT ACQKDLRINT ACQKDLRINT ACQKDLRINT ACQKDLRINT AAHCONGINA AAHTNNRLNI AAHTNNRLNIYT	YRALLKELSL ALLKELSLVI YRALLRKLSK YSALLRKLSK YSALLRKLSK YTALLAKLAN YTALLQELSK YTALLQELSK YTALLQELSK YTALLQELSK YTALLQELSK YTALLRUSF ALLKRLSF	VIKYNQKEFV KYNQKEFVSQ VIKYNQKEFV KVNYNQKQFV KVNYNQKQFV KVNYNQKQFV KYEVKKFVAH VIKYRQKEFV VIKYRQKEFV VIKYRQKEFV UIKYRQKEFVQ LIKLRQKFFV XYHQKEFVQ	SQSNCQOFIN SNCQOFINTV AQSNCQOFIN AHPICQOVIS AHPICQOVIS THITCQOVIS AHPNCQOOIL PNCQQUITI AQPNCQOILA AQPNCQOILA AHPNCQOILA AHPNCQOILA	TVUIHTPFMK WIHTPFMKFI TVUHTPFIK SIGLKIPVIK SIGLKIPVIK SIGLKIPVIK SIGLKIPVIK SIGLKIPVIK SIGLKIPFIK SIGLKIPFIK SIGLKIPFIK SIGLKIPFIK WIKKFFIK	SIIHGASYFT IHGASYFTFL SIIHSASYFT SLLHSASYMW SLLHSASYMW SLLHSASYMW SLHSASYMW SVAHAASFII AHAASFIIFL SICHTASYLT SICHTASYLT SICHTASYLT SLSHSGSYIF CHTASYLTFL	SLILLNLYRI LLLNLYRIDY SLIFILGEVW SLIFILGEVW SLIFILGEVW SLIFILLGEV SLGLUVFNWT GLLVFNWTEM SLFILLLAIV SLFILLLAIV SLFILLLAIV SLFILLLAIV SLFILLLAVV	DYLLILWIGMI DYLLILWIGMI DYLLILWIG BSLEMIWWTG HSFHWWVVG HSEHWWVVG DMILPWVLG DMILPWVLG DWMILPWVLG DWMILPWVLG DWMILPWVLG DWMILPWVLG MILDWVLGFI
Ava26160_2 TRPC1_Hsap TRPC1_Mrus TRPC2_Mrus TRPC2_Drer TRPC2_Drer TRPC3_Isap TRPC4_Hsap TRPC4_Hsap TRPC4_Hsap TRPC4_Mrus TRPC4_Mrus TRPC4_Drel TRPC4_Celle TRPC5_Mrus	AAHRNNRLDI HRNNRLDIYR AAHRNNRLDIYR ACQKDLRINT ACQKDLRINT ACQKRLRINT AAHCQKRINA HCHKRINAYI AAHTNNRINI AAHTNNRINI AAHTNNRINI AAHRNNRINA AAHRNNRINA	YRALLKELSL ALLKELSIVI YRALLKELSIVI YSALLRKLSK YSALLRKLSK YTALLAKLANI ALLAKLANI YTALLQELSK YTALLQELSK YTALLRKLSF YYALLKRLSF ALLKELSKVI ALLKELSKVI	VIKYNQKEFV VIKYNQKEFVQ VIKYNQKEFV KVNINQKQFV KVNINQKQFV IIKYEVKKFV IIKYEVKKFV VIKYNQKEFV VIKYNQKEFV VIKYNQKEFV IIGLSQRFFV KYHQKEFVAQ KYHQKEFVAQ	SQSNCQQFIN SNCQQFINTV AQSNCQQFIN AHPICQQVIS HHPICQQVIS HHPICQQVIS AHPNCQQUITI AQPNCQQUITI AQPNCQQUITI AQPNCQQUITI AQPNCQQUIA AHSNVQQIIA AHSNVQQIIA AHSNVQQIIATI PNCQQUIATI	TVOIHTPFMK WIHTPFMKFI SICLKIPVIK SICLKIPVIK SICLKIPVIK SICLKIPVIK SICLKIPVIK SICLKIPVIK SICLKIPVIK SICLKIPVIK SICLKIPVIK SICLKIPVIK SICLKIPVIK SICLKIPVIK SICLKIPVIK SICLKIPVIK	JIIHGASYFTI IHGASYFTI JIHSASYTW JLHSASYTW JLHSASYTW JLHSASYTW JVAHAASYIT IGHTASYIT JICHTASYIT JICHTASYIT JICHTASYIT JCHTASYITFL CHTASYITFL CHTASYITFL	LLLINLYRI LLINLYRIDY LLILLNLYFI SLIFLLGEFU SLIFLLGEFU SLIFLLGEFU SLIFLLLAFV SLFLLLAFV SLFLLLAFV SLFLLLAFV SLFLLLAFV SLFLLLAVVEW	DYLLILWIGMI DYLLILWIGMI DYLLILWIGMI SSLHMIWVG SSLHMIWVVG HSLEMVWVG MILIMVWUG DMILIPWVLG DWMILPWVLG SWMILPWVLG SCALFLWVLG MILPWVLGFI MILPWVLGFI
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Ava26160_2 TRPC1_Hsap TRPC1_Muus TRPC2_Drer TRPC2_Muus TRPC2_Muus TRPC4_Hsap TRPC4_Hsap TRPC4_Hsap TRPC4_Muus TRPC4_Drer TRPC4_Drel TRPC5_Hsap TRPC4_Cele TRPC5_Hsap TRPC6_Hsap TRPC6_Hsap TRPC6_Cele	AAHRNNRLDI HRNNRLDIYR AAHRNNRLDI ACQRDLRINT ACQRDLRINT ACQRDLRINT ACQRDLRINT AAHCQRRINA HCHRRINAY AAHTNNRLNI AAHTNNRLNI AAHTNNRLNIYT HCQERINAYT HCQERINAYT HCQERINAYT HCQERINAYT HCQERINAYT	YRALLKELSL ALLKELSLVI YRALLKELSLVI YSALLRKLSK YSALLRKLSK YTALLAKLAN ALLAKLANI YTALLQELSK YTALLQELSK YTALLQELSKVI ALLKELSKVI ALLKELSKVI ALLAVLANII YAALLASLAN YTALLAVLANII YAALLASLAN YTALLAVLANII	VIKYNQKEFVS VIKYNQKEFVSQ VIKYNQKGFV KVNYNQKQFV KVNYNQKQFV KVNYNQKQFV IIKYEVKKFVAH VIKYNQKEFV VIKYNQKEFV VIKYNQKEFVA KYHQKEFVAQ KYHQKEFVAQ KYEVKKFVAH KYEVKKFVAH IIKYELKKFV IIKYELKKFV	SQSNCQOFEN SNCQOFENTV AQSNCQOFENTV AHPTCQOVIS AHPTCQOVIS THFICQOVIS AHPNCQOFE ANDROQOFEA AQPNCQOFEA AQPNCQOFEA ALSNVQOFEA AHSNVQOFEA AHSNVQOFEA SHSNCQOFES PNCQQLEATL PNCQQLEATL PNCQQUEST PNCQQUEST PNCQQUEST AHPNCQQOFE SHPRCQOFEA	TVOIHTPFMK WIHTPFMKFI TVOIHTPFMKFI SICLKIPVIK SICLKIPVIK SICLKIPVIK SICLKIPVIK SICLKYPIK SRUTKKPFIK SIMKKPFIK DIGAKKPFIK WIKKPFIKFI WIKKPFIKFI WIKKPFIKFI WIKKPFIKFI SICHSOFPKKY SICHSOFPKKY SICHSOFPKKY SICHSOFPKKY	SIIHGASYFT IHGASYFTI SIHSASYFW SLHSASYIW SLHSASYMW SVARAASFII HAAASFIIFI SICHTASYLT SICHTASYLT SICHTASYLT SICHTASYLTFI AHAASFTIFI AHAASFTIFI AHAASFTIFI SVARAASFTI SVARAASFTI SVARAASFTI SVARAASFTI	LLILNLYRI LLINLYRIY SLIFLLCEVW SLIFILCEVW SLITILCEU SLIALLTEIL SLGLVENWT GLIVENWT SLFILLLAIV SLFILLLAIV SLFILLLAIV SLFILLLAVU MLLLAVVEW GLIVMNWMEM GLIVMNWMEM SLGLIVNNWM	DYLLILWIGMI DYLLILWIGMI DYLLILWIGMI DYLLILWIG HSEHMVWVG HSEHMVWVG HSEHMVWVG DMLILWVLG DMMILPWVLG DMMILPWVLG SMMILPWVLG GAIFLWVIG MILPWVLGFI LIISWVIGMI LIISWVIGMI LIISWVIG MMLISVVIG SMLIISVVIG SMLIISVVIG
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Ava26160_2 TRPC1_Hsap TRPC1_Mrus TRPC2_Drer TRPC2_Drer TRPC2_Drer TRPC3_Hsap TRPC3_Hsap TRPC4_Hsap TRPC4_Drer TRPC4_Cele TRPC6_Hsap TRPC6_Mrus TRPC6_Drer TRPC6_Drer TRPC6_Orer TRPC6_Ores TRPC7_Hsap TRPC7_Mrus TRPC7_Dren TRPC7_Dren TRPC7_Dren	AAHRNNRLDI HRNNRLDIYR AAHRNNRLDI ACQRDLRINT ACQRDLRINT ACQKDLRINT AACQKDLRINT AAHCQKRINA HCHRRINAYT AAHTNNRLNI AAHTNNRLNIYT HTNNRLNIYT HTNNRLNIYT HCQERINAYT HCQERINAYT ASHCHERINA ASHCHERINA AAHCQERMNAYT AAHCQERMNAYT AAHCCERMNA	YRALLKELSL ALLKELSLVI YRALLKELSK YSALLRKLSK YSALLRKLSK YSALLRKLSK YTALLQELSK YTALLQELSK YTALLQELSK YTALLQELSK YTALLQELSK ALLKELSKVI ALLKELSKVI ALLAVLANII ALLAVLANII ALLAVLANIA YTALLAVIAN FSALLQRLAF STALLQRIAF	VIKYNQKEFVSQ VIKYNQKEFVSQ VIKYNQKGFV KVNYNQKQFV KVNYNQKQFV KVNYNQKQFV XYYNKKFVAH VIKYRQKEFV VIKYRQKEFV VIKYRQKEFVAQ KYHQKEFVAQ KYHQKEFVAQ KYHQKEFVAQ IIKYELKKFV IIKYELKKFV IIKYELKKFV IIKYELKKFV IIKYELKKFV IIKYELKKFV IIKYELKKFV IIKYELKKFV IIKYEVKFVAH IIKYEVKKFVAH IIKYEVKKFVAH	SQSNCQQFLNTV AQSNCQQFLNTV AQSNCQQFLNTV ALPICQQVIS AHPICQQVIS AHPICQQVIS AHPNCQQULTI AQPNCQQIJ AQPNCQQIJ ALPNCQQIJ ALPNCQQIJATL PNCQQLLATL PNCQQLLATL PNCQQULSI PNCQQULSI SHPNCQQUISI SHPNCQQUISI SHPNCQQUISI AHPNCQQUISI AHPNCQQUISI AHPNCQQUISI AHPNCQQUISI AHPNCQQUISI AHPNCQQUISI AHPNCQQUISI AHPNCQQUISI AHPNCQQUISI AHPNCQQUISI AHPNCQQUISI	TVUIHTPFMK WIHTPFMKFI TVIHTPFIK SITLKIPVLK SITLKIPVLK SITLKIPVLK SITLKIPVLK SITLKSPFMK WIRSPFMKFV WIRGPFMFFV WIRGPFMKFV WIRGPFMKFV WIRGPFMKFV SIWMGGPFLK SIWMSSPFMK WIRSPFMKFV WIRSPFMKFV TLTLRSPFMK WIRSPFMKFV TLTLRSPFMK	IIHGASYFT IHGASYFTI IHGASYFTI ILHSASYMW ILHSASYMW ILHSASYMW VAHAASFI ICHTASYLT ICHTASYLT ICHTASYLT ICHTASYLT ICHTASYLTFI AHAASFTIFI AHAASFTIFI AHAASFTIFI SVAHAASFTI IVAHAASFTI ISVAHASFTI IAHAVSFTI IAHAVSFTIFI AHAVSFTIFI AHAVSFTIFI INTINIY	SLILLNIYRI LLINLYRIDY SLIFILGEVW SLIFILGEVW SLIFILGEVW SLIFILGEV SLIFILLGEV SLIFILLAIV SLIFILLAIV SLIFILLAIV SLIFILLAIV SLIFILMAII MILLAVVEW MILLAVVEW SLIFILMAII SLILLIVNWM SLGLIVMNWMEM SLGLIVMNWM SLGLIVMNWMEM SLGLIVMNWMEM SLGLIVMNWMEM SLGLIVMNWMEM	DYLLILWIG LLILWIGMI DYLLILWIG SLEMIWVTG HSEHNVWVG HSEHNVWVG ILWVVG DMILPWVLG DMILPWVLG DMILPWVLG DWILPWVLG DWLILAWVG DLILSWVIG MILPWVLGFI LIISWVIG DMLISWVG DMLISWVG DMLISWVG DMLISWVG DMLIMKVVLG DMLIMKVLGMI DMLIMKVLGMI
Ava26160_2 TRPC1_Hsap TRPC1_Drer TRPC2_Drer TRPC2_Drer TRPC2_Drer TRPC3_Hsap TRPC4_Hsap TRPC4_Hsap TRPC4_Mmus TRPC4_Orer TRPC4_Oren TRPC5_Mmus TRPC6_Hsap TRPC5_Mmus TRPC6_Drer TRPC6_Drer TRPC6_Drer TRPC6_Oren TRPC6_Cele TRPC7_Mmus TRPC6_Cele TRPC7_Mmus TRPC7_TRP3_	AAHRNNRLDI HRNNRLDI YR AAHRNNRLDI XC QKDLRINT ACQKDLRINT AACQKRLRIN AACQKRLNA HCHRINAINI AAHTNNRLNI AAHTNNRLNI AAHTNNRLNI AAHTNNRLNI HTNNRLNI YT HTNNRLNI YT HTNNRLNI YT HCORRINAYT ASHCHERINA ASHCHERINA ASHCHERINA AAHQERMNA AAHCKERNNA AAMGFHISV	YRALLKELSL ALLKELSL YAALLRELSL YAALLRELSK YSALLRKLSK YTALLQELSK YTALLQELSK YTALLQELSK YTALLQELSK YTALLQELSK YTALLRELSKVI ALLKELSKVI ALLKELSKVI ALLKUANII YTALLAVLANI YTALLAVLANI YTALLAVLANI YTALLAVLAN YTALLAVLAN YTALLAVLAN YTALLAVLAN YTALLAVLAN YTALLAVLAN YTALLAVLAN YTALLAVLAN YTALLAVIN	VIKYNQKEFVQ VIKYNQKEFVQ VIKYNQKEFV KVNINQKQFV KVNINQKQFV IIKYEVKKFV IIKYEVKKFV VIKYNQKEFV VIKYNQKEFV VIKYNQKEFV VIKYNQKEFVAQ KYHQKEFVAQ KYHQKEFVAQ KYHQKEFVAQ IIKYELKKFV IIKYELKKFV IIKYELKKFV IIKYELKKFV IIKYEVKKFVAH IIKYEVKKFVAH IIKYEVKKFVAH	SQSNCQOFIN SNCQOFINTV AQSNCQOFINTV AQSNCQOFINTV ALPICQOVIS AHPICQOVIS THITCQOVIS HIPICQOUIS PNCQQUITI AQPNCQOIIA AQPNCQOIIA ALPNCQOIIA PNCQQUISI PNCQQUISI PNCQQUISI PNCQQUISI SHPNCQQUISI SHPNCQQUI SHPNCQQUI SHPNCQQUITSI AHPNCQQUI SHPNCQQUITSI AHPNCQQUITSI AHPNCQQUITSI AHPNCQQUITSI AHPNCQQUITA AHPNCQQUITA AHPNCQQUITA AHPNCQQUITA	TVUIHTPFMK WIHTPFMKFI TVUHTPFMKFI TVUHTPFIK SIGLKIPVIK SIGLKIPVIK SIGLKIPVIK SIGLKIPVIK SIGLKIPVIK SIGLKIPFIK SIGLKIPFIK SIGLKIPFIK WIKKPFIKFI WIKKPFIKFI WIKKPFIKFI WIKKPFIKFI SIGLGFPMKFV SIGLGFPMKFV SIGLGFPMKFV TULSSPFMK ELGNKVPIK	SIIHGASYFT IHGASYFTI SIHSASYFW SLHSASYMW SLHSASYMW SLHSASYMW SLHSASYMW SLHSASYMW SLHSASYMW SICHTASYLT SICHTASYLT SICHTASYLT SICHTASYLTFI CHTASYLTFI CHTASYLTFI CHTASYTFI AHAASFTIFI SYAHAASFTI SYAHAASFTI SYAHASFTI SYAHASFTI SYAHASFTI SYAHASFTI SYAHASFTI SYAHASFTI SYAHASFTI SYAHASFTI SYAHASFTI SYAHASFTI SYAHASFTI SYAHASFTI SYAHASFTI SYAHASFTI SYAHASSTIFI SYAHASTIFI SYAHASSTIFI S	LLILNLYRI LLINLYRIDY LLILLNLYFI LIFILGEVW SLIFILGEVW SLIFILGEVW GLVFNWTEM SLFILLAIV SLFILLLAIV SLFILLLAIV SLFILLAVEW MILLAVVEW MILLAVVEW CLIVINNMEM GLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE SLGLIVNNWE	DYLLILWIGMI DYLLILWIIGMI DYLLILWIIGMI DYLLILWIIG HSFHMVWVG HSFHMVWVG LIMVWVLGMI DMILPWVLG DMILPWVLG DMILPWVLG DMILPWVLGFI MILPWVLGFI LIISWVIG DMLIISWVIG SLIPTWVIG DMLIISWVIG DMLIISWVIG DMLIMKWVLGMI DMLIMKWVLGMI
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Ava26160_2 TRPC1_Hsap TRPC1_Muss TRPC2_Drer TRPC2_Drer TRPC2_Muss TRPC4_Hsap TRPC4_Hsap TRPC4_Hsap TRPC4_Hsap TRPC4_dol TRPC4_Drer TRPC4_Drer TRPC4_Dref TRPC5_Hsap TRPC6_Hsap TRPC6_Hsap TRPC6_Drer TRPC6_Drer TRPC6_Drer TRPC6_Drer TRPC6_Drer TRPC6_Drer TRPC6_Dref TRPC7_Hsap TRPC7_Hsap TRPC7_Muss TRPC7_Muss TRPC7_Muss TRPC7_Muss TRPC7_Muss TRPC7_Muss TRPC7_Muss TRPC7_Muss TRPM1_Hsap TRPM2_Muss TRPM3_Isap TRPM3_Drer TRPM3_Dref TRPM3_Cele TRPM3_Cele TRPM3_Cele	AAHRNNRLDI HRNNRLDI XA ACQRDLRIMT ACQRDLRIMT ACQRDLRIMT ACQRDLRIMT ACQRDLRIMT ACQRDLRIMT AAHCQRINA HCHRRINAI AAHCQRINAI AAHTNNRLNI AAHTNNRLNI AAHTNNRLNI HTNNRLNIYT HCQERINAYT HCQERINAYT HCQERINAYT HCQERINAYT HCQERINAYT HCQERINAYT AAHCHERINA ASHCHERINA ASHCHERINA AAHCQERMNA HCQERMNAY AAHCQERMNA HCQERMNAY AAHCGEHMAY EELINTELMY EELINTELMY EELINTELMY EELINTELMY EELINTELMY EELINTELMY EELINTELMY EELINTELMI EELINTELMI	YRALLKELSL ALLKELSL YAALLRKLSK YSALLRKLSK YSALLRKLSK YSALLRKLSK YTALLAKLAN ALLAKLANI YTALLQELSK YTALLQELSK YTALLQELSK YTALLKRLSF YYALLKRLSF ALLKELSKVI ALLAVLANII YAALLASLAN YTALLAVLANI YTALYNN YTALYNN YTALYNN YTALYNN YTALYNN YTALYNN YLANI YTALANI YTALAVLANI YTALAVLANI YTALYNN YTALYNN YTALYNN YLANI YTALANI YLANI YTALA	VIKYNQKEFVS VIKYNQKEFVSQ VIKYNQKGFV KVNYNQKQFV KVNYNQKQFV IIKYEVKKFV VIKYRQKEFV VIKYRQKEFV VIKYRQKEFV UIKYRQKEFVA IIQLSQKRFV IIQLSQKFV IIQLSQKFV IIQLSQKFV IIKYEKKFVAH KYEVKKFVAH KYEVKKFVAH IIKYELKKFV IIKYELKKFV IIKYELKKFV KIENEQKEVI KIENEQKEVI KIENEQKEVI KIENEQKEVI KIENEQKEVI KIENEQKEVI KIENEQKEVI EVAAKHRDFI	SQSNCQOFEN SNCQOFEN ADSICOOFIN ALPICQOVIS AHPICQOVIS THPICQOVIS THPICQOVIS AHPNCQOFIL PNCQOLIAT PNCQOLIATL PNCQOLIATL PNCQQLIATL PNCQQLIATL PNCQQLIATL SHPNCQOFIL AHPNCQOFIL AHPNCQOFIL SHPRCQOFIL AHPNCQOFIL AHP	TVOILHTPFMK WIHTPFMKTI TVOILHTPFIK SIGLKIPVIK SIGLKIPVIK SIGLKIPVIK SIGLKIPVIK SIGLKYPIK SRITKPFIK SRITKPFIK SIGNFPIK SIGNFFIKFI WIKKPFIKFI WIKKPFIKFI WIKKPFIKFI WIKKPFIKFI WIKKPFIKFI WIKKPFIKFI WIKKPFIKFI WIKSPFMK SIGNFFIKFI WIKSPFMK ELNKVPIK EVNTIPIVK DMVNAPIVK DV	JIIHGASYFT IHGASYFTI JIHGASYFTI JIHSASYTW JLHSASYMW JLHSASYMW JLHSASYMW JLHSASYMW JLHSASYMW JCHTASYLT JICHTASYLT JICHTASYLT JICHTASYLT JICHTASYLTFI AHAASFTIFI AHAASFTIFI YVAHAASFTIFI YVAHAVSFTIFI YVAHAVSFTIFI HAYSFTIFI YVAHAVSFTIFI HMSILTSHIY YVCHIVSHIF WFYTISYLG FWFYTISYLG WFYTISYLG WFYTIAYIG WFYTIAYIG WHTILAYG WHSTIFII WSATISFII WSATISFII WMSTIFII	LLILNLYRI LLINLYRIDY LLINLYRIDY LIFILCEVW LIFILCEVW LIFILCEVW LGILVFNWTG LFILLAIV SLGILVNNWM SLGILVNNWM SLGILVNNWM SLGILVNNWM SLGILVNWY STILLFNVVC SLCFAYWC SLCFAYWC SLCFAYWC SLGFAYWC SLMFFNTY SLMFSFTWO SLFFTTVI SLTFFTTVI	DYLLILWIG LLIWIGMI DYLLILWIG SLEMIWVTG HSEHWVVG HSEHWVVG HSEHWVVG USLEMIVVG SMILPWVG SMILPWVG SMILPWVG SMILPWVG SMILPWVG SMILSWVG SLIPWVG SLIPWVG SLIPWVG SLIPWVG SLIPWVG SLIPWVG SLIPWVG SLIPWVG SLIPWVG SLIPWVG SLIPWVG SUFI SUFIG SUFIWVG SUFI SUFIWVG SUFIWVG SUFIWVG SUFI SUFI SUFI SUFI SUFI SUFI SUFI SUFI

TDDMA Hear	NOT VENDT T	WCAATDUMAD	THOADADADEE	AODOUOS		MONTO VIT T	DITTERDUCT	
TRPM4_Hsap	AQLISADILL	WSAALKVMAR	LMQADARAFF	AQDGVQSIIII	QKWGAPVII	IGNVVSILL	LLLFSRVSL	SLLLIF WAFT
TRPM4_Mmus	AQLISADLLI	WSAALKVMAR	LMQADARAFF	AQDGVQSIIIT	QKWWGAPVTA	LGNVVSILL	SLLLFAHVVS	SLLLIFWAFT
TRPM4_Drer	EKLYNSSLFI	WTAGLVELSK	QIAADARIFF	SHDGVQS	QINWYAPVTS	GIGNLLMYFL	BLFLYAYVVS	DYVLYFWVFT
TRPM4_Drer	EILYNSCLFI	WTAGLLELSK	QIAADARIFF	SHDGVQSIIIS	QIOWYAPVTS	FIGNLLMYFL	PLFLYAYVVS	DYVLYFWVFT
TRPM4_Drer	EKLYNSCLFI	WTAGLLELSK	QIAADAQIFF	SHDGVQS	QIWWYAPVTS	FIGNLLMYFL	FLFLYAYVVS	DYVLYFWVFT
TRPM4_Drer	ESLYSSSLFI	WSAGLRELSK	LTSADARLFF	SHDGVQT	EIWWFAPVTS	FLGNVLMYFL	PLFLFAYVPL	DLVLYFWVFT
TRPM5 Hsap	QELYRSDLFL	WAAALKEMSH	LTEADAKAFF	AHDGVQAFUT	RIWWGAPVTV	FLGNVVMYFA	PLFLFTYVGP	VTLYFWVFT
TRPM5 Mmus	QQLYHSDLFL	WAAAIKEMSH	LTEADAKAFF	AHDGVQAFIT	KIWWGAPVTV	FLGNVVMYFA	FLFLFTYVGS	DVTLYFWVFT
TRPM5 Drer	QELYCSDLFL	WAAGMKEMAH	LTLAEAKCFF	AHDGVQAMT	KV WWSAPVTV	DMGNVIMYFA	BLILFSYVAA	DIILYFWVFT
TRPM6 Hsap	EELYNTDLLV	WKAAYRAMAH	EVSGGLRPFV	SHTCTOMOUT	DMOYSAPIVK	WFYTMAYLA	JIMLETYTVO	WLVSIYIFT
TRPM6 Mmus	EELYNTDLLV	WKAAYRAMAR	EVSCGLEPEV	SHSCTOMMET	DMOYSAPEVK	WFYTMAYLA	DT.MT.FTYTVH	WLVITTTTT
TREPM7 Hear	FELVNTELLT	WKAAVDOMAV	FUCCDI DDFV	AUTOTOMIUS	DMAYHADTUK	WENTLAXIC	DI MI VTENNO	WINTYTAVIET
TRENT Mous	FET VNTET T	WKAAVDCMAV	FUCCDI DDFV	AUTOTOMIUS	DMAYHADTVK	INFINIT AVI C	DI MI VTENNO	WINTYTAVIET
TREM7 Pullus	BELINIEBUI	WINAAIKSMAI	EVSSKERFFV	AUTOTOM	DIMINIALITY	WENTLATING		
TRPM/ Drer	EELINTELLV	WKAALKSLGD	EVSSRLRPFV	AHTCTOMINS	DMWIHAPIVK	SWENTLETIG	LMLISEVPQ	WVVILIIFT
TRPM8_Hsap	TELFSNALFI	WAAALKTLAK	VVEATDQHFI	AQPGVQNETS	KQWFTSPFVV	SWNVVFYIA	BLLLFAYVPP	PLATASTALA
TRPM8_Mmus	TELFSTALFI	WAAALKTLAK	VVEATDQHFI	AQPGVQNFUS	KQMFTSPFVV	SWNVVFYIA	BLLLFAYVTP	DIILYALVFV
TRPA_Hsap_	TASASHDKVV	NKAHLALHNK	VQNNRIELLN	HPVCKEYIJIM	KWLAYGFRAH	MMNLGSYCLG	LIPMTILTCM	ILVFLSSIFG
TRPA_Mmus_	TASASHDKVV	NKAHIALHNK	VQHNRIELLN	HPVCREY	KWCAYGFRAH	MMNLGSYCLG	LIPMTLLICM	ILVFLSSIFG
TRPA_Drer_	ATSCGAHVKV	VNKAHEAVHN	AVNFNRVNLL	THPVCKKYLE	MKSAYGIKA	HLLNMTVYAL	GVFPLTYLSS	MLLVLAMNMY
TRPA Drer	ASSCSAHAQV	VNDNHEAVRN	EVRYNRLELL	IHPLSRKYLE	MKOTAYGSKV	HFLNLAIYLL	GLLPLTYLVC	IIMVIVMNVY
TRPA Dmel	AASRSGHTRV	VNVMDYAIYY	KVTHGRVELL	AHPLSQKYLQ	MKONSYGKYF	HLANLLIYSI	BLVFVTIYFC	AVVIVVYILL
TRPA Cele	THDSHDATTD	EKDIACENDA	DAEKLHLLNH	PLSKALLKYK	WNRLGRPMYY	ALFMYLVFI	VSLTQYVWKI	IIQTLAVCQI
TRPV1 Hsap	AACTNOKIGV	LTCKLEVIAY	SETPNRHDML	LVEPLNR	DKODREVKRI	TYFNFLVYCL	YMIIFTMATG	DILSVLGGVY
TRPV1 Mmus	AACTNOKIGV	LTCKLEVIAY	SETPNRHDML	LVEPLNRU	DKODREVKRI	YFNFFVYCL	YMIIFTTATG	PILSVSGGVY
TRPV1 Drer	AACTNOKLCL	FTYKLETVVY	CET DNRLEMI.	OTEPLNPTTE	FKODOFAHRM	DIFNETVYVT	VIETETASTC	HTISTTCAFY
TREVI Diei	AACTNOKIET	FROFIETTAF	GETFINKLEML	VIEDINK	THE DITTOR	THE NET CUT T	VMETETAVTC	HTTTTCCTV
TRPV2_Hsap	AACIKQKIEI	FSCELEIIAF	INCOMPANY	VLEPENK	AKW-DLLIPK	TELNELCNLI	IMPIPIAVIG	HILILLGGII
TRPV2_Mmus	AACTKQKIEI	FSWKLEITAF	HKSPHRHRMV	VLEPLNKI	EKW-DRLIPR	DEFNEACYLV	YMIIFTIVLG	HILIFIGGIA
TRPV3_Hsap	AACTNQKAEI	LTTDLEITVY	NNIDNRHEML	TLEPLHTONH	MKOKKFAKHM	FLSFCFYFF	YNITLTLVLG	RMFVLIWAMC
TRPV3_Mmus	AACTNQKAEI	LTTDLEIIVY	NNIDNRHEML	TLEPLHT	TKOKKFAKYM	FLSFCFYFF	YNITLTLVLG	RMFVLIWATC
TRPV4_Hsap	AACTNQKIGI	FTCELEILVY	NKIENRHEML	AVEPINE	DKWRKFGAVS	TINVVSYLC	AMVIFTLTAG	DVITLFTGVL
TRPV4_Clup	AACTNQKIGV	FTCELEILVY	NKIENRHEML	AVEPINE	DKWRKFGAVS	FYINVVSYLC	AMVIFTLTAG	DIITLFTGVL
TRPV4 Mmus	AACTNQKIGV	FTCELEILVY	NKIENRHEML	AVEPINE	DKORKFGAVS	TYINVVSYLC	AMVIFTLTAG	VITLFTGVL
TRPV4 Drer	AACTNOKIGV	FTCELEILVY	NKIENRHEML	AVEPINE	AKOKFAAVT	YISVFSYLV	TMIIFTLVGG	DIITVGSGLF
TRPV5 Hsap	AACVNSNTVM	FSWELELVVS	SDKREAROIL	EOTPVKEVS	FKONKYGRPY	CILAALYLL	YMICFTTCVG	LVSIVGAVI
TRPV5 Mmils	AACVGSNTVM	FSWELELVVS	SKKKEABOTT	EOTPVKEUVS	LKOKKYGOPY	CLLGALYTE	YMVCFTTCVG	TVTVTGAVT
TRPV6 Hsap	AACVNSNTVM	ESSELELITT	TKKREAROTL	DOTPVKEUVS	LKOKRYGRPY	CMLGATYLL	YTTCFTMCVG	DIVTVIGATI
TREVO_HSup	ANCUCONTUM	FCCDIFITU	THUUCHINGTH	DOTTOWNER	INARDYCODY	DOM CATVUT	VIICEMOUC	TUCTUCAUT
TREVO Pillus	AACVGSNI VH	FORTETTAT	CURREARDIT	ET TOWNOUT	LIGHT VORUN	DOLMITYI	VICTERVCIC	TTOLICATI
TRPV6_Drer	AACVGNNV	FSRELEIIAT	SHKKEARRIL	ELTPVRQUIT	LAWNLIGHT	RSLMVIILV	TISTFTVCIG	BIISLIGAII
TRPMLI_HSa	CORVYHNLTL	K	-ITFONKAHS	GRIPISLET-	VFQHG	DNSFRLLFDV	VVILTCSLLC	ASTTKGLTTL
TRPMLI_Mmu	CORYYHNLTL	K	-ITFDNKAHS	GRIPIRLET-	VSRHG	DNSFRLLFDV	VVILTCSLLC	ASLLRGFLLF
TRPML1_Dre	CQRYFKNITL	N	-ILFDNKAHS	GKVKLSLUN-	VSGHG	DSYARVAFDV	LVAVVCGLLC	GSILKGIMLY
TRPML2_Hsa	CKQHYKFFRL	E	-IIFDNKAHS	GKIKIYFDS-	IFGSTQK	NAQYVLVFDA	VIVICLALC	TSIVLALRLF
TRPML2_Mmu	CKQHYKFFRL	D	-ITFDNTAHS	GKIKIYLNS-	ISGSTQR	STHYLLVFDV	FVIMICLALC	TSIVLALRLF
TRPML2_Dre	CKKSYKFFEL	D	-IDFDNSCHS	GKMKLSLGF-	ISGTAQK	NTLYLLIFDG	FVILVCLILC	TSIILAVKLF
TRPML3 Hsa	CQHFYKNLTL	D	-ITFDNKAHS	GRIKISLDN-	VSGSIQK	NTHYMMIFDA	FVILTCLVLC	ISVIRGLQLF
TRPML3 Mmu	CQHFYRNLSL	D	-ITFDNKAHS	GRIKISLDN-	VSGSIQK	NTHYMMIFDA	VILTCLALC	ASVIRGLQLF
TRPML3 Dre	COOFYHNFTL	Н	-IQFDNKAHS	GRILVDLDN-	MTGASAR	NMYMMVLFDA	VVILILSTLC	ISVKAGVLLF
TRPML3 Dme	CLONYRDVEV	N	-ITFNNRDHD	GOMLISLDA-	IS-DANF	DSMLRSVLNI	VLLTCALLC	TALWRAYLLF
TRPML3 Dme	CLONYRDVEV	N	-TTENNEDHD	COMULISIDA -	TS-DANE	DSMLRSVLNT	DVLLTCALLC	TALWRAYLLE
TREPMI 3 Col	TTOPTOFTOF	D	TKEDNODUT	COMPARE ST-	KCVCWSF	DTLICCTDI	WITICILLC	CALTRAULTY
TREMES_CEL	STOANUDTIM	DWAADCCANC	AVWHDNKCIS	DAWET OUVIN	AMOCDAVETE	TERREDAVCT	VTIDILCIDDC	-WCTTTEAW
TRPP_PRDI_	SIQANVRILM	RWAARSSANS	AVWIDNKGLS	PAWFLQHVIN	AVTSRAVELL	LIRISPAVGL	VILKLIS	-VCLLLFAVH
TRPP_PKDI_	SIQANVRILM	RQAAQSSHNP	VVWHDNKGLS	PAWFLQHIIN	AVWSRAVEVE	LTRISPAVGL	VTLRLTS	-VCLLLFALY
TRPP_PKD1_	AACLQLRILM	LTGAKAVLPP	ALWHDNKGLS	PAWLLQYVIA	AVWIRALFLE	SLININTDL	SFLLLT	-LILLVLLIY
TRPP_PKD2_	KECYDVGSSH	WATGYLDLSR	TREE	TAAQVASUKK	NVOTRATFID	SVYNANINL	CVVRLLVAC	DIIFCFFIFY
TRPP_PKD2_	KECYDVGSSH	WASGYLDLSR	TREE	TAAQLAGURR	NEWTRAAFID	SVYNANINL	ECVVRLLAAC	DIIFCFFIIY
TRPP_PKD2_	YDCYNVESSY	WSTGYQDLSR	TREK	SANQLQEIKN	NLWTRAVFLD	SIYNGNVNL	FCIVRLLVMC	VSFCLFVLY
TRPP_PKD2_	KECFANNLKT	VASGVQRLPV	AGSTE	AQSAIATIKA	NR	BALYNANINL	FCVVKLLFIF	GIFCGFILY
TRPP_PKD2L	LSCYDVGFSH	WTSGYLDLPG	SRQG	SAEALRANQE	GLWTRVVFID	SVYNANINL	FCVLRLVVGC	DVIFCVFIFY
TRPP PKD2L	LSCYDVGSSH	WTSGYLDLPG	SRQA	SAEALQDLQE	GLWTRVVFID	SVYNANINL	FCVLRLVVGC	DIIFCIFIVY
TRPP PKD2L	LNCYDVGSSH	WTSGYLDLPG	SRQA	SAEALQGLQE	GLTRVVFID	SVYNANINL	FCILRLVVGC	DVVFCVFIFY
TRPP PKD2L	SDCFDVGSSH	WTTGYODLTT	TRDE	SAALLED	NLOTRVLFID	TAYNANINL	CVIRLVVGC	DIVFCVFILY
TRPP_PKD2L	SECYGKSPWH	WGVNIFTLSK	SKSE	TKNKFIDURL	NSOTRVIFID	SLYNANVNL	CITRLVASC	DITECTELEV
TRPP PKD21	SDCYSKAPWH	WGVDIVTT.SK	SKSF	TKAKEVDUPT	NNOTRAVETO	SLYNANVNT	CITRLIASC	PVIECTELEV
TREE DED21	NTCVAACTDT	WAFTTUNIDY	DKDB	NUKTINDUKD	THEST CIVE	INT ENENTDT	DOSTRI TAVI	VIEWVIMUTV
Coo7050	FIGTORNET	ATDAVOVETN		VDVEAEAVIA	ET TI I MUEVT	EWITT AVUT A	TINEEVET	DECHEVETDI
Cca/UJU	FISIGKVKLT	ALDAVQIELN	DOWINEDITT	VEAPAIVA	FULLEMVERL	LIVIETEVES	LINEFVILV	NEGRE IFTRL
CCd21/84	MISDRCKKET	AUVOATK	LOWINEPIII	TIANVISISV	EAAPPTTTTTTT	TTATE TEARC	PTPOFIKSE,	ALLERE IF SGL
CCa260897	THLLPES	RRQAARV	IAELKDNMWS	RVVFLDFTVY	NANINLFCVV	KLIVFCEVVF	CLFIIYYIVE	PVLEIYLHRM
S⊥a36613_6								
Sycon24227	KMNKKLECKD	KELQRHNVVR	MLIYNKWVEY	GERMAILNEG	LYLLFMLCVT	SVLEVISLL	GVMVNLYDEA	KECYREKTAY
Sycon24228	NKKLECKDKE	LQRHNVVRML	IYNKWVEYGE	RMAILNLGLY	LLFMLCVTFS	VLEVISLLGV	MVNLYDEAKE	CYREKTAYVT
Sycon9763_								
Ava16635_4	HVTGRCMTFL	SHPCVQSLLD	EQWYTSPSIK	FITYVLAFIL	YLTLYSFV	EWIFIVWSLT	YILEEVRQLF	AGNSAYLNDR
Ava9904 1	KIKGDCKHFI	AHPLIQDYAN	QKWYNAPKIK	YWLHFLSH	YTILFTIVII	ELIVWVWTFT	IIMEECSQLL	HEKRGYISSA
Ava7536_5	-VQFKRFELV	LHPIFKKLLE	MKWRKYGFLF	AIIQTVFYFT	FWSLFTIH	-FVCIAFLVF	QIVEEFTEIF	QNNPYTADF
Ava6620 1	ESTAGKOLFF	THEGVOGHUR	NVWYISPSTT	FYIHSLVYFT	FLVLYTVHTF	DVIYFLYMVA	YILDEVFOIE	DKTFEYLSSG
Cca31351	EF	SHTPMEKMVT	SVW		FWLIPPTP	-VIYEKWVKT	JLGDMVEKHT	YEG
Cca30070 2	NF	ACETTECTOR	SPWTPAUTUO	FTUYNANENT	FSTGLITURG	FARVETEV	VTVKATDATU	KUKCAFTUED
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Ava26193_2 Ava26160_2	-ARSGYEEIV	YHDTVRLLLR	MKWKKFGRFR	FLLQFLTY <mark>I</mark> L	HILAMSVSLC	EIVYYVFLLW	NLAAEIFQMF	RHRLRYLLDW
TRPC1 Hsap	MIWSDIKRLW	YEGEDFLEES	RNQLSFVMNS	YLATFALKV	VATLVAEGLF	AFANVLSYLR	LFFMYTTSSI	LCPLQISMGQ
TRPC1_Mmus	WSDIKRLWYE	GEDFLEESRN	QLSFVMNSLY	LATFALKVVA	TLVAEGLFAF	ANVLSYLRLF	FMYTTSSILG	PLQISMGQML
TRPC1_Drer TRPC2_Mmus	FLWFECKEVW	IEGRSYLLDW	NFLDVVILS	YLATFALKI	LLOFLAEVLF	AVTSMLSFTR	LAYILPAHES	LEPLQISMGQ LETLOISIGK
TRPC2_Drer	FFWFECKEVW	IEGRSYFLDW	WNCLDVMVLS	MYLASFALRL	VIQFISEVLF	AVTSMLSFTR	LAYILPAHES	l <mark>g</mark> tlqisigk
TRPC2_Drer	FFWFECKEVW	IEGKSYFLDL	NILDMMVLS	MYLASFTLRI	LIQLIAETLF	AVTSMLSFTR	LAYILPAHES	LGTLQISMGR
TRPC3_Mmus	WSECKELWLE	GREYIVQLWN	VLDFGMLSIF	IAAFTARFLA	QIISEGLYAI	AVVLSFSRIA	YILPANESFG	PLQISLGRTV
TRPC4_Hsap	FIWGEIKQMW	DGGQDYIHDW	WNLMDFVMNS	TYLATISLKI	VATLVAEALF	AIANIFSSLR	LISLFTANSH	LGPLQISLGR
TRPC4_Mmus TRPC4_Drer	FIWTEIKOMW	DGGQDYIHDW	WNLMDFVMNS	IYLATISLKI	VATLVAEALF	AIANIFSSLR	LISLFTANSH	LGPLQISLGR
TRPC4_Dmel	LIWSEVKQLW	DVGQEYLNDM	W <mark>NVIDFVTNS</mark>	I YVATVALRV	VSMLISEGLF	SAANIFSSLK	LVYIFSVNPH	l <mark>g</mark> plqvslsr
TRPC4_Cele	LIWVEIKQLW	ECGYNYCRNL GTEYTHDWWN	MNILDFITNS	TYLCTTALRV	VATLLSECFF	ATANIFSSLK	LVHIFTVSPH SLFTANSHLG	LCPLKISLGR PLOISLGBML
TRPC5_Mmus	WGEIKEMWDG	GTEYIHDWWN	LMDFAMNSLY	LATISLKIVA	TLIAEALFAI	SNILSSLRLI	SLFTANSHLG	PLQISLGRML
TRPC6_Hsap	WAECKEIWTQ	GKEYLFELWN	MLDFGMLAIF	AASFIARFMA	QIISEGLYAI	AVVLSFSRIA	YILPANESFG	PLQISLGRTV
TRPC6 Drer	MIWAECKEIWTQ	SOGREYLLEP	MLDFGMLAIF	IFVASFISRI	MAQLVSEGLY	AIAVVLSFSRIA	IAYILPANES	FEPLOISLGR
TRPC6_Drer	MIWAECKEIW	SLGREYLLEP	WNLLDFGMLA	IFVTSFIARF	MAQLISEGLY	AIAVVLSFSR	IAYILPANES	F <mark>G</mark> PLQISLGR
TRPC6_Cele TRPC7_Hsap	MIWSEIKQLW	EEGKRYMRQW	WNWLDFLMIC	IFVASFTARF	SAMLVAEALF	AVGNVFSFAR	IIYLFQTNPY	LCPLQISLGC FCPLOISLGR
TRPC7_Mmus	WSECKEIWEE	GREYVLHLWN	LLDFGMLSIF	VASFTARFMA	QIISEGLYAI	AVVLSFSRIA	YILPANESFG	PLQISLGRTV
TRPC7_Drer	MIWTECKEVW	ADGREYIMHL	NVLDFGMLS	VFVASFTARL	MAQLISEGLY	SIAVVLSFSR	IAYVLPANES	FGPLQISLGR
TRPN Cele	NLVSELSTVG	GGSG	LGIVKVLILV	ISAMAIAVHV	LALYLKNQLF	AFALLFAFVE	YLDFLTVHHL	FGPWAIIIGD
TRPN_Drer_	MLVSELTFPG	ERTG	LAWIRLLLLG	FSAAALLCHL	LALFARNVLL	AVAMTLGFIQ	LLEFLTFHHL	FGPWAIIIRD
TRPM1_Hsap TRPM1_Mmus	LALEKIREIL	MSEKVWLQEY	INITDLVAIS	TFMIGAILRL MFMVGAILRL	QNMGYGRVIY OSMGYGRVIY	CVDIIFWYIR	VLDIFGVNKY	LEPYVMMIGK
TRPM2_Hsap	LVCEEMRQLF	YDPALYFSDF	WNKLDVGAIL	FVAGLTCRL	IPLYPGRVIL	SLDFILFCLR	LMHIFTISKT	LGPKIIIVKR
TRPM2_Mmus	LVCEETRQLF	YDPSLYFSDF	WNKLDVGAIL	LFIVGLTCRL	IPLYPGRIIL	SLDFIMFCLR	LMHIFTISKT	LGPKIIIVKR
TRPM3 Mmus	LGIEKMREIL	MSEKVWLQEY	WNVTDLIAIL	LFSVGMILRL	QDRSDGRVII	CVNIIYWYIR	LLDIFGVNKY	LGPYVMMIGK
TRPM3_Drer	NGIEKMREIL	MSEKVWLQEY	WNITDLMAIL	IFSIGMVLRL	QDMSYGRVIY	CVNIIYWYIR	LLDIFGVNKY	L <mark>G</mark> PYVMMIGK
TRPM3_Dme1 TRPM3_Cele	LGFEKVREII	SSESVWAWNM MSDRTYVCSF	NPCDGAAII	EFVIGLAFRF FYIVGFFMRC	REMDIGRVIY FGVAYGRVIL	CVDSIYWYLR ACDSVLWTMK	ILNILGVNKY LLDYMSVHPK	LGPLVTMMGK LGPYVTMAGK
TRPM3_Cele	LEIGRKIMMD	TRVFFFQYRN	GLLAFGLLTY	IAYFIRLSP	KTLGRILIIC	NSVIWSLKLV	DYLSVQQGLG	PYINIVAEMI
TRPM3_Cele	VEHIRKLMTS	EKVFYAKWYN	IWTSAALLFF	CELLGYGCRI	HSWGRVLLSF	SNVLFYMKIF	EYLSVHPLLG	PYIQMAAKMV
TRPM4_Mmus	LLCEELRQGL	GGGHLYLSDT	WNQCDLLALT	CFLLGVGCRL	TPFDLGRTVL	CLDFMIFTLR	LLHIFTVNKQ	LGPKIVIVSK
TRPM4_Drer	LVCEEIQEAS	IAGIVYAQDM	WNKFDVLAIC	FIAGLCCRM	FSFNMGRGIL	CVDYMVFTLR	LIHIFAIHKE	LGPKIIILGK
TRPM4_Drer TRPM4_Drer	LVCOEIOEAF	IAGFVIAQDM	WNKFDVLAIS	IFITGLCCRM	FSFNMGRGIL	CVDYMVFTLR	LIYIFAIHKE	LGPKIIILGK
TRPM4_Drer	LACEEIRQSF	FVGKVYIQDI	WNKCDITALG	I FVLGLLCRM	FPYNFGRAVM	CVDYTVFTLR	LIHIFAVHKQ	LGPKIIIVGK
TRPM5_Hsap TRPM5_Mmus	LVLEEIRQGF	FTDTLYVGDN FTDTLYVEDN	*NKCDMVAIF	DFIVGVTCRM DFIVGVTCRM	LPFEAGRTVL VPFEAGRTVL	AMDFMVFTLR	LIHIFAIHKQ	LEPKIIVVER
TRPM5_Drer	LVLEEIRQSF	FTDKLYVEDN	WNKCDMVAIS	LFVVGLSCRM	AMYEAGRTVL	ALDFMVFTLR	LIHIFAIHKQ	L <mark>G</mark> PKIIIVER
TRPM6_Hsap	NAIEVVREIC	ISEKVWISEY	WNLTETVAIG	LFSAGFVLRW	GDHTAGRLIY	CIDIIFWFSR	LLDFFAVNQH	AGPYVTMIAK
TRPM7_Hsap	YAIEKVREIF	MSEKVWFSDY	FNISDTIAII	SFFIGFGLRF	GAFVAGRLIY	CLNIIFWYVR	LLDFLAVNQQ	AGPYVMMIGK
TRPM7_Mmus	YAIEKVREVF	MSEKVWFSDY	FNVSDTIAII	SFFVGFGLRF	GAFVAGRLIY	CLNIIFWYVR	LLDFLAVNQQ	AGPYVMMIGK
TRPM7_Drer TRPM8_Hsap	LFCDEVRQWY	VNGVNYFTDL	NISDFLAIL	YFIAGIVFRL	HSLYSGRVIF	CLDYIIFTLR	LIHIFTVSRN	LGPKIIMLQR
TRPM8_Mmus	LFCDEVRQWY	MNGVNYFTDL	WNVMDTLGLF	YFIAGIVFRL	HSLYSGRVIF	CLDYIIFTLR	LIHIFTVSRN	L <mark>G</mark> PKI IMLQR
TRPA_Hsap_ TRPA_Mmus	YCKEAGQIFQ	QKRNYFMDIS OKRNYFLDYN	NVLEWIIYTT	GIIFVLPL SIIFVLPL	HLQWQCGA YMOWOCGA	IAVYFYWMNF	LLYLQRFENC	GIFIVMLEVI
TRPA_Drer_	AVGKEILQMF	QQRLNYLRDL	SNYMDWAAAI	CALLFVVPL-	SWHWQAG	ALAALTSWLN	LLLYLQRFER	ICIYVVMFRE
TRPA_Drer_	SICKEVVQLA	QQRVNYFTDF	SNPADWSAAI	SALVFVVPM-	TWQWEAG	AYAILTSWIG	FLLYFQRFER	IGIYVVMFNG
TRPA_Cele_	LVECFQLFQR	KFAYLVNWEN	WIDCFIYSTA	TITVYDFSEC	QNWQWILAAL	CIFFGWINLL	FMIRKMPRFG	IFVVMFVDIV
TRPV1_Hsap	FFFRGIQYFL	QRRTLFVDSY	SEMLFFLQSL	FMLATVVLYF	SHLKEYVASM	VFSLALGWTN	MLYYTRGFQQ	MGIYAVMIEK
TRPV1 Drer	FFIRGLIDMV	RKRSLIIDGY	TDQLFFVQGL	FLASVVLYC	YGQYEYLAFL	VICLALSWIN	LLYFSRGSKN	LGIYNVMIQK
TRPV2_Hsap	LLVGQLWYFW	RRHISFIDSY	FEILFLFQAL	LTVVSQVLCF	LAIEWYLPLL	VSALVLGWLN	LLYYTRGFQH	TGIYSVMIQK
TRPV2_Mmus TRPV3_Hsap	LLLGQLWYFW	RRRISFMDSY LLRSILSDAW	FEILFLVQAL	ITVLSQVLRF	VETEWYLPLL FAYKEYLACL	VSSLVLGWLN	LLYYTRGFOH	TGIYSVMIQK
TRPV3_Mmus	ISVKEGIAIF	LLRSILSDAW	FHFVFFVQAV	LVILSVFLYL	FAYKEYLACL	VLAMALGWAN	MLYYTRGFQS	MGMYSVMIQK
TRPV4_Hsap	FFFTNIKDLF	MKKSLFIDGS	FQLLYFIYSV	IVIVSAALYL	AGIEAYLAVM	VFALVLGWMN	ALYFTRGLKL	TGTYSIMIQK
TRPV4_Mmus	FFFTSIKDLF	TKKSLFVDGS	FQLLYFIYSV	LVVVSAALYL	AGIEAYLAVM	VFALVLGWMN	ALYFTRGLKL	TGTYSIMIQK
TRPV4_Drer	FFVTNIKDLF	LKKSIFVDGS	FQLLYFIYSV	IVVGSAALYL	SGIEAYVSVM	VFALTLGGMN	PLYFTRGLKL	TGTYSIMIQK
TRPV5_Hsap TRPV5_Mmus	ILLLEIPDIF	RVGKTILGGP	FHVIIITYAS	IVLLTMAMRL	TNTNGEVVPM	SFALVLGWCS	VMYFARGFOM	LGPFTIMIQK
TRPV6_Hsap	ILLVEVPDIF	RMGQTILGGP	FHVLIITYAF	MVLVTMVMRL	ISASGEVVPM	SFALVLGWCN	VMYFARGFOM	LGPFTIMIQK
TRPV6 Mmus	ILLVEIPDIF	REGOTILGGP	FHVIIITYAF	MVLVTMVMRL	TNVDGEVVPM	SFALVLGWCN	VMYFARGFOM	LEPTIMIOK

TRPV6_Drer	ILLIEIPGIL	AVGQTALGGL	FHVTLISYAL	VLLLCGLRV	TGIQGELIPM	AFSLILGWFS	LVYFARGFEM	LEPYVIVIQK
TRPML1_Hsa	MWRQRGRVIS	LWERLEFVNG	<b>YILLVTSDV</b>	TISGTIMKI	GIYDVCSILL	GTSTLLVWVG	VIRYLTFFHN	YNILIATLRV
TRPML1_Mmu	MWRRRGREIS	LWERLEFVNG	*YILLVTSDV	TISGTVMKI	GIYDVCSILL	GTSTLLVWVG	VIRYLTFFHK	YNILIATLRV
TRPMLI_Dre	FRVSLGRSVS	LGDRLEFING	WYLLLIISDV	TILASFIKI	AIYDVCSILM	GTSTLLVWVG	VIRTESFEOR	YNILIVTLRA
TRPML2_Hsa	FLEKYKRPVC	CIDOWEFING	AVULVIISDL	MTTTGSTLKM	EIYDLCSIFL	GTSTLLVWVG	VIRILGIFUA	YNVLILTMQA
TRPML2 Dro	CLONVNHKVC	FEDOREFING	OVVIVITSDU	MATTGSTLKM	ETTDVCSTLL.	GTSTLMVWVG	VIRILGIEVE	VNVLTLTMRA
TRPML3 Hsa	FLLHYKKEVS	VSDOMEFVNG	VIMIISDI	TIIGSILKM	EIYDVCSILL	GTSTMLVWLG	VIRYLGFFAK	YNLLILTLOA
TRPML3 Mmu	FLLHYKKEVS	ASDOMEFING	WYIMIIISDI	TIVGSVLKM	EIYDVCSILL	GTSTMLVWLG	VIRYLGFFAK	YNLLILTLQA
TRPML3 Dre	SLRRYRKCVS	LSERLEFING	WYLLIIVSDV	TISGSVLKI	VIYDLCSILL	GTGTMLVWIG	VLRYMGXXCV	VQILIITLRV
TRPML3_Dme	FRSQFGKELS	FDGRLEFVNF	WYIMIIFNDV	LIIGSALKE	QIWDTCSLFL	GIGNLLVWFG	VLRYLGFFKT	YNVVILTLKK
TRPML3_Dme	FRSQFGKELS	FDGRLEFVNF	WYIMIIFNDV	LIIGSALKE	QIWDTCSLFL	GIGNLLVWFG	VLRYLGFFKT	YNVVILTLKK
TRPML3_Cel	FENVLKNKIT	VTDQLDFLNL	<b>YVMIVVNDA</b>	IIIGTVAKI	SIFTLTSIFL	GMGALLVYVG	VLRYFGFFSQ	YNILMLTLKR
TRPP_PKD1_	FAVAEARTWH	REGRWRVLRL	GAWARWLLVA	TAATALVRL	AQSSAARGLA	ASLLFLLLVK	AAQQLRFVRQ	WSVFGKTLCR
TRPP_PKD1_	FSMAEVQTWR	KDGCACTARP	DTWARCLLVI	TAATGLVRL	AQGSVARGLA	ASLLFLLLVK	AAQQLRFVRQ	WSVFGRTLCR
TRPP PKD2	VVVFFTLFTP	THELEVERSE	NCLOWIT	SWATCINI	VROTOFNNTA	AUTVEEVWIK	LEKEINENET	MSOLSTTMSP
TRPP_PKD2_	YVVEETLETR	THRUSYFRSF	NCLOVVIVV	SVVAMVINI	YROTOFNNTS	AVMVFLVWTK	LEKEINENRT	MSOLSTIMSR
TRPP PKD2	YLVEEALEIR	LHRLRYFKSL	NCLDVLIVA	SVPAIIMNI	CROVHFNNLA	AIIVFLSWVK	LFKFINFNKT	MNQLSTTMSR
TRPP PKD2	FIFEELFAIG	RHRLHYLTQF	NLVDVVLLG	FSVATIILSV	NRENSYLNIK	ACVVFVAWVK	VFKFISVNKT	MSQLSSTLTR
TRPP_PKD2L	YVVEEILELH	IHRLRYLSSI	WNILDLVVIL	SIVAVGFHI	FRQTQYNNMN	AVNLFFAWIK	IFKYISFNKT	MTQLSSTLAR
TRPP_PKD2L	YMVEEILELH	IHRLHYLSSI	WNILDLVVIM	<b>I</b> SIVAVGFHI	FRQTQYNNMN	AVNLFFAWIK	IFKYISFNKT	MTQLSSTLAR
TRPP_PKD2L	YVVEEILEIH	LHRLRYLSSV	WNILDLVVIL	ISIVAVGFHI	FRQTQYNNMN	AVNLFFAWIK	IFKYISFNKT	MTQLSSTLAR
TRPP_PKD2L	YIVEEILEFR	IHKLSHFTSI	*NILDIVVIL	AVVAIVFSA	FRQTQYNNMN	AVNLFFAWIK	IFKYISFNKT	MTQLTSTLAR
TRPP_PKD2L	FTTQEVKKIK	EFKSAYFKSI	NWLELLLL	CFVAVSFNT	YYHIYYNNII	AITIFFAWIK	IFKFISFNKT	MSQLSSTLSR
TRPP_PKD2L	VELEKKVN	LERSAIFRSV	INTIDCATLL	CFLAVSFIA	ICHIIINNVI WHNTTYWDMM	ATTIFFAMIK	TEXELORNET	NSQLSSTLSR
Cca7050	CHETNCIIT	METTEVIVEL	TVLBLTSVLL	AVASTMSCIP	T.LOYLEVHEV	TCPTOKSVCK	WONMACEW	TLETVIMAEA
Cca21784	DYKMDTSMLV	LEVI.FETT.BA	TALRGSCYFL	GPATVLACVR	VLRYLSWHPV	TGPVORATSK	IVEETLIFIV	TLMVFLTAFA
Cca260897	KYFKNVWNCL	DILMILIAIV	CMAFNIYROV	QFNHMSAVLI	FFAWFKLFKY	ISFNKTMNQL	SSTLSKCAKD	VLGFCVMFFI
Sla36613 6			YCYLL	AFVVFMSTLK	FINMLKFNRR	MGLLTETIKA	SVADMKGFAI	TFFIYVMAFA
Sycon24227	VTDGNNYLQV	GSILLILAIV	PLRWLDQDAQ	WHVACFAYIF	VCLRILQLIS	VTRMVGIYLQ	ILTRILKDIS	RFVIIFGIFL
Sycon24228	DGNNYLQVGS	ILLILAIVPL	RWLDQDAQWH	VACFAYIFVC	LRILQLISVT	RMVGIYLQIL	TRILKDISRF	VIIFGIFLLT
Sycon9763_								SF
Ava16635_4	WNQFDTAFAL	FFIMGTVLRL	IPLSYSRHMY	AVIGFVLFFR	LLQFLVIIKD	SGPFVYMVFR	MLKNLGSFLI	LALIFLLAYG
Ava9904_1	WNILDLALIL	LFLLAFSIKL	GCSAWVHRVY	ALIILILYIR	IFQYLIMSAY	FGVIVLIIFA	LAEEVVYFVF	VLLLSMIGFG
AVa/536_5	WNYIDWLAYI	LMVATIVSHV	ADADWHARIG	VVNIIVLWFR	FLKILRPFEF	IGWEITIVIY	LKADIIRFAI	FLMTLLIPYS
Ava0020_1	WNILDIAIAI	GEVAIISLEI	SVNVIARLVF	TEMT DTCWTH	AUVETHOENT	FCOLUCETE	AFKKUDI KEDV	DEFUENTWUV
Cca30979 3	WNWVEMLVIV	LGWTTTGVYI	ARDTIYLTGS	SLVVFFSFLK	ILRLLOFNRR	MLLLAGTLRR	SGMOLIAFAI	AFLIVMVAFA
Ava26193 2	YNYLDMGAIV	CSLLIIPLRF	SQENAQWFFA	AIAYLLNVMR	GYKFAVVLRT	TGAYVEIIGS	ILYDIVPFSI	VFIMFLFGFS
Ava26160 2			ADADWHARIG	VVNIIVLWFR	FLKYLRPFEF	IGWFITIVIY	LKADIIRFAI	FLMTLLIPYS
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TRPC1_Hsap	MLQDFGKBLG	MFLLVLFSFT	IGLTQLY	DTFHSFIGTC	FALOWYIFSL	VAIFVTRLQS	FVGAVIVGTY	NVVVVIVITK
TRPC1_Mmus	QDFGKFLGMF	LLVLFSFTIG	LTQLYDT	FHSFIGTCFA	LFWYIFSLVA	IFVTRLQSFV	GAVIVGTYNV	VVVIVLTKIL
TRPC1_Drer	MLQEFGRELG	LFLLVLISET	IGLTQLYGKD	DTEHTEMGTC	OFTOWTHEM	VNLFVTRLRS	FVGALIVGTY	TTYMUTY
TRPC2 Drer	MTDDMMRIME	TLVIICTAFI.	CGINNITVPI	INLOKINETE	SELOWTMECM	ADOTYVDLAF	LVGRTLVGTV	TLTTVIN
TRPC2 Drer	MIDOMMROMF	ILMIIGTAFL	CGINNIYVPY	IHLGRLNETF	NELOWIMECM	ANOGYVDLAE	FVGRIFYGIF	TLLIVIV
TRPC3 Hsap	TVKDIFKEMV	LFIMVFFAFM	IGMFILYSYY	GAFTTVEESF	KTLEWSIFGL	SEVTSVVFIE	NIGYVLYGIY	NVTMVVV
TRPC3_Mmus	KDIFKFMVLF	IMVFLAFMIG	MFILYSYYGA	FTTVEESFKT	LFWSIFGLSE	VTSVVFIENI	GYVLYGIYNV	TMVVVLLNML
TRPC4_Hsap	MLLDILKELF	IYCLVLLAFA	NGLNQLYFYY	EAFSTLFETL	QSLEWSIFGL	INLYVTNFTE	FVGATMFGTY	NVISLVVIIIN
TRPC4_Mmus	MLLDILKELF	IYCLVLLAFA	NGLNQLYFYY	EAFSTLFETL	QSLEWSIFCL	INLYVTNFTE	FVGATMFGTY	NVISLVV
TRPC4_Drer	MLLDILKalf	IYCLVLLAFA	NGLNQLYFYY	NAFSTLFETL	QSLOWSIFCL	ISLYVTNFTE	FVGATMFGTY	NVISLVVIIIN
TRPC4_Dmei	MVMD1MKBFF	LYVLVLFAFG	SGLNQLLWYY	DRESNLEETT	QTLIWAVEGL	IDLDSFEFTR	FWGMLMFGTY	SVINIVULL
TRPC5_Hsan	LDILKFLATY	CLVLLAFANG	LNOLYFYYTA	FSTLFETLOS	LEWSVEGLUN	LYVTNETEEV	GATMFGTYNV	TSLVVLLNML
TRPC5 Mmus	LDILKFLOIY	CLVLLAFANG	LNOLYFYYTA	FSTLFETLOS	LFWSVFGLLN	LYVTNFTEFV	GATMFGTYNV	ISLVVLLNML
TRPC6 Hsap	KDIFKFMVIF	IMVFVAFMIG	MFNLYSYYGA	FTTVEESFKT	LFWAIFGLSE	VKSVVFIENI	GYVLYGVYNV	TMVIVLLNML
TRPC6_Mmus	KDIFKFMVIF	IMVFVAFMIG	MFNLYSYYGA	FTTVEESFKT	LFWAIFGLSE	VKSVVFIENI	GYVLYGVYNV	TMVIVLLNML
TRPC6_Drer	TVKDIFKEMV	IFILVFLAFM	IGMFNLYSYY	GAFTTVEESF	KTLEWAIFGL	SEVKSVVFIE	NIGYVLYGVY	NVTVVIVII
TRPC6_Drer	TVKDIFKOMV	IFIMVFVAFM	IGMFNLYSYY	GAFTTVEESF	KTLEWAIFCL	SEVKSVVFIE	NIGYVLYGVY	NVTMVIVION
TRPC6_Cele	MLVDVAKECF	IFVLIISSFS	IGLAQLYWYY	PVFSSIADSY	LTLLWSLFSI	TKPEDTDITQ	WVGQGMFIMY	HCTSIIVIIIN
TRPC/_Hsap	TVKDIFKOMV	IFIMVFVAFM	IGMENLYSYY	GAFTTVEESF	KTLIWSIFEL	SEVISVVFIE	NIGYVLYGVY	NVTMVVVIAN
TRPC7 Drer	TVENTERIOMY	IMVFVAFMIG	TOMENLISIIGA	CAFTTVEESFRT	KTLOWSTER.	SEVISVVETE	NICYTLYCVY	NVTMVVVLLNML
TRPN Dmel	LLKDLARDLA	VLAIEVEGES	MHIVALNOSE	NYFSDPINSF	ELLEFAVECO	TTTEOTOWVE	YLFKIVFGTY	MLVSVVVTTN
TRPN Cele	LMYDLARGLV	ILMLFVAGET	LHVTSIFOPA	QRLASPSOTL	EMLEFSLEEL	VEPDSMPFAK	IILKLLFGIY	MMVTLIV
TRPN Drer	LIKDLCREAV	ILMLFHTAFT	LSLTALCOPL	PTVPGPLNMS	VLLFFALFCL	TEPDKIPATA	VLAKMVFGVY	LVVTFIVLIN
TRPM1 Hsap		THEFT	VAROAILHPE	ESWKLARNIF	YMPYWMIYGE	VFADQIDPGA	WLTPALMACY	LLVANIL
	MMIDMLYDVV	TWTAATW2LG	~		and an an an an an and the			and the second second second second
TRPM1_Mmus	MMIDMLYFVV MMIDMLYFVV	IMLVVLMSFG	VARQAILHPE	ESWKLARNIF	INDIMUTICE	VFADQIDPGA	WLTPALMACY	LLVANIL
TRPM1_Mmus TRPM2_Hsap	MMIDMLYFVV MMIDMLYFVV MMKDVFFFLF	IMLVVLMSFG IMLVVLMSFG LLAVWVVSFG	VARQAILHPE VAKQAILIHN	ESWKLARNIF EVDWLFRGAV	YMPYWMIYGE YHSYLTIFGQ	VFADQIDPGA IP-GYIDFPE	WLTPALMACY WLTVLLLCLY	LLVANILLVN LLFTNIL
TRPM1 Mmus TRPM2 Hsap TRPM2 Mmus	MMIDMLYEVV MMIDMLYEVV MMKDVFFELF MMKDVFFELF	IMLVVLMSFG IMLVVLMSFG LLAVWVVSFG LLAVWVVSFG	VARQAILHPE VAKQAILIHN VAKQAILIHN	ESWKLARNIF EVDWLFRGAV EVDWIFRGVV	YMPYWMIYGE YHSYLTIFGQ YHSYLTIFGQ	VFADQIDPGA IP-GYIDFPE IP-TYIDFPE	WLTVLLLCLY WLTVTLLCLY	LLVANILLVN LLFTNILLLN LLFANILLLN
TRPM1_Mmus TRPM2_Hsap TRPM2_Mmus TRPM3_Hsap	MMIDMLYFVV MMIDMLYFVV MMKDVFFFLF MMKDVFFFLF MMIDMMYFVI	IMLVVLMSFG IMLVVLMSFG LLAVWVVSFG IMLVVLMSFG IMLVVLMSFG	VARQAILHPE VAKQAILIHN VAKQAILIHN VARQAILFPN	ESWKLARNIF EVDWLFRGAV EVDWIFRGVV ESWKLAKNIF	YMPYWMIYEE YHSYLTIFGQ YHSYLTIFGQ YMPYWMIYGE YMPYWMIYGE	VFADQIDPGA IP-GYIDFPE IP-TYIDFPE VFADQIDTGA	WLTPALMACY WLTVLLLCLY WLTVTLLCLY WIVPAIMACY	LLVANILLVN LLFTNILLLN LLFANIL <mark>HLN</mark> LLVANILLVN
TRPM1_Mmus TRPM2_Hsap TRPM2_Mmus TRPM3_Hsap TRPM3_Mmus TRPM3_Drer	MMIDMLYSVV MMIDMLYSVV MMKDVFFSLF MMKDVFFSLF MMIDMMYSVI MMIDMMYSVI MMIDMMYSVI	IMLVVLMSFG IMLVVLMSFG LLAVWVVSFG IMLVVLMSFG IMLVVLMSFG IMLVVLMSFG	VARQAILHPE VAKQAILIHN VAKQAILIHN VARQAILFPN VARQAILFPN VARQAILFPN	ESWKLARNIF EVDWLFRGAV EVDWIFRGVV ESWKLAKNIF ESWKLAKNIF	YMPYWMIYCE YHSYLTIFGQ YHSYLTIFGQ YMPYWMIYCE YMPYWMIYCE FMPYWMIYCE	VFADQIDPGA IP-GYIDFPE IP-TYIDFPE VFADQIDTGA VFADQIDTGA	WLTPALMACY WLTVLLLCLY WLTVTLLCLY WIVPAIMACY WIVPAIMACY WIVPAIMACY	LLVANILLVN LLFTNILLLN LLFANILLLN LLVANILLVN LLVANILLVN LLVANILLVN
TRPM1 Mmus TRPM2 Hsap TRPM2 Mmus TRPM3 Hsap TRPM3 Mmus TRPM3 Drer TRPM3 Dme1	MMIDMLYSVV MMIDMLYSVV MMKDVFFSLF MMKDVFFSLF MMIDMMYSVI MMIDMMYSVI MMIDMMYSVI MVKNMIYSVV	IMLVVLMSFG IMLVVLMSFG LLAVWVVSFG IMLVVLMSFG IMLVVLMSFG IMLVVLMSFG LLAVVLMSFG	VARQAILHPE VAKQAILIHN VAKQAILIHN VARQAILFPN VARQAILFPN VARQAILNPN VSRQAILYPN	ESWKLARNIF EVDWLFRGAV EVDWIFRGVV ESWKLAKNIF ESWKLAKNIF ESWMLARNIF KTWSLIKEVT	YMPYWMIYEE YHSYLTIFO YHSYLTIFO YMPYWMIYE YMPYWMIYE FMPYWMIYE FOPYFMLYE	VFADQIDFGA IP-GYIDFFE IP-TYIDFFE VFADQIDTGA VFADQIDTGA VFADQIDTGA	WLTPALMACY WLTVLLLCLY WLTVTLLCLY WIVPAIMACY WIVPAIMACY WVVPAIMACY WVTPITMSMY	LLVANIDLVN LLFTNILLLN LLFANILLLN LLVANILLVN LLVANILLVN LLVANILLVN LLTANILLIN

TRPM3_Cele	and a start store where	the second se			a ser an	State of the second		and a second Plane
$m_{D} D M^{\prime} \rightarrow 0 - 1$	MIQNMSYIIV	MLVVTLLSFG	LARQSITYPD	THWILVRNIF	LKPYFMLYCE	VYADEIDPGY	WIPPLLMTFF	LLIANIL
TRPMS_CEI	PTMIPLCVLV	FITLYAFGLL	RQSITYPYDH	WILVRNIFLQ	PYFMLYGEVY	AAEIDPGYWI	APVGLTVFML	ATNVLLMNVM
TRPM3_Cele	WSMCYICVLL	LVPLMAFGVN	RQALTEPNKH	WLLVRNIFYK	PYFMLYGEVY	AGEIDPGYFI	PPLLMVIFLL	VANILLLNIL
TRPM4_Hsa	MMKDVFF9LF	FLGVWLVAYG	VATEGLLRPR	DFPSILRRVF	YRPYLQIFGQ	IPQEDMDYAN	WLVVLLLVIF	LLVANILLVN
TRPM4 Mmu:	5 MMKDVFF9LF	FLCVWLVAYG	VATEGILRPQ	DLPSILRRVF	YRPYLQIFGQ	IPQEEMDYAN	WLVVLLLIVF	LLVANIL
TRPM4 Dre:	MIKDAFFOLF	FLLVWLIAYG	VANQALLYQY	DPARVFRRVL	YRPYLHIFGD	IPVEEIDSHN	WLVVVLLVIF	LLVTNILLIN
TRPM4 Dre:	MIKDAFFIELF	FLLVWLSAYG	VANOALLYOY	DPARTFRRVL	YRPYLHIFCO	IPVEEIDSHN	WLVVVLLVIF	LLVTNILLVN
TRPM4 Dre	MIKHAFFOLF	FLLVWLIAYG	VANOALLYOY	DPARVFRRVL	YRPYLHIE	IPVEEIDSHN	WLVVILLVIF	LLVTNILI IN
TRPM4 Dre	MVKDVFFDLF	FLGVWLMAYG	VANOALLYSY	DPGWVARRVF	YRPYMHIYGO	IPLDEIDDAN	WLVLILLSVY	LLVTNILIVN
TRPM5 Hear	MMKDVFFDLF	FLSVWLVAYC	VTTOALLHOH	DT.EWTERRUT.	VERVIOTEO	TRLOFTOVAN	WINTLINTE	LUVTNVLUMN
TRPM5 Mmu	MMKDVFFDLF	FLSVWLVAYC	VTTOALLHDH	DI.FWIFPPVI.	VERVIOLECO	TPLOFTOVAN	WINTLIANE	LLVTNVLIMN
TRENS_DEC.		FLOWETAYC	VIIQALLUDN	DIDWIFDDAI	VDDVIUTEO	TOLEETDYAN	WINTETTTY	
TREMS_DIC.	MTANNEYTUT	TMATUTIEEC	VADEATIODE	FOWSTADDTV	FEDVENTVEE	VYACETDECS	FITDELONUY	LEVOYTEMUN
TRENO_HSA		THATVILLEG	VARIATIOPK	LONDIND	FEFINALICE	VIAGEIDEGS	FLIFFLQAVI	LEVQIIIMU
TRPM6_Mmu:	5 MAANMETIVI	IMAIVLLSFG	VARKAILSPK	ESWRLARDIV	FEPIWMMIGE	VIASDIDPGS	FLTPFLQAVY	TEAGATIWAN
TRPM/_Hsaj		IMALVLLSFG	VPRKAILIPH	ESWILARDIV	FHPIWMIFCE	VIAIEIDPGT	WLTPFLQAVY	TEAGATIWAN
TRPM/_Mmu:	5 MVANMFYIVV	IMALVLLSFG	VPRKAILYPH	ESWSLAKDIV	FHPYWMIFCE	VYAYEIDPGT	WLTPFLQAVY	LEVQYIIMV
TRPM/_Dre:	C MVANMFYIVV	IMAVVLLSFG	VPRKAILYPE	ESWTLAKDVV	FQPYWMMYCE	VYAYEIDTGV	WLTPLLQAVY	LEVQYILMVN
TRPM8_Hsap	D MLIDVFFPLF	LFAVWMVAFG	VARQGILRQN	EWRWIFRSVI	YEPYLAMFGQ	VP-SDVDFPE	WITIPLVCIY	MLSTNILLVN
TRPM8_Mmu:	8 MLIDVFF9LF	LFAVWMVAFG	VARQGILRQN	EWRWIFRSVI	YEPYLAMFGQ	VP-SDVDFPE	WITIPLVCIY	MLSTNILUVN
TRPA_Hsap	LKTLLRSTVV	FIFLLLAFGL	SFYILLN	PFSSPLLSII	QTFSMMLGDI	NYRESFAHPV	LSFAQLVSFT	IFVPIVLMNL
TRPA_Mmus	FKTLLRSTGV	FIFLLLAFGL	SFYVLLN	AFSTPLLSLI	QTFSMMLGDI	NYRDAFAYPV	LTFGQLIAFT	MEVPIVLMNL
TRPA_Drer	ISRTLLSIIV	LFFYLILGFA	LSFYALMI	-HFGRMFLSL	LQTHVMMVGE	MNYQDNFPFP	DLTLAIFVWF	VLLVPILLMN
TRPA Drer	IVRTLVCIMV	LFVFLLLAFG	LAFYALML	-EFSSISLAL	AQTIVMTVGE	LNYQSTFAFP	AITYFVFVFF	VLLMPILIMN
TRPA Dmel	ILQTLIKVLM	VFSILIIAFG	LAFYILLSKI	DSFSNIPMSL	LRTESMMLCE	LDFVGTYKVP	MTSFLILSVF	MILMPILLMN
TRPA Cele	KTFFRFFPVF	VLFIIAFSSS	FYVILQE	FSTIFMSPLK	TTVMMIGEFE	FTGIFAHTAV	ACALFFFFCI	IMTILLMN
TRPV1 Hsa	MIRDLCROMF	VYIVFLFGFS	TAVVTLIEDG	NSYNSLYSTC	LELSKFTICM	GDLEFTEDFK	AVFIILLAY	VILTYIL
TRPV1 Mmu	MIRDLCROMF	VYLVFLFGFS	TAVVTLIEDG	NSYNSLYSTC	LELOKFTICM	GDLEFTEDFK	AVFIILLAY	VILTYIL
TRPV1 Dre	MVGEIRROLV	VYMVFLIGFS	AALVTLLDOE	ISYKNIYFTT	LELEKFTICM	GDLEFTDKYK	EVFYVLLIVY	IVMTYILMUN
TRPV2 Hsau	VIBILIBILI	TYLVFLEGEA	VALVSLSOFA	BOYRGILEAS	LELOKETICM	GELAFOEHER	GMVLLLLAY	VILTYTLINE
TRPV2 Mmil	VIRILIRIALI	VYLVFLEGEA	VALVSLSREA	SPYGGTLDAS	LELOKETICM	GELAFOERFR	GVVLLLLAY	VI.I.TYVI.
TRIV2_PARA	VIII VIII VIIII	WITNELLCEC	VAL AST TEKC	KEVCEFEDAV	TELEVITET	CDINIOOKYP	TIFIFITTTY	VIII TTVI UN
TREVS_HSA	VIII VIII KOTE	WYTEFTCEC	VALASITEKC	KEVCEFEDAV	TRUNKITION	CDINIQQUIF	TIFIFITTTY	VILLE VLUM
TRPV5_MIIU:		VIILFLLGFG	VALASLIERC	NDODEDODED	LELINKLIIGL	GDLNIQQIIP		
TRPV4_HSaj	5 ILKLIFRELL	VILLEMIGIA	SALVSLLNPC	NDSETFSTFL	LDLEKLTIGM	GDLEMLSKIP	VVFIILLVIY	
TRPV4_CIU	) ILN LFRELL	VILLEMIGIA	SALVSLLNPC	NDSETFSTFL	LDLGKLTIGM	GDLEMLSKIP	VVFIILLVIY	TILTEVELLE
TRPV4_Mmu:	5 ILKOLFRIGLL	VYLLFMIGYA	SALVTLLNPC	NDSETFSAFL	LDLIGKLTICM	GDLEMLSKYP	AAE.IFFFA.A	
TRPV4_Dre:	ILKOLFROLL	VYVLFMIGYA	SALVSLLTIC	NDTNTFSEFL	LDLSKLTICI	GDLDMLKQYP	AVFLILLVTY	IILTEVPINE
TRPV5_Hsa	D MIGDLMRDCW	LMAVVILGFA	SAFYIIFQTE	PQFYDYPMAL	FTTEELFLTV	IDAPNYDDLP	FMFSIVNFAF	AIIATLLMON
TRPV5_Mmu:	5 MIGDLLRECW	LMAMVILGFA	SAFYIIFQTE	PEFSDYPTAM	FSTEELFLTI	IDGPNYRDLP	FMYSVTYATF	AIIATLLMIN
TRPV6_Hsa	D MIGDLMRDCW	LMAVVILGFA	SAFYIIFQTE	PHFYDYPMAL	FSTEELFLTI	IDGPNYNDLP	FMYSITYAAF	AIIATLLMUN
TRPV6_Mmu:	MIGDLMRGCW	LMAVVILGFA	SAFYIIFQTE	PHFYDYPMAL	FSTEELFLTI	IDGPNYDDLP	FMYSVTYAAF	AIIATLLMUN
TRPV6_Dre:	SIGDITKEMW	LSIIFLIGSS	AALWIFYMTQ	PQYRSFPITL	FSQEEVSVGQ	IDLPDHTFTH	PVVYWTHVCF	SLISNVLLFN
TRPML1_Hsa	a ALPSVMRECC	CVAVIYLGYC	FCGWIVLGPY	VKFRSLSMVS	ECLESLINCD	DMFVTFALVW	LFSQLYLYSF	ISLFIYMVIS
TRPML1_Mm	1 ALPSVMRECC	CVAVIYLGYC	FCGWIVLGPY	VKFRSLSMVS	ECLESLINCD	DMFVTFALVW	LFSQLYLYSF	ISLFIYMVIS
TRPML1 Dre	AFPNVIR	CAAAIYMGYC	FCGWIVLGPY	AKFRSLSTVS	ECLESLINCD	DMFATFSLVW	VFSQIYLYTF	ISLFIYMVIS
TRPML2 Hsa	a SLPKVLRFCA	CAGMIYLGYT	FCGWIVLGPY	DKFENLNTVA	ECLESLVNCD	DMFATFALVW	LFSRLYLYSF	ISLFIYMI
TRPML2 Mm	1 SLPKVLRECA	CAGMIYLGYT	FCGWIVLGPY	EKFENLNIVA	ECLISSIVNED	DMEATEATIN	a second second second	
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		CAGMIYLGYT	FCGWIVLGPY	EKFEDLSRVA	ECLESLVNGD	DMFATFAMVW	LFSRLYLYSF LFSRVYLYSF	ISLFIYMVIS ISLFIYMVIS
TRPMLS HS	ALPNVIRGCC	CAGMIYLGYT CAAMIYLGYC	FCGWIVLGPY	EKFEDLSRVA DKFRSLNMVS	ECLESLVNCD	DMFATFAMVW DMFATFALVW	LFSRLYLYSF LFSRVYLYSF LFSRIYLYSF	ISLFIYMVIS ISLFIYMVIS ISLFIYMIIS
TRPML3_HS3	ALPNVIRECC	CAGMIYLGYT CAAMIYLGYC CAAMIYLGYC	FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY	EKFEDLSRVA DKFRSLNMVS EKFRSLNRVS	ECLESLVNGD ECLESLINGD ECLESLINGD	DMFATFALVW DMFATFALVW DMFATFALVW	LFSRLYLYSF LFSRVYLYSF LFSRIYLYSF LFSRVYLYSF	ISLFIYMVLS ISLFIYMVLS ISLFIYMILS ISLFIYMILS
TRPML3_HS TRPML3_Mm TRPML3_Dre	ALPNVIRFCC ALPNVMRFCC ALPNVMRFCC	CAGMIYLGYT CAAMIYLGYC CAAMIYLGYC CAAMIYLGYC	FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY	EKFEDLSRVA DKFRSLNMVS EKFRSLNRVS TKFRTLNTVS	ECLESLVNGD ECLESLINGD ECLESLINGD ESLESLINGD	DMFATFALVW DMFATFALVW DMFATFALVW DMFATFKVVW	LFSRLYLYSF LFSRVYLYSF LFSRIYLYSF LFSRLYLYSF LFSRLYLYTF	ISLFIYMVIS ISLFIYMVIS ISLFIYMIS ISLFIYMIS VSLFIYMVIS
TRPML3_Mm TRPML3_Dre TRPML3_Dre	A ALPNVIRECC ALPNVMRECC ALPNVIRETC AAPKILRELI	CAGMIYLGYT CAAMIYLGYC CAAMIYLGYC CAAMIYLGYC AALLIYAGFY	FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWLILGPY	EKFEDLSRVA DKFRSLNMVS EKFRSLNRVS TKFRTLNTVS MKFRSLATTS	ECLESLINGD ECLESLINGD ECLESLINGD ESLESLINGD ECLEALINGD	DMFATFANVW DMFATFALVW DMFSTFALVW DMFATFKVVW DMFATFAWLW	LFSRLYLYSF LFSRVYLYSF LFSRIYLYSF LFSRVYLYSF LFSRLYLYTF WFCOIYLYSF	ISLFIYMVIS ISLFIYMVIS ISLFIYMIIS ISLFIYMIIS VSLFIYMVIS ISLYIYVVIS
TRPML3_HS3 TRPML3_Mmi TRPML3_Dro TRPML3_Dmo TRPML3_Dmo	ALPNVIRFCC ALPNVMRFCC ALPNVMRFCC ALPNVIRFTC AAPKILRFLI AAPKILRFLI	CAGMIYLGYT CAAMIYLGYC CAAMIYLGYC CAAMIYLGYC AALLIYAGFV AALLIYAGFV	FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWLILGPY FCGWLILGPY	EKFEDLSRVA DKFRSLNMVS EKFRSLNRVS TKFRTLNTVS MKFRSLATTS MKFRSLATTS	ECLFSLINGD ECLFSLINGD ECLFSLINGD ESLFSLINGD ECLFALINGD ECLFALINGD	DMFATFAMVW DMFATFALVW DMFATFALVW DMFATFAVW DMFATFAWLW DMFATFAWLW	LFSRLYLYSF LFSRVYLYSF LFSRLYLYSF LFSRLYLYSF WFCQIYLYSF WFCQIYLYSF	ISLFIYMVIS ISLFIYMVIS ISLFIYMIIS ISLFIYMIS ISLFIYMVIS ISLYIYVVIS ISLYIYVVIS
TRPML3_HS; TRPML3_Mm TRPML3_Dre TRPML3_Dme TRPML3_Dme TRPML3_Dme	A ALPNVIRECC ALPNVMRECC ALPNVMRECC ALPNVIRETC AAPKILRELI AAPKILRELI SAPNIMREMT	CAGMIYLGYT CAAMIYLGYC CAAMIYLGYC CAAMIYLGYC AALLIYAGFV AALLIYAGFV CATVLYAGFL	FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWLILGPY FCGWLILGPY IAGWVIIGPY	EKFEDLSRVA DKFRSLNMVS EKFRSLNRVS TKFRTLNTVS MKFRSLATTS MKFRSLATTS MKFRSLAESS	ECLFSLVNGD ECLFSLINGD ECLFSLINGD ESLFSLINGD ECLFALINGD ECLFALINGD EALESLINGD	DMFATFANVW DMFATFALVW DMFATFALVW DMFATFAVLW DMFATFAWLW DMFATFAWLW DMFATFYVIK	LFSRLYLYSF LFSRVYLYSF LFSRLYLYSF LFSRLYLYSF WFCQIYLYSF WFCQIYLYSF WFCQIYLYSF	ISLFIYMVIS ISLFIYMVIS ISLFIYMILS ISLFIYMVIS VSLFIYMVIS ISLYIYVVIS USLFIYVVIS
TRPML3_HS; TRPML3_Dro TRPML3_Dro TRPML3_Dmo TRPML3_Dmo TRPML3_Cel TRPML3_Cel	ALPNVIRECC ALPNVMRECC ALPNVIRETC AAPKILEALI AAPKILEALI SAPNIMEMT ALPELLCVTT	CAGMIYLGYT CAAMIYLGYC CAAMIYLGYC CAAMIYLGYC AALLIYAGFV AALLIYAGFV CAIVLYAGFL GLVULGVAYA	FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWLILGPY FCGWLILGPY IAGWVIIGPY OLATLIVSSC	EKFEDLSRVA DKFRSLNMVS EKFRSLNRVS TKFRTLNTVS MKFRSLATTS MKFRSLATS MKFRTLAESS DSLWSV	ECLESLINGD ECLESLINGD ECLESLINGD ESLESLINGD ECLEALINGD EALESLINGD EALESLINGD	DMFATFALVW DMFATFALVW DMFATFALVW DMFATFAVWW DMFATFAWLW DMFATFAWLW DMFATFYVIK	LFSRLYLYSF LFSRVYLYSF LFSRLYLYSF LFSRLYLYFF WFCQIYLYSF WFCQIYLYSF VFGTVYIYLF LICVCL	ISLFIYMVIS ISLFIYMVIS ISLFIYMIS ISLFIYMVIS ISLFIYMVIS ISLYIYVVIS VSLFIYVVIS VSLFIYVVIS
TRPML3_HS; TRPML3_Dre TRPML3_Dre TRPML3_Dme TRPML3_Dme TRPML3_Ce: TRPP_PKD1 TRPP_PKD1	ALPNVIRJCC ALPNVMRJCC ALPNVMRJCC AAPKILRJI AAPKILRJI AAPKILRJI ALPELLGVTL ALPELMGATU	CAGMIYLGYT CAAMIYLGYC CAAMIYLGYC CAAMIYLGYC AALLIYAGFV AALLIYAGFV CAIVLYAGFL GLVVLGVAYA GLVLLGVAYA	FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWLILGPY FCGWLILGPY IAGWVIIGPY QLAILLVSSC OMAILLISSC	EKFEDLSRVA DKFRSLNMVS EKFRSLNRVS TKFRTLNTVS MKFRSLATTS MKFRSLATTS DSLWSV DSLWSV DTLYNM	ECLISLINGD ECLISLINGD ECLISLINGD ESLISLINGD ECLIALINGD ECLIALINGD EALISLINGD AQAL-IVIC ARAD-IVIC	DMFATFALVW DMFATFALVW DMFATFALVW DMFATFAVVW DMFATFAWLW DMFATFAWLW DMFATFYVIK LSP	LFSRLYLYSF LFSRLYLYSF LFSRLYLYSF LFSRLYLYFF WFCQIYLYSF WFCQIYLYSF VFGTVYIYLF LLCVGL LLCVGL	ISLFIYMVIS ISLFIYMVIS ISLFIYMIS ISLFIYMIS VSLFIYMVIS ISLYIYVVIS VSLFIYVVIS WALRLWGAR WALRUWGAR
TRPMLS H3S TRPML3_Dre TRPML3_Dre TRPML3_Dme TRPML3_Ce TRPP_PKD1 TRPP_PKD1 TRPP_PKD1	A ALPNVIRGCC ALPNVMRGCC ALPNVMRGCC AAPKILRGLI AAPKILRGLI SAPNIMRGMT ALPELLGVTL ALPELMGATL SEWFLIMGATL	CACMIYLGYC CAAMIYLGYC CAAMIYLGYC CAAMIYLGYC AALLIYAGFV AALLIYAGFV CAIVLYAGFL GLVVLGVAYA TLLUFLIAYS	FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWLILGPY FCGWLILGPY IAGWVIIGPY QLAILLVSSC QMAILLISSG	EKFEDLSRVA DKFRSLNMVS EKFRSLNRVS TKFRTLNTVS MKFRSLATTS MKFRSLATTS DSLWSV DTLYNM ECYCTV	ECLESLINGD ECLESLINGD ESLESLINGD ECLEALINGD ECLEALINGD EALESLINGD AQALLVLC ARAELVLC SSTOFFIT	DMFATFANVW DMFATFALVW DMFATFALVW DMFATFAVLW DMFATFAWLW DMFATFAWLW DMFATFAWLW DMFATFYVIK LSP DC9	LFSRLYLYSF LFSRLYLYSF LFSRLYLYSF LFSRLYLYSF WFCQIYLYSF WFCQIYLYSF VFGTVYIYLF LLCVGL LLCVGL	ISLFIYMVIS ISLFIYMVIS ISLFIYMIS VSLFIYMVIS ISLYIYVVIS ISLYIYVVIS VSLFIYVVIS WALRLWGAMR WALRVWGAMR
TRPMLS_H3 TRPML3_Dre TRPML3_Dre TRPML3_Dre TRPML3_Dre TRPML3_Ce TRPP_PKD1 TRPP_PKD1 TRPP_PKD1 TRPP_PKD1	A ALENVIRCC ALENVIRTCC ALENVIRTCC AAPKILRII SAPKILRII SAPKILRII ALPELLGVIL ALPELLGVIL ALPELMGATL STWELLMVAV CANTFECAN	CACMIYLGYT CAAMIYLGYC CAAMIYLGYC CAAMIYLGYC AALLIYAGFU CAIVLYAGFU GLVVLGVAYA GLVLLGVAYA TLLVFLLAYS	FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWLILGPY FCGWLILGPY IAGWVIIGPY QLAILLVSSC QMAILLISSC UMAILLISSC	EKFEDLSRVA DKFRSLNRVS EKFRSLNRVS TKFRTLNTVS MKFRSLATTS MKFRSLATTS DSLWSV DTLYNM EGYGTV	ECLESLINCD ECLESLINCD ECLESLINCD ECLESLINCD ECLEALINCD ECLEALINCD EALESLINCD AQAL-LVLC ARAELVLC SSTCFKLIES	DMFATFANVW DMFATFANVW DMFATFANVW DMFATFAVVW DMFATFAWLW DMFATFAWLW DMFATFAWLW DMFATFYVIK LSP PCS PCS	LFSRLYLYSF LFSRLYLYSF LFSRLYLYSF LFSRLYLYSF WFCQIYLYSF WFCQIYLYSF WFCQIYLYSF LLCVGL LLCVGL LLCVGL UCCVGL	ISLFIYMVUS ISLFIYMUS ISLFIYMUS VSLFIYMUS ISLYIYVVUS ISLYIYVVUS VSLFIYVVUS WALRLWGADR WALRLWGADR TLLRLVUDWI
TRPMLS_H3 TRPML3_Dre TRPML3_Dre TRPML3_Dre TRPML3_Ce TRPP_PKD1 TRPP_PKD1 TRPP_PKD1 TRPP_PKD1 TRPP_PKD2	A ALPNVIRCC ALPNVIRCC ALPNVIRTCC ALPNVIRTCC AAPKILRII AAPKILRII AIPELLGVTI ALPELMGATI SFWELLMVAV CANLFGATI CANLFGATI	CACMIYLGYC CAAMIYLGYC CAAMIYLGYC CAALIYAGFU AALLIYAGFU CAIVLYAGFL GLVVLGVAYA GLVLLGVAYA TLLVFLLAYS MFFIIFLAYA	FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWLILGPY FCGWLILGPY IAGWVIIGPY QLAILLVSSC QMAILLISSG HTGHLLFHSV QLAYLVFGTQ QLAYLVFGTQ	EKFEDLSRVA DKFRSLNMVS EKFRSLNRVS TKFRTLNTVS MKFRSLATTS MKFRTLAESS DSLWSV DTLYNM EGYGTV DDFSTFQECI	ECLESLINGD ECLESLINGD ESLESLINGD ESLESLINGD ECLEALINGD ECLEALINGD AQAL-IVIC ARAE-IVIC SSTOFKLIGS FTOFRIIGP	DMFATFANVW DMFATFALVW DMFATFALVW DMFATFKVVW DMFATFAWLW DMFATFAWLW DMFATFAWLW DMFATFYVIK LSP PCS INFAETEANR	LFSRLYLYSF LFSRVYLYSF LFSRLYLYSF LFSRLYLYTF WFCQIYLYSF WFCQIYLYSF UFCTVYIYLF LLCVGL LLCVGL GSCFIFYISF VLGPLYFTTF VLGPLYFTTF	ISLFIYMVIS ISLFIYMVIS ISLFIYMIS ISLFIYMIS ISLYIYVVIS ISLYIYVVIS VSLFIYVVIS VALRVMCAIR TLLRLVIDWI VFFMFFIMN
TRPMLS_HS TRPML3_Dr TRPML3_Dr TRPML3_Dr TRPML3_Dr TRPML3_Cr TRPP_PKD1 TRPP_PKD1 TRPP_PKD1 TRPP_PKD2 TRPP_PKD2 TRPP_PKD2	A ALENVIR CC ALENVIR CC ALENVIR CC ALENVIR TC ALENVIR TC ALEN	CACMIYLGYC CAAMIYLGYC CAAMIYLGYC CAALIYLGYC AALLIYAGFV AALLIYAGFV CAIVLYAGFU GLVVLGVAYA GLVLLGVAYA TLLVFLLAYS MFFIIFLAYA MFFIIFLAYA	FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWLILGPY QLAILLGPY QLAILLYSC QMAILLISSG HTGHLLFHSV QLAYLVFGTQ QLAYLVFGTQ QLAYLVFGTQ	EKFEDLSRVA DKFRSLNMVS EKFRSLNRVS TKFRTLNTVS MKFRSLATTS MKFRSLATTS MKFRTLAESS DSLWSV DTLYNM EGYGTV DDFSTFQECI DDFSTFQECI DDFSTFQECC	ECLESLINCD ECLESLINCD ECLESLINCD ECLEALINCD ECLEALINCD ECLEALINCD EALESLINCD AQAL-LVLC ARAE-LVLC SSTCFKLICS FTQFRIILCD FTQFRIILCD	DMFATFALVW DMFATFALVW DMFATFAVVW DMFATFAVVW DMFATFAWLW DMFATFYVIK LSP PCS INFAEIEANR INFAEIEANR	LFSRLYLYSF LFSRVYLYSF LFSRLYLYSF LFSRLYLYSF WFCQIYLYSF WFCQIYLYSF WFCQIYLYSF UFGTVYIYLF LLCVGL LLCVGL GSCFIFYISF VLGPLYFTTF VLGPLYFTTF	ISLFIYMVUS ISLFIYMVUS ISLFIYMIUS VSLFIYMVUS ISLYIYVVUS ISLYIYVVUS VSLFIYVVUS VALRLWGAUR TLLRLVIJWI VFFMFFILIN VFFMFFILIN
TRPML3_Mail TRPML3_Dri TRPML3_Dri TRPML3_Dri TRPML3_Ce: TRPP_PKD1 TRPP_PKD1 TRPP_PKD1 TRPP_PKD2 TRPP_PKD2 TRPP_PKD2 TRPP_PKD2	A ALPNVIR CC ALPNVIR CC ALPNVIR CC ALPNVIR TC APRILR II AAPRILR II AAPRILR II AAPRILR II ALPELMGATL SFWELLMAW CAN LFG AI CAN LFG AI CAN LFG CON	CAGMIYLGYC CAAMIYLGYC CAAMIYLGYC CAAMIYLGYC AALLIYAGFV AALLIYAGFV GIVULGVAYA GLVLLGVAYA GLVLLGVAYA MFFIIFLAYA MFFIIFLAYA MFFIVFLAYA	FCGMIVLGPY FCGMIVLGPY FCGMIVLGPY FCGMIVLGPY FCGWLILGPY FCGWLILGPY QLAILLGPY QLAILLYSSC QMAILLISSG QLAYLVFGTQ QLAYLVFGTQ QLAYLVFGTQ	EKFEDLSRVA DKFRSLNRVS EKFRSLNRVS TKFRTLNTVS MKFRSLATTS MKFRSLATTS DSLWSV DTLYNM EGYGTV DDFSTFQECI DDFSTFQECI DDFSTFQECI DDFSTFQECI	ECLISIINCD ECLISIINCD ECLISIINCD ECLISIINCD ECLISALINCD ECLISALINCD EALISIINCD EALISIINCD EALISIINCD EALISIINCD EALISIINCD FTORRILLOD FTORRILLOD FTORRILLOD	DEFATFANVW DMFATFALVW DMFATFALVW DMFATFAVW DMFATFAVW DMFATFAVW DMFATFAVW DMFATFAVW DMFATFAVW INFATFAVW INFATEANR FDFSETEADS	LFSRVILYSF LFSRVILYSF LFSRVILYSF LFSRVILYSF LFSRLYLYFF WFCQIVLYSF WFCQIVLYSF WFCQIVLYSF WFCQIVLYSF ULCVGL LLCVGL GSCFIFYISF VLGPLYFTTF VLGPLYFTTF VLGPLYFTTF	ISLFIYMVIS ISLFIYMVIS ISLFIYMIS ISLFIYMIS ISLYIYVVIS ISLYIYVVIS ISLYIYVVIS VSLFIYVVIS WALRUWGAP TLILLVIIWI VFFMFTIIM VFFMFTIIM VFFMFTIIM
TRPML3_Mmi TRPML3_Drr TRPML3_Drr TRPML3_Drm TRPML3_Ce: TRPP_FKD1 TRPP_FKD1 TRPP_FKD1 TRPP_FKD2 TRPP_FKD2 TRPP_FKD2 TRPP_FKD2	A ALPNVIR CC ALPNVIR CC ALPNVIR TC AAPKILR II AAPKILR II SAPKILR II SAPKIR SIPELGVIL ALPELGVIL SFFELMVAV CANDLFG TI CANDLFG TI CANDLFG TI SANDIGGAV	CAGMIYLGYC CAAMIYLGYC CAAMIYLGYC CAAMIYLGYC AALLIYAGFU CAIVLYAGFL GLVVLGVAYA TLLVFLAYS MFFIIFLAYA MFSIIFLAYA MFSIIFLAYA MFSUFFFAYA	FCGMIVLGPY FCGMIVLGPY FCGMIVLGPY FCGMILLGPY FCGMLILGPY IAGWVIIGPY QLAILVSSC QMAILLSSG QMAILLSSG QLAILVFGTQ QLAYLVFGTQ QLAYLVFGTQ QCAVLVFGTQ	EKFEDLSRVA DKFRSLMVS EKFRSLMVS TKFRTLNVS MKFRSLATTS MKFRSLATTS MKFRTLAESS DTLYNM EGYGTV DDFSTFQECI DDFSTFQECI DDFSTFQECI ADFSNLYNSA	ECLISIVNED ECLISIINED ECLISIINED ECLISIINED ECLISALINED ECLISALINED EALISIINED AQAL-IVIC ARAE-IVIC ARAE-IVIC STOFRIIED FTORRILED FALRILED FALRILED	DEFATFAIVE DEFATFAIVE DEFATFAIVE DEFATFAIVE DEFATFAIVE DEFATFAIVE DEFATFAIVE DEFATFAIVE DEFATFAIVE DEFATFAILEANR INFAETEANR INFAETEANS FNFSALECAN	LFSRVIIYSF LFSRVIIYSF LFSRVIIYSF LFSRVIIYSF WFCQIYLYSF WFCQIYLYSF WFCQIYLYSF UFGTYIYLF LLCVGL LLCVGL LLCVGL VLGPLYFTTF FFGRAFFIAY	ISLFIYMVUS ISLFIYMUS ISLFIYMUS VSLFIYMUS VSLFIYMUS VSLFIYVVUS ISLYIYVVUS VSLFIYVVUS WARRUGAPR WARRUGAPR WARRUGAPR TLIRVULWI VFFMFTILIN VFFMFTILIN VFFMFTILIN VFFIFTILIN
TRPML3_Mm TRPML3_Mm TRPML3_Dmc TRPML3_Dmc TRPML3_Dmc TRPM_S_Ce. TRPP_PKD1 TRPP_PKD1 TRPP_PKD2 TRPP_PKD2 TRPP_PKD2 TRPP_PKD2 TRPP_PKD2 TRPP_PKD2	A ALENVIR CC ALENVIR CC ALENVIR CC ALENVIR CC ALENVIR TO ALENTIR TI APRILR TI APRILR TI ALELIGTI ALELIGTI ALELIGTI ALELIGTI CANDLEGAI CANDLEGAI CANDLEGAV CANDLEGAV CANDLEGAV CANDLEGAV	CAGMIYLGYC CAAMIYLGYC CAAMIYLGYC CAAMIYLGYC AALLIYAGFV AALLIYAGFV CAIVIYAGFU GLVVLGVAYA GLVLLGVAYA GLVLLGVAYA MFFIFLAYA MFFIFLAYA MFFIFFLAYA MFFUFFFAFA MFFUFFFAFA	FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWLILGPY FCGWLILGPY FCGWLILGPY FCGWLILGPY ULATLIVSSC QMAILLISSG HTGHLFHSV QLAYLVFGTQ QLAYLVFGTQ QLAYLVFGTQ QLGYLVFGTQ QLGYLVFGTQ QLGYLLFGTQ	EKFEDLSRVA DKFRSLNRVS EKFESLNRVS MKFRSLATTS MKFRSLATTS MKFRTLAESS DSLWSV DSLWSV DDFSTFQECI DDFSTFQECI DDFSTFQECI DDFSTFQECI DDFSTFQECI DDFSTFQECI DDFSTFQECI DDFSTFQECI	ECLESIVNCD ECLESIINCD ECLESIINCD ESLESIINCD ECLESIINCD ECLESIINCD EALESIINCD EALESIINCD AQAL-IVIC ARAE-IVIC SSTCFKIIES FTORRIICD FTORRIICD FTORRIICD FTORRIICD	DEFATFANYW DMFATFALVW DMFSTFALVW DMFATFALVW DMFATFAVLW DMFATFAVLW DMFATFAVLW DMFATFAVLK LSP CS INFAEIEANR INFAEIEANR FDFSEIEADS FDFSEIEADS FDFSAIECNR FDVNAIDANR	LFSRVIIYSF LFSRVIIYSF LFSRVVIYSF LFSRVVIYSF WFCQIYLYSF WFCQIYLYSF WFCQUYLYSF UFGTVYIYL LICVGL LICVGL GSCFIFYISF VLGPLYFTF VLGPLYFTTF VLGPLYFTTF VLGPLYFTTF VLGPLYFTTF VLGPLYFTTF VLGPLYFTY	ISLFIYMVUS ISLFIYMVUS ISLFIYMUS VSLFIYMVUS ISLYIYVVUS ISLYIYVVUS VSLFIYVVUS WALRUKALR WALRUKALR WALRUKALR VFFMFTILN VFFMFTILN VFFMFTILN VFFMFTILN VFFVFTULN VFFVFTULN
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CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV CANDIGGAV	CAGMIYLGYC CAAMIYLGYC CAAMIYLGYC CAAMIYLGYC CAAMIYLGYC CAIVLYAGFL GLVVLGYAYA GLVLLGYAYA GLVLLGYAYA GLVLLGYAYA MFFIYLLAYS MFFIYLLAYS MFFIYLLAYS MFFIYFLAYA MFFIYFFAYA MFFIYFFAYA MFFIYFFAYA MFFIYFFAYA MFFIYFFAYA MFFIYFFAYA MFFIYFFAYA MFFIYFFAYA MFFIYFFAYA MFFIYFFAYA MFFIYFFAYA MFFIYFFAYA FGFUFFAYA FGFUFFAYA FGFUFFAYA FGFUFFAYA FGFUFFAYA FGFUFFAYA 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GLVLLGVAYA TLLWFLLAYS MFFIFLAYA MFFIFLAYA MFFIFFLAYA MFFIVFFAYA MFFIVFFAYA MFFIVFFAYA MFFIVFFAYA MFFIVFFAYA MFFIVFFAYA MFFIVFFAYA MFFIVFFAYA MFFIVFFAYA MFFIVFFAYA MFFIVFFAYA MFFIVFFAYA MFFIVFFAYA MFFIVFFAYA MFGIVFLAYA MFGIVFLAYA MFGIVFLAYA MFGIVFLAYA MFGIVFLAYA MFGIVFLAYA	FCGWIVLGPY FCGWIVLGPY FCGWIVLGPY FCGWILLGPY FCGWLILGPY FCGWLILGPY FCGWLILGPY CLATLUSSC QMATLLISSC QLATLVFGTQ QLATLVFGTQ QLAYLVFGTQ QLGYLFGTQ QLGYLFGTQ QLGYLFGTQ QLGYLFGTQ QLGYLFGTQ QLGYLFGTQ QLGYLFGTQ QLGYLFGTQ QLGYLFGTQ TFGDSVFLFT TSLFLFVLGT HFTSNYGFILT FVYLFRLAIG FRPYFQVFGE	EKFEDLSRVA DKFRSLNRVS EKFESLNRVS TKFRTLNTVS MKFRSLATTS MKFRSLATTS MKFRSLATTS DCSLWSV DSLWSV DDFSTFQECI DDFSTFQECI DDFSTFQECI DDFSTFQECI DDFSTFQECI ENFSTFIKCI ENFSTFIKCI ENFSTFIKCI ENFSTFIKCI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI ENFSTFIKCI ENFSTFVKI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI DDFSTFQNSI 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DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNSI DFSTFQNS	ECLESIINGD ECLESIINGD ECLESIINGD ESLESIINGD ECLEAINGD ECLEAINGD EALESIINGD EALESIINGD EALESIINGD FAILRINGD FTORNING FTORNING FTORNING FTORNING FTORNING FTORNING FTORNING FTORNING FTORNING FTORNING FTORNING FAORIVIGD FAORIVIGD TAGKIYGLW ALEANRIGU FIGPVFFFL VSFSWGIVIN PGWAVAFFCI FFVFFLAW	DEFATFANVW DMFATFANVW DMFATFANVW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW PMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW DMFATFAVIW	LFSRVIJYSF LFSRVIJYSF LFSRVJIYSF LFSRVJIYSF WFCQIYLYSF WFCQIYLYSF WFCQIYLYSF WFCQIYLYSF WFCQIYLYSF VLGPLYFTF VLGPLYFTTF FVGGAFFIAY ILGPAYFTY ILGPAYFTY ILGPAYFTY ULGPLYFTF MLIALVTNKF MLIALVTNKF MLIALVTNKF MLIALVTNKF MLIALVTNKF MLIALVTNKF INTLIALS SQLIAMMAT ILIALFNNTY	ISLFIYMVUS ISLFIYMVUS ISLFIYMUS ISLFIYMUS VSLFIYMUS VSLFIYVUS VSLFIYVUS VSLFIYVUS VSLFIYVUS VFWFFILM VFFWFFILM VFFWFFILM VFFWFFULM VFFVFFULM IFVFFVLM IFVFFVLM IFVFFVLM IFVFFVLM IFVFFVLM IFVFFVLM IFVFFVLM IFVFFVLM IFVFFVLM IFVFFVLM ILVFFKVLM IFVFFVLM ILVFXSIL INDTYGEVK ETVRTVKQK SDTYADVKADQ HQRVEKDREA VEESSNATY

Ava6620 1	IIEVTLTSTN	NGWNLLRILL	FSPYYQIFGE	FGLANIRSTT	FIAYVFLIIL	QLIANVLLLN	LMIAYFTKI
Cca31351	LSQYA	EHVEM	FGLLSDNDGW	DELSAIDAVH	PTGINQLSMY	EIRGLLSLVE	LLVKMLLRG
Cca30979 3	SLHMGVFGAS	YRFSSMFSAL	QYQIEMILGK	FEANRSRDYP	IAAPLIFIMF	VLTGAMLLSN	LFIVLINET
Ava26193 2	GATYLALKFE	VASSLTYLVS	EWWFVFFNGL	VIESPVFGFG	WFSLILHATF	LFFVIVVFLN	LIIAOMSDTY
Ava26160_2	TOWNTYOFO	RDENTEYSTV	FTVFRTTVTD	TDE	WMTYFTTGSY	TSTVSTVSLN	LETALLSNTE
	1011111212					101101101	
MDDC1 Hear	THE MET WEEK	OT TANHEDRE	AND AD ANT MT	OVEDDET DNE	TRDI		
mppol Maure	LIV, MLHKSP	QLIANHEDKE	TAPARAKLWL	SIFUURLENE	TRDL		
TRPCI_Mmus	VAMLHKSFQL	TANHEDKEWK	FARAKLWLSI	FUDKLENEIR	DL		
TRPCI_Drer	L VOMLHKSF	RQIANHEDKE	7KFARAKLWL	SYFDDKLRNE	MRDL		
TRPC2_Mmus	MINAMITNSF	QKIEDDADVE	<b>☆KFARSKLYL</b>	SYFREGVQSE	VASV		
TRPC2_Drer	MIIIAMITNSF	QKIEDDADVE	<b>KFARSKLYL</b>	SYFREGIHTE	MKQI		
TRPC2_Drer	M <mark>LIA</mark> MISNSF	QRIEDDADVE	KFARSKLYL	SYFREGVHTE	MKDF		
TRPC3 Hsap	MIIIAMINSSY	QEIEDDSDVE	KFARSKLWL	SYFDDGIRYE	LLED		
TRPC3 Mmus	IAMINSSYQE	IEDDSDVEWK	FARSKLWLSY	FDDGIRYELL	ED		
TRPC4 Hsap	M MMNNSY	OLIADHADIE	KFARTKLWM	SYFEEGIRFE	VLGL		
TRPC4 Mmus	MUTAMMINISY	OLTADHADTE	KFARTKLWM	SYFEEGIBFE	VLGL		
TRECA Dror	MUTAMMINISY	OUTADUADIE	CKEA DTKI WM	SVEFFCIEVE	VICM		
TRIC4_DIEL	TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	QUITADIADIE	ANDADOWI	STFEEGIKIE	VIGH TIMT		
TRPC4_Dille1	LITT MINING	QUISERADVE	AKFARSKLWI	SIFLEGIRCE	PART		
TRPC4_Cele	MITTOMMSNSI	QIISDQADIE	TREARSREEL	EIFDDTL			
TRPC5_Hsap	IAMMNNSYQL	IADHADIEWK	FARTKLWMSY	FDEGIRYEVL	DL		
TRPC5_Mmus	IAMMNNSYQL	IADHADIEWK	FARTKLWMSY	FDEGIRYEVL	DL		
TRPC6_Hsap	IAMINSSFQE	IEDDADVEWK	FARAKLWFSY	FEEGIRYELL	EE		
TRPC6 Mmus	IAMINSSFQE	IEDDADVEWK	FARAKLWFSY	FEEGIRYELL	EE		
TRPC6 Drer	MINNSF	QEIEDDADVE	KFARAKLWF	TYFEEGIRYE	LLEE		
TRPC6 Drer	MUTAMINNSF	OEIEDDADVE	KFARAKLWF	SYFEEGIRFE	LLEE		
TRPC6 Cele	MITAMMSHSF	OIINDHADLE	KEHRTKLWM	AHFDEGIRYE	LRDD		
TRPC7 Hean	MITTAMINISY	OFTEEDADVE	KEAPAKLWI.	SYFDECTRYE	LIFE		
TRPC7_Mmus	TAMINISVOF	TEEDADVEWK	FADARTWICY	FORCTOVELL	PP		
TRPC/_Millus	TAMINNSIQE	ILEDADVEWK	FARARLWLSI	FDEGIRIELL	EE		
TRPC/_Drer	MITAMINHSY	QEIEEDADVE	<b>KFARAKLWL</b>	SYFDEGIRYE	LLEE		
TRPN_Dmel_	LIGHAMMSDTY	QRIQAQSDIE	*KFGLSKLIR	NMHRTTSSDA	ESGS		
TRPN_Cele_	LIIIAMMSDTY	QRIQAQSDKE	KFGRAILIR	QMNKKSRDVD	LAMA		
TRPN_Drer_	L <mark>LIA</mark> MMSDTY	QRIQAQSDTE	<b>KFGRAVLIR</b>	DMSRKSTDE-			
TRPM1 Hsap	LLIAVFNNTF	FEVKSISNQV	KFQRYQLIM	TFHDRPLSNR	MVNA		
TRPM1 Mmus	LLIAVFNNTF	FEVKSISNQV	KFQRYQLIM	TFHDRPLSGR	MVSA		
TRPM2 Hsap	LUIAMENYTE	OOVOEHTDOI	KFORHDLIE	EYHGRPTLHW	IVRT		
TRPM2 Mmus	LUIAMENYTE	OEVOEHTDOT	KFORHDLTE	EYHGRPVLHW	TVTT		
TREPMS Hear	TUTATENNEE	FEVENTENOV	KEORVOLTM	TENEDDI TCD	MATTA		
TREMS_HSap	TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	FEVELSINGV	AREODVOLTM	TEHERPLICK	MADA		
TRPMS_MILLS	LUIAVENNIE	FEVESISNOV	MRFQRIQLIM	TEREFLICK	MAIA		
TRPM3_Drer	TITT AAA ENNIE	FEVESISNQV	*KFQRYQLIM	TFHERPMIGR	IAVA		
TRPM3_Dmel	LINIAVENNIE	NEVNSVSHQV	MFQRFTVVM	EYQQKPMSEQ	ILSH		
TRPM3_Cele	MULAIFNHIF	DATDEMSQQI	LFQRYKQVM	EYESTPVQNE	ILEC		
TRPM3_Cele	VAGCTYIFEK	HIQSTREIFL	FERYGQVMEY	ESTPMHKEQM	NL		
TRPM3_Cele	IAIFNNIYND	SIEKSKEIWL	FQRYQQLMEY	HDSPISDEVV	QI		
TRPM4 Hsap	LLIAMFSYTF	GKVQGNSDLY	KAQRYRLIR	EFHSRPCLGW	VAEA		
TRPM4 Mmus	L <b>LIA</b> MFSYTF	SKVHGNSDLY	KAQRYSLIR	EFHSRPCLTW	MAEA		
TRPM4 Drer	LUIATESYTE	TKVOEHSDKY	KFORYNLIV	EYHSRPCLOW	IMET		
TRPM4 Drer	LUIATESYTE	SKVOERSDTY	KFORYNLIV	EYHSRPCLOW	IMET		
TRPM4 Drer	LUTATESYTE	TRUCEHSDRY	KEORYNLTV	EVHSEDW	TMET		
TREMA Dror	TUTOMESYTE	NEWOFDODUV	KEORVNI TV	EVUEDDCT CW	TVEN		
TRENG DICI	LINE MESTIF	NICVQERSDVI	ANDODIDU TU	EINSKECLOW	IVEA		
TRPM5_Hsap	LITAMESTIE	QVVQGNADMF	TREORINLIV	EIHERPCVSS	VADV		
TRPM5_Mmus	THAME SALE.	QVVQGNADMF	WREQRIHLIV	EIHGRPCLSS	MTDT		
TRPM5_Drer	LUUAMFSYTF	QVVQENADIF	KFQRYNLIV	EYHSRPCLSW	IAEC		
TRPM6_Hsap	LUIAFFNNVY	LDMESISNNL	<b>KYNRYRYIM</b>	TYHEKPLSAL	TVDT		
TRPM6_Mmus	LLIACFNNIY	LDIKSISNKL	<b>KYNRYRYIM</b>	TYHQKPLSAI	TVDT		
TRPM7_Hsap	LLIA FFNNVY	LQVKAISNIV	KYQRYHFIM	AYHEKPLSAL	TVDT		
TRPM7 Mmus	LLIA _{FFNNVY}	LQVKAISNIV	KYQRYHFIM	AYHEKPLSAL	TVDT		
TRPM7 Drer	LLIAFFNNVY	LOVKSISNLV	KYORYHFIL	AYHDKPLSAL	TVDT		
TRPM8 Hsap	LIVAMEGYTV	GTVOENNDOV	KFORYFLVO	EYCSRL			
TRPM8 Mmus	LUVAMEGYTV	GTVOENNDOV	KFORYFLVO	EYCNBL			
TRPA Hean	LICLAVCDIA	FUOKHASLKR	TAMOVELHTS	LEKKLOTKLT	TOK		
TREA_HSap_	LIGLAVODIA	EVQNIASLIKK	TAMOVELINIS	DERREQUENT	TOK		
TRPA_Mmus_	LIGLAVGDIA	EVQKHASLKR	TAMQVELHTN	LEKKLQIKLI	IQK		
TRPA_Drer_	LIT GLAVGDI	AEVQTNACLK	RIAMQIELHT	NLEERLQLKL	IVQK		
TRPA_Drer_	LMIGLAVGDI	AEVQRNAELK	RIAMQIDLHT	ALEEKLQLKL	IIQK		
TRPA_Dmel_	LUUGLAVGDI	ESVRRNAQLK	RLAMQVVLHT	ELERKLQVRL	IVQK		
TRPA_Cele_	VGLAVDDIKG	VQEKAELKRL	AMQVDLVLQI	EASLQLKNIQ	EN		
TRPV1 Hsap	MILLALMGETV	NKIAQESKNI	KLQRAITIL	DTEKSFAEVY	LRQF		
TRPV1 Mmus	MUTALMGETV	NKIAQESKNI	KLORAITIL	DTEKSFTEVO	LKHY		
TRPV1 Drer	MUTALMNOSV	EMMSVESTST	KLOBAITTI.	DMEWILLSSS	v		
TRPV2 Hear	MINALMSETV	NSVATOSWST	KLOKATSVI	EMENGY			
TRPV2 Mmus	MINIMSET	NSVATDSWET	KLOKATSVI	EMENGY			
THE VZ PHILUS	MULLAIMORT	FUNCKEGEDT	PT OPAPTT	EFERMI			
INFV3_nsdp	MUTUTIOLIV	ENVORESERI	ADIODARTIL	SFERMIL			
TRPV3_Mmus	MILLALMGETV	LNVSKESERI	RLORARTIL	EFEKML			
TRPV4_Hsap	MINISTAL	GQVSKESKHI	KLQWATTIL	DIERSFEPLD	SMGN		
TRPV4_Clup	MILLALMGETV	GQVSKESKHI	KLQWATTIL	DIERSFEPLD	NMGN		
TRPV4_Mmus	MUIALMGETV	GQVSKESKHI	KLQWATTIL	DIERSFEPLD	NLGN		
TRPV4 Drer	MLIALMGETV	GQVSKESKKI	KLQWATTIL	DIERSFTEPL	TGRH		
TRPV5 Hsap	LF <b>IA</b> MMGDTH	WRVAQERDEL	RAQVVATTV	MLERKLGSEG	DGEE		
_ *							

NEISENADSI NIQYNYMSTV SAVKRDNQTQ QNVWSDAQRK QTVYDNSKAT

MD DIVE Marrie				MT EDIMOGEO	DODD
TRPV5_Mmus	LFIAMMGDTH	WRVAQERDEL	RAQVVATTV	MLERNMGGEG	DGEE
TRPV6_Hsap	LITAMMGDTH	WRVAHERDEL	RAQIVATIV	MLERKLGGES	WEIQ
TRPV6_Mmus	LIT AMMGDTH	WRVAHERDEL	RAQVVATTV	MLERKLGGEG	WEYQ
TRPV6_Drer	LI VAMMSDTQ	WRVTQERDEL	RTQVVATTL	MLERKLEC	EKEE
TRPMLI_Hsa	LFIALITGAY	DTIKHPGGAG	AEESELQAYI	AQ-CPTS	GKFR
TRPMLI_Mmu	LFIALITGAY	DTIKHPGGTG	TEKSELQAYI	EQ-CPTS	GKFR
TRPMLI_Dre	LFIALITGAY	DTITQQTQDV	PQVSELHRFI	AE-CPTS	GNFR
TRPML2_Hsa	LFIALITDSY	DTIKKFQQNG	FPETDLQEFL	KE-CSSK	EEYQ
TRPML2_Mmu	LFIALITDSY	HTIKKYQQHG	FPETDLQKFL	KE-SGSK	DGYQ
TRPML2_Dre	LFIALITDAY	ETIKGYQTTG	FPMTELHWFL	KGQKE-CQGQ	EEME
TRPML3_Hsa	LFIALITDTY	ETIKQYQQDG	FPETELRTFI	SE-CPNS	GKYR
TRPML3_Mmu	LF <u>UA</u> LITDTY	ETIKHYQQDG	FPETELRKFI	AE-CPNS	GKYR
TRPML3_Dre	LFUTLITDTY	DTIKHQQLDG	EPVSDLQAFV	LQ-CPDS	GEFS
TRPML3_Dme	LFUAVIMDAY	DTIKAYYKDG	FPTTDLKAFV	GTRTISS	GVFM
TRPML3_Dme	LFUAVIMDAY	DTIKAYYKDG	FPTTDLKAFV	GTRTISS	GVFM
TRPML3_Cel	LF <mark>IA</mark> IIMDAY	EVVKDRYSDG	LRAIEKRGCL	RDFVE-PSAY	APSN
TRPP_PKD1_	LGAVILRWRY	HALRGELRPA	WEPQDYEMVE	LFLRRLVEQQ	LHSL
TRPP_PKD1_	LGAILLRWRY	HALRGELRPA	WEPQDYEMVE	LFLRRLVEQQ	LQSL
TRPP_PKD1_	LMSALLR-NY	RRARAELRPA	VDLQDYEMVE	LFLRRLLEYR	IERL
TRPP_PKD2_ 1	MFLAIINDTY	SEVKSDLQQK	AEMELSDLIR	KGYHKAIIDA	VIVK
TRPP_PKD2_ 1	MFLAIINDSY	SEVKSDLQQK	AEMELSDLIR	KGCQKAIIDA	VIVK
TRPP_PKD2_ 1	MFLAIINDTY	SEVKADMQQR	SEMEITDLIK	KSYNRAIIDA	VIVK
TRPP_PKD2_ 1	MFLAIINDSY	VEVKAELRKK	DGEGILDWFM	NKVRGLIIEG	VNAT
TRPP_PKD2L 1	MFLAIINDTY	SEVKEELGQK	DELQLSDLLK	QGYNKTVIDA	VGSK
TRPP_PKD2L 1	MFLAIINDTY	SEVKEELGQK	DELQLSDLLK	QGYNKTVVDA	VGSK
TRPP_PKD2L 1	MFLAIINDTY	SEVKEELGQK	DQLQLSDFLK	QSYNKTVIDA	VGSK
TRPP_PKD2L 1	MFLAIINDTY	SEVKSELSQK	DEFQIADLIK	QSYAKTILDF	VMEK
TRPP_PKD2L 1	MFLAIINDTY	SEVKADYGRR	LDFELGKMIK	QSYKNVEC	LTKR
TRPP_PKD2L 1	MFLAIINDTY	SEVKADYGRR	PDFELGKIIQ	KSCFNVVLNQ	LMRK
TRPP_PKD2L 1	MFLAIIMETY	NTVKGEI-TQ	GRSHLGSYIY	RKLSGMLMDD	ILKR
Cca7050	WKASFGATVI	DVQKSQ			
Cca21784	WKFTRAELLM	QVKHTH			
Cca260897	AETRDDDEMT	VTDYFKKSYN	KL		
Sla36613_6 1	NDYEVFDYIL	GKFKNI			
Sycon24227	AQRELEQNWA	ASLRNLEQGT	TRQSLDEQ		
Sycon24228	RELEQNWAAS	LRNLEQGTTR	QSLDEQ		
Sycon9763_	vwx				
Ava16635_4	WKYKFFNSVK	EFRDKPSRRI	LIRY		
Ava9904_1	WKFTRYSAIE	EFRLKPVCHT	LLDH		
Ava7536_5 .	ATMEKARILL	SFERKLLMGE	LEKR		
Ava6620_1	YTTQFLEVVD	EYQRKSVGVK	SVNL		
Cca31351	WKEERLKTVS	SDFLS-DCRF	CLDM		
Cca30979_3	NKYEVVEYIK	ELVGL			
Ava26193_2	LYKNRAWILA	RIEHNSILQA	RDKQ		
Ava26160_2 .	ATMEKARILL	SFERKL			

### A1.4 Phylobayes alignment of data in 2-5c.

(Tree has been split into four pages for viewing. For the full scale complete tree see http://www.biomedcentral.com/1471-2148/14/3/additional)









0.5

### A1.5 Full alignment of sequences in Figure 2-5c and list of Sponge TRP Fastas

### Supplementary Figure S4

TRPC1_Hsap_NP_003295.1 TRPC4_Mmus_NP_035773.1 TRPC4_Mmus_NP_03297.1 TRPC4_Mmus_NP_058680.1 TRP_Spur XP_793901 TRP_Stow_XP_002733765.1 TRP_Stow_XP_002733765.1 TRP_Lflor_emb CAA11261.1 TRP_Bflo_XP_002511405.1 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec1_XP_001637374.1 Cca7050 Cca21784 Ava16635_4 Ava6620_1	    	    		 	     FTASPRDNYT  NKT	
TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4_Mmus_NP_03680.1 TRPC4_Mmus_NP_058680.1 TRP_Spur XP_793901 TRP_Stow_XP_002733765.1 TRP_Stow_XP_002733765.1 TRP_Bflo_XP_002611405.1 TRP_Bflo_XP_002611405.1 TRP_Stow_XP_002576849.1 TRP_Mvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409						    IMIVTMIGGE
Ava904_1 Ava6620_1	DLQVMDNPTP	SPTGSQTDRL	ISSSLTPQTS	ERNVTKSLNN	LEASRLRPRL RL	PFVKQAMGNK DFISRA
TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4_Hsap_NP_003297.1 TRPC4_Mmus_NP_058680.1 TRP_5lpur XP_793901 TRP_Cint XP_002124651.2 TRP_Slow_XP_002733765. 1 TRP_Eflor_emb[CAA11261.1 TRP_Bflo_XP_002611405.1 TRP_Bflo_XP_002611405.1 TRP_Mvec4_XP_001640409 TRP_Nvec1_XP_001640409 TRP_Nvec1_XP_001637374.1 Cca7050 Cca21784 Ava16635_4 Ava904_1 Ava6620_1	M M CVSCTSLQSN 	GAPPPSPGLP   GHGNKPTHGV  GHGNKPTHGV  AVPFSGSLPR 	MMAAL PSWAAMMAAL   PPIATNMAAT   KRVMLQRIES 	YPSTDLSGAS YPSTDLSGVS	SSSLPSS – - SSSLPSS – -   ADRIPLRVVH   ARELKNSMDT 	- MMELSSSTL HESDLS EAEK
TRPC1_Hsap_NP_003295.1 TRPC4_Mmus_NP_035773.1 TRPC4_Mmus_NP_03297.1 TRPC4_Mmus_NP_058680.1 TRP_Spur XP_793901 TRP_Stow_XP_002733765.1 TRP_Stow_XP_002733765.1 TRP_Lflor_emb CAA11261.1 TRP_Bflo_XP_002516849.1 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec1_XP_001640409 TRP_Nvec1_XP_001637374.1 Cca7050 Cca21784 Ava6635_4 Ava6620_1 TRPC1_Hsan_NP_003295.1	 ELVTPPTRGD RFLVSVERGD   NNQEALNRAD  E	 SPMMFPRNAN YATVRKILED   TEVIKRQTIL 	Y QNRGV Y QNRGV YGPGEQSGRL  MSRHENKENI TM	PSSS PSSS MAQF MAQF  ASGLLNAAFT FVCLFNMAAT  TSVNENETQS TSCSLQEKDW	SPNEVMALKD SPNEVMALKD YYKRNVNAPY YKRNVNAPY QRRSASVISG IPDEVLQEED 	VREVK VREVK RDRIPLRIVR RDRIPLRIVR  ADRIPLRVVH  FSKMKIDHAS FSRLSITSGN
TRPC1_Mmus_NP_03297.1 TRPC4 Hsap_NP_003297.1 TRPC4 Hmus_NP_058680.1 TRP_Spur XP_793901	E A A					

TRP_cint XP_002124651.2 TRP_Skow_XP_002733765.1 TRP_Lflor_emb CAA1261.1 TRP_Bflo_XP_002611405.1 TRP_Mvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec1_XP_001637374.1 Cca7050 Cca21784 Ava16635_4 Ava904_1 Ava6620_1	E H PGDHVEMNKL EKAEFLEEQL	MSTDCLD FTVPD-SISN QNVLSVTYQG	VDMLVMLCQS TEITPLLDQH SDISEIPCVH	DVDLLLSDEN TGNVENEIEK SKALKKSDEI	NITAMHHMVE TVDGHIHFPT EIDTDFEYSC	KHRPTDAHLV RHGRKDANYL GNVKFEGAYE
TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4_Hsap_NP_003297.1 TRPC4_Msap_NP_058680.1 TRP_Spur_XP_793901 TRP_Cint XP_002124651.2 TRP_skow_XP_002733765.1 TRP_fbio_meb CAA11261.1 TRP_fbio_XP_002611405.1 TRP4_Sman_XP_002576849.1 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_001640409 TRP_NVec4_XP_00040409 TRP_NVec4_XP_00040400409 TRP_NVec4_XP_00040400400400400000000000000000000	HTLASERP IIIPPQASPS- VADPAKKPKI		LLDVLSKTWK QLPKIHKYFK			IISLPGTSQ- TLILPSTTDH
TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4_Hsap_NP_003297.1 TRPC4_Mmus_NP_058680.1 TRP_5pur XP_793901 TRP_cint XP_002124651.2 TRP_Skow_XP_002733765.1 TRP_Eflor_emb CAA11261.1 TRP_Bflo_XP_002611405.1 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001637374.1 Cca7050 Cca21784 Ava16635_4 Ava9604_1 Ava6620_1	LSQG CPENAIRNRD	SRFRQMLKEN PNYMKNFLSD	LIRIAATTKA MRQIIRNTDT	WFLTEGVNKG WVLINGLNWG	ISAFVGSCLQ LTRIIGENIA	SHAYKRFAKK TRVLSPFTAE
TRPC1_Hsap_NP_003295.1 TRPC1_Mnus_NP_035773.1 TRPC4_Mnus_NP_003297.1 TRPC4_Mnus_NP_05860.1 TRP_Cint_XP_002124651.2 TRP_Spur_XP_703901 TRP_Cint_XP_002133765.1 TRP_Lflor_emb CAA11261.1 TRP_Bflo_XP_002611405.1 TRP4_Sman_XP_002576849.1 TRP_Nvec1_XP_001637374.1 Cca7050 Cca21784 Ava16635_4 Ava9604_1 Ava6620_1		TGFGDYDAPI	PIIGMVNPEN PIIGMVNPEN PIIGKVKDS	I YKGTLFQNP LPATVRNC HTVMARNEEL	TDSITYGKDN ISRLSMKAQL IPLREREEIQ	ENT ESE ESE GNR MSKKPPRKRD SD YDF SSLCFPDRNL EEDTIP-RGC EVLPIRHSDN
TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4_Hsap_NP_003297.1 TRPC4_Mus_NP_05860.1 TRP_Spur XP_793901 TRP_Cint XP_002124651.2 TRP_Stlor_emb(CA11261.1 TRP_Bflor_menb(CA11261.1 TRP_Bflor_XP_002611405.1 TRP4_Sman_XP_002576849.1	LNEKIFIL ISPSEKAYIN ISPSEKAYIN SNHKEFGFIL ITAKERMFME INNEERQFIG ISEAEKRFIV	ACDKGDYYMV ACDKGDYYMV AVEKGDYASV AVEKGDYASV ARSPMTETER ARSONATI AAEKGDNATI AVARGDVGSV SVERGDYATV	KK KK PR QK RK RK			

TRP_Nvec4_XP_001640409 TRP_Nvec1_XP_001637374.1 Cca7050	NTIRDSL <mark>E</mark> LH	ACVHGSKATL	 QE			
Cca21784 Ava16635 4	DANHSHITV	LSKSISGNSL	DO-WSC			IE
Ava9904_1	LEENHSL <mark>B</mark> LS	LKDNLDRDEI	ETFWDT			IE
Ava6620_1	TMKHWEYVE	ARLDNREQQ	PNFWKIPFAF	GHSLVDDSKD	DRLVTHYKHV	PQKSIHQETK
TRPC1_Hsap_NP_003295.1						
TRPC1_Mmus_NP_035773.1 TRPC4_Hsap_NP_003297.1						
TRPC4_Mmus_NP_058680.1						
TRP_Spur_XP_793901 TRP_Cint_XP_002124651.2						
TRP_Skow_XP_002733765.1						
TRP_Lfloremb CAA11261.1 TRP_Bflo_XP_002611405_1						
TRP4_Sman_XP_002576849.1						
TRP_Nvec4_XP_001640409 TRP_Nvec1_XP_001637374_1						
Cca7050						
Cca21784						
Ava9904 1	HTQIIKRIED	IKAATCRESI	ILDLEQKWDK	NREAPNTPKT	KTSLVELSTK	RNSEVGEPKP
Ava6620_1	DEGDLVKKPS	TKFYDIVEIP	ILDDPSNIDF	LKYAKSLKQI	LEVGKDLAYD	RFNYRSKIDF
TRPC1 Hsap NP 003295.1						
TRPC1_Mmus_NP_035773.1						
TRPC4 Hsap_NP_003297.1 TRPC4 Mmus NP 058680.1						
TRP_Spur XP_793901						
TRP_Cint XP_002124651.2 TRP_Skow XP_002733765 1						
TRP_Lfloremb CAA11261.1						
TRP_Bflo_XP_002611405.1						
TRP_Nvec4_XP_001640409						
TRP_Nvec1_XP_001637374.1						
Cca21784						
Ava16635_4		-VSNHLKIGK	EPL			PIVRI
Ava9904_1	DGDLIEMGKL	EKANFVIFED	EPTRVGRTID	SGPRIPSEFQ	NLWFKQIEFK	DPDINPAVCL CRITNIVLES
MV00020_1	1 10111111111111	INTONOLLINV		-		-
TRPC1_Hsap_NP_003295.1			ILEENS	SG-DLNINCV	DVLG	RN
TRPC4 Hsap NP 003297.1			SLEEAE	IYFKININCI	DPLG	RT
TRPC4_Mmus_NP_058680.1			SLEEAE	IYFKININCI	DP <b>lg</b>	<mark>R</mark> T
TRP_Spur_XP_/93901 TRP_Cint_XP_002124651.2			NLLRAF	TNRNIGLGVI	GFN <b>G</b>	NV
TRP_Skow_XP_002733765.1			CLKHPD	PVNVNVT	NI <mark>LC</mark>	<b>R</b> S
TRP_Lfloremb CAA11261.1			ALAEAE	ERF-IDISCK	DSLG	RS
TRP4_Sman_XP_002576849.1					MG	
TRP_Nvec4_XP_001640409						
Cca7050						
Cca21784			ADV VICONE	IMPREMENTE		
Ava9904 1	LLDNSIDGLR	HTLHAIRNRV	PTILVIGSGI	AADMIHQIM-	-L <b>I</b> S	RD
Ava6620_1	LERAKHDGVK	QITERIQNRL	NFL-GFYDKP	LKQDIDPEAP	NA <mark>LG</mark> NKRYLL	STDGCRELKS
TRPC1 Hsap NP 003295.1	AVTUTIENEN	LDILQ <mark>I</mark>			<b>IT</b> D-Y	
TRPC1_Mmus_NP_035773.1	AVTITIENES	LDILQ <mark>L</mark>			LLD-Y	
TRPC4 Hsap_NP_003297.1 TRPC4 Mmus_NP_058680_1	ALLIAIENEN	LELIEN				
TRP_Spur XP_793901	TRGG	IDIIVV			<b>II</b> E-H	
TRP_Cint XP_002124651.2	AAGIAVELKD	DLLIK <mark>L</mark>			IVVEH	
TRP Lflor emb CAA11261.1	SLVIAIENEN	DDLVSL			LIN-Y	
TRP_Bflo_XP_002611405.1	all <mark>i</mark> aienen	LELVG <mark>L</mark>			IVS-Y	
TRP4_Sman_XP_002576849.1 TRP Nvec4 XP 001640409		TEMTD				
TRP Nvec1 XP 001637374.1						
Cca7050 Cca21784					<b>ILL</b> Q	

Ava9904_1 Ava6620_1	HEV <mark>I</mark> SISNEV MASSSISKVL	REYLKQNYPL KGCIV <mark>I</mark> RHDH	QALRLPEDLL NDGKLVKEHL	RRVISSVVDN LYETSCLLKI	EENFTFY PGNKIEFIVE	PGKRTCHEVQ
TRPC1 Hsap NP 003295.1						
TRPC1_Mmus_NP_035773.1						
TRPC4 Hsap_NP_003297.1						
TRP Spur XP 793901						
TRP Cint XP 002124651.2						
TRP_Skow_XP_002733765.1						
TRP_Lflor_emb CAA11261.1						
TRP4 Sman XP 002576849 1						
TRP_Nvec4_XP_001640409						
TRP_Nvec1_XP_001637374.1						
Cca7050						
Ava16635 4						
Ava9904 1						
Ava6620_1	IDFLDPHYKE	TDDRVYNFYR	KEPELYQMIL	QKADEYFYRD	ESDFKGWNTM	TTALFLRDQY
MDDC1 Haar ND 002205 1		CC	0			
TRPC1_HSap_NP_003295.1 TRPC1_Mmus_NP_035773.1		GC	OSADATTVAT	DS		
TRPC4 Hsap NP 003297.1		NV	YVGDALLHAI	RK		
TRPC4_Mmus_NP_058680.1		NV	YVGD <mark>ALL</mark> HAI	RK		
TRP_Spur_XP_793901		GI	QLGDALLRAV	DE		
TRP_CINC_XP_002124651.2		LIKQPSMA	KIGDALLUAT	BE		
TRP Lflor emb CAA11261.1		DV	DLEDSLLHAI	RE		
TRP_Bflo_XP_002611405.1		NV	RVGDALLHAI	KR		
TRP4_Sman_XP_002576849.1						
TRP_NVeC4_XP_001640409		GA	DVGA	5K		
Cca7050		LGASIDGK	DGASG	LAASSAVNQT	AIENVNILMA	NGADLHVTSS
Cca21784						
Ava16635_4		DMNMTYGA	DLSKAIVVAL	LKSRKSTGKE	KLKEALDLVI	DWNRVDLAEQ
Ava9904_1 Ava6620_1	RVRRALERT	HPLRHGIH	OTGRITRYAL	EXGSPEIVEN	TF	RWKRPSLALE
		£	2			
TRPC1_Hsap_NP_003295.1						KLME
TRPC1_Mmus_NP_035773.1			EV	VGAVDILLNH	RPKRS	SRPTIVKLME
TRPC4 Mmus NP 058680 1			EV	VGAVELLLNH	KKPS	GERQVPPI
TRP Spur XP 793901			QF	IYAAQIICEH	IKQKNIPEFL	
TRP_Cint XP_002124651.2			GY	LRIAEILMNH	PSFCVNQRLT	TSPGELMLID
TRP_Skow_XP_002733765.1			GV	YKMVEMMVNH	PSISREML	GGEWS-KMTK
TRP_LIIOFemb(CAAII261.1			EI	VGAVENILIH	QLKKF	TEDKTOYM
TRP4 Sman XP 002576849.1						
TRP_Nvec4_XP_001640409			DN	VLYVKALLAY	ENNN-DRF	SRRSSSCV
TRP_Nvec1_XP_001637374.1	N					
Cca21784	IN	GQN	LCHIAAILON	MOTATD-		
Ava16635_4	NIFTESMVW-	GDTDLFQH	-YFAILILNQ	VDFLELMLER		
Ava9904_1	KIFIGREKWI	SEDDTRAVQR	IFFSALTTNN	TGFVHRMLES		
Ava6620_1			NN	SDIQQRLIKK		
TRPC1 Hsap NP 003295.1	RION	PEYSTTMDVA	PVILAAH	RNNYEILTML	IKODVSLPKP	AVGCECTLO
TRPC1_Mmus_NP_035773.1	RIQN	PEYSTTMDVA	PVILAAH	RNNYEILTML	IKQDVSLPKP	HAVGCECTLC
TRPC4 Hsap_NP_003297.1	LLDK	QFSEFTPDIT	PIILAAH	TNNYEIIKLL	VQKGVSVPRP	HEVRONOVEC
TRPC4_Mmus_NP_058680.1	LLDK	QFSEFTPDI	PIILAAH	TNNYEIIKLL	VQKGVSVPRP	EVRONOVEC
TRP_Cint_XP_002124651.2	PNSDFYAYDN	DGTRFSPDIT	PITLAA0	COEFDIVYEI	IRRGATIOHP	PYRCOCTEC
TRP_Skow_XP_002733765.1	DPQE	ESSDYSPDIS	PVILAAH	CNQFEILQLL	LTRCATISTP	HNVTCGCEHC
TRP_Lflor_emb CAA11261.1	QIEF	KSNTFTADIT	PIILAGH	IDNYEIIKML	LDRGYRIPKP	HDLTCHCDDC
TRP_Bflo_XP_002611405.1	KYVQ	KESDFTEDM	BIILAAH	KNNYETIKII RDNYVIIVI	LQKGHPIPKP	DVROTONEC
TRP Nvec4 XP 001640409	NLSK	NTNDSNRYM	PLILASH	NNSYDIVKII	ISKCHTIDRV	DRGCLOPWO
TRP_Nvec1_XP_001637374.1			PLVVAAQ	lg <mark>nye</mark> vlnml	VSKGFQLVKP	HNVLORCEEC
Cca7050	ARVD	HTYQDKEGST	PLHYACAA	PENDAVISLI	IEAGLDMNEP	NSDGLTPLNL
UCa21/84 Ava16635 4	KGVD	HIKSDREGN	BLHY AAA-AV	DDNHDVIEIL RNNDLT FZCT	IGDACDTNAA	NSKAQTPLCF
Ava9904 1	KIIN	FRYFG	NMYYLSO	LYKRT	FDKLSDSEED	IIANKMLRLN
Ava6620_1	REEN	LTSVFKKSGQ	EL <b>TI</b> FQR	LMFA	TKDEEYVEK	KIKG <mark>C</mark> KAEFT
MDDC1 Hoop ND 000005 1	CAUNIER					
TRPC1_Mmus_NP_035773.1	SAKNKKDSI-					

TRPC4 Hsap_NP_003297.1	VSSSDVDSI-					
TRPC4_MMUS_NP_058680.1 TRP Spur XP 793901	AFSTETNTI-					
TRP Cint XP 002124651.2	TAMRRDDAL-					
TRP_Skow_XP_002733765.1	TEKQHEDSL-					
TRP_Lflor_emb CAA11261.1	LRGSLVDVL-					
TRP_BIIO_XP_002611405.1 TRPA Sman_XP_002576849_1	TKARRENCE-					
TRP Nvec4 XP 001640409	OSLGRI-					
TRP_Nvec1_XP_001637374.1	QA <b>D</b> NF-					
Cca7050	SIKSQHVNNV	IPLIRAMVDI	TKC			
Cca21784	AVLSNQV'I'NI	VPLIRSSADI	RKA		OKIDINE	
Ava9904 1	FSESKHRKDP	ROILYEIGKL	IKELMGNDYV	CFYNHLPISR	KKREYEEENI	KKNVNSCYNF
Ava6620_1	ASLE					
TRPC1_Hsap_NP_003295.1					RHSRFREDIY	RCLASPA
TRPC4 Hsap NP 003297 1					RHSRSRINTY	KALASPS
TRPC4 Mmus NP 058680.1					RHSRSRLNIY	KALASPS
TRP_Spur XP_793901					Q <b>HS</b> LGMLNIY	r <mark>alas</mark> qa
TRP_Cint XP_002124651.2					NFCLSRLNAY	KGLASPV
TRP_SKOW_XP_UU2/33/65.1 TRP_Lflor_emblCA11261_1					CHSRARINTY	RALASPA
TRP Bflo XP 002611405.1					RHSRORLNVY	RALASPS
TRP4 Sman XP 002576849.1					QHSTIRINTY	RALTSPS
TRP_Nvec4_XP_001640409					GTSLHRLYTY	RALASPVYMS
TRP_Nvec1_XP_001637374.1					RESORREDIY	RGLANPV
Cca21784					GTORI BIERI	OLLARDE
Ava16635 4	IGKLLKY	VLK	YSFKDVYV	ENEGMHDIIE	NEPIDNEFIW	AVITORWRMA
Ava9904_1	LRHIATLMKQ	CLKRFRVRKL	TAQTKKLKLV	RAEKAQRLFE	QFPEEQVFIW	CLIFHRWEMA
Ava6620_1	VVKFLQL	AIEKLMGDGF	LWNIPDVQRH	DMQLNLTHYE	VYFAEYIMVW	G <mark>AL</mark> SQRYEVA
TPDC1 Hear NP 003295 1					TRAFFICART	12
TRPC1_Mmus_NP_005295.1	T.T.VT.T			EEDEI	LRAFELSADI.	K
TRPC4 Hsap NP 003297.1	LIALS			SEDPF	LTAFCLSWEL	Q
TRPC4_Mmus_NP_058680.1	LIALS			SEDPF	ltafolswel	Q
TRP_Spur XP_793901	YISIT			SLDPI	NTGERCVKL	R
TRP_CINC_XP_002124651.2					TTAEKI SWEL	F
TRP Lflor emb CAA11261.1	LIALS			SKDPI	LTAFELSWEL	R
TRP_Bflo_XP_002611405.1	LIMLS			SDDPI	LTAFQLSWEL	RGSVTTRLFN
TRP4_Sman_XP_002576849.1	FUILT			SNDPI	LTAFELSWEL	K
TRP_Nvec4_XP_001640409	LTELS			CKDPV	ROAFELNKEL	V
Cca7050	ITEA			SPKPL	EYTLMLSSEF	E
Cca21784	MIQA			SAEPL	KFVL <b>ELS</b> YLY	R
Ava16635_4	evl <mark>i</mark> sntnsv	I		FNAV-AAKAL	IAGMHHHLKD	D
Ava9904_1	ILILKYCNKT	C		LTTVLSAARL	IRGMKIKYQS	R
AV86620_1	ELFEISGGH	LQELLTRDRE	FIRIQKGVIQ	IANALAISRL	IGVOQELRE	D
TRPC1 Hsap NP 003295.1		EISLVEV	EFRNDYEELA	ROCKMFAKDL	LAQARNS	RELEVILN
TRPC1_Mmus_NP_035773.1		ELSLVEV	efrndyeela	RQCKMFAKDL	LAQARNS	RELEVILN
TRPC4 Hsap_NP_003297.1		ELSKVEN	EFKSEYEELS	RQCKQFAKDL	IDQTRSS	RELEIILN
TRPC4_Mmus_NP_058680.1 TRP_Spur_XP_793901		ELSKVDN	EEKSEMEELS EESVEENTIA	GOCEOFARDL	GHIBNO	ABOTCVIY
TRP Cint XP 002124651.2		KMATMOK	EFKKDYLKIV	HOLYDYLEKI	IDICRNS	EDVNAMUS
TRP_Skow_XP_002733765.1		HIAMRIN	EFKDVYQQLS	h <u>q</u> sktyAvdl	LEQCRSS	EEVIAVLN
TRP_Lfloremb CAA11261.1		NLSEMEN	EFRAEYEELG	ITCQNFAVDL	LEQIRGS	KELEVILN
TRP_Bilo_XP_002611405.1	SFHHQFLAKT	FLLTLSTLON	EFKSEYEQLS	KQCKKFASDL	LSHTRGT	RELQVILN
TRP Nvec4 XP 001640409		ELADIBY	EFRSDYLOUS	COCEEFAVAL	DOCRDM	SEIEOMMS
TRP Nvec1 XP 001637374.1		VIARRED	EYEKDYLQLS	QQCSQFTIGL	IDECRTS	REQRCILN
Cca7050		RMAKERM	RLKESYMALS	VQLEDAAIDL	IEGLHSS	QLQGLVLH
Cca21784		HWGYNHP	LOKARMEALS	MEMEELAVSM	VDSAPPV	LLLKVLTN
Ava9904 1		QIVSE	LARDRINNA	NDFENIAT 7	CEFSVSDH	POAHEINO
Ava6620 1		TAVST	DDRETLIQKA	AYFEELAVGL	DNAIGK	NEFTLNELFN
_						
TRPC1_Hsap_NP_003295.1		HTSS	-D	EPLDKRGL	LEE	
TRPC1_Mmus_NP_035773.1		HTSS	-D	EPLDKRGL	LEE	
TRPC4 Mmus NP 058680.1		YRDD		NSLIEE	-05	
TRP_Spur XP_793901		HDPC		-FYSIGES	~	
TRP_Cint XP_002124651.2	GNYSDSWKGL	ARKQSGRTSS	NEITNNHLMK	SFSNVADE	HID	
TRP_Skow_XP_002733765.1		RDND	SE	DGFAEEDV	MGG	

TRP_Lfloremb CAA11261.1 TRP_Bflo_XP_002611405.1 TRP4_Smar_XP_002576849.1 TRP_Nvec4_XP_001640409 TRP_Nvec1_XP_001637374.1 Cca7050 Cca21784 Ava16635_4 Ava9904_1 Ava620_1		HDCR HSDD HYTG YPDM YPGE 	ADVSGCHVSG -D L VECSELIGLE	-SPDQDEE MVES INQSLSED -GALTKN NGSVEDYA-  VAACQDDKPP	-KE ATS ISE    VEGDNLLMRE	QDDSTTYIWP
TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4_Hsap_NP_003297.1 TRPC4_Mmus_NP_058680.1 TRP_Spur XP_793901 TRP_Cint XP_002124651.2 TRP_Skow_XP_002733765.1 TRP_Lflor_emb CAA11261.1 TRP_Bflo_XP_00251405.1 TRP_Mvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001647374.1 Cca7050 Cca21784 Ava16635_4 Ava964_1 Ava6620_1	RMNUSRLKLA RMNUSRLKLA GNDJARLKLA GNDJARLKLA GNDJARLKLA GIGPYKNUR HPRUYCLKLA KKITUIRLKLA LKKUSRLKLA SNSJARLKLA SNSJARLKLA SNSJALKUNA SKISUCUDYA AGNVLEMA EIVEMA YDDINCIEMA WHENNAFDMA WHENTATELA	IKYNOKESVS IKYNOKESVS IKYNOKESVS IKYROKESVA IKECKESVA IKECKESVA IKECKESVA IKYEOKESVA IRYCOKESVA ISTORKESTA ISTORKESTA ISTORKESTA ISTORKESTA STORKESTA STORKESTA STORKESTA	QSNCQCFUNT QSNCQCFUNT CENCQCLUAS HEHCQCLIAS HEHCQCLIAS HENCQCLIAS HENCQCLIAS HENCQCLIAS HENCQCLIAS HENCQCLIAS HECQCLIAS HEFCOHLUMQ TDAV0YEENR HEFCOHLUMQ TDAV0YEENR HECVSLIDE HECVGGHWRN HECVGGHWRN	VN VN RN RN RN IN IN IN IN IN IN IN IN IN I	-FGQMSGYRR FGQMSGYRR YDEFPGMSR YDEFPGMSR WECIPSWRQ HECIPSWRQ YECIPSWR YECFPSMSR YECFPSMSR FGDITGMT -HE	KPTCKKIMTV KPTCKKIMTV RHWAVKMVTC RHWAVKMVTC RHWAVKMUTC LSIGYKFLLA HNAFVKLLIC KPILKQITVA KHWAVKVIIC KPVFAOLTTI MGVTLKIIFA VNFLYRIAVV QEPSYKALLK NSIPLRILIS QNKLWKKLS QNKLWKLISC INIGVQLKNS
TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4_Hsap_NP_003297.1 TRPC4_Mmus_NP_05860.1 TRP_Cint XP_002124651.2 TRP_Skow XP_002733765.1 TRP_Lflor_emb CAA11261.1 TRP_Bflo_XP_002611405.1 TRP4_Sman_XP_002576849.1 TRP_Nvec1_XP_001637374.1 Cca7050 Cca21784 Ava9604_1 Ava6620_1	LTVGIFWEVL LTVGIFWEVL FIIGLLFVF SAIGFGEIN VGMSLFMEVL LAVILIJELM FGILGELFIL LLFTFISVW LTVVIFFVL LTFVFILQAI LIFTVFILQAI LIFVFILQAI LIFVFILQAI LIFVFILQAI	S LCMLIA S VCMLIA S VCMLIA C LLMLIY S LLMLIY S LAMFUA A LCMLLF S GIMMLA A TVMIA A TVMFT A VIMPFT A VIMPFT A VIMPFT N SFSDPQ L ELFQR N FF	FKS           FKS           FKS           FWG           FWG           FHT           FHS           FS		ULNIQ 	QF PL NI KI KI KI KL KL 
TRPC1_Hsap_NP_003295.1 TRPC4_Hsap_NP_003297.1 TRPC4_Hsap_NP_003297.1 TRPC4_Hsap_NP_003297.1 TRPC1_Msus_NP_05860.1 TRP_Spur_XP_793901 TRP_Cint_XP_002124651.2 TRP_Skow_XP_002733765.1 TRP_Lflor_emb CAA11261.1 TRP_Bflo_XP_002611405.1 TRP4_Sman_XP_002576849.1 TRP_Nvec1_XP_001637374.1 Cca7050 Cca21784 Ava16635_4 Ava9604_1 Ava6620_1	CRIIHTPOMK CLFIRKPIK CLFIRKPIK CLFIRKPIK CLFIRKPIK CLLRTPOMK CLLCRKPIK CLLRTPOMK CKLIRKPIK CKLIRKPIK CKLIRKPIK CKLIRTPIK CKLIRPIK CKLIRPIK CKLIRPIK CKLIRPIK CKLIRPIK CKLIRPIK CKLIRPIK CKLIRPIK CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP CKLIP	III CASYFT III CASYFT IICTASYIT ICTTASYIT ICTISSII ISSI ISSI ISSI ISSI ISSI ISS	FILLINGUS FILLINGUS FILLINSQ FILLINSQ FILLINSQ FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS FILLINSS F	V H DRVEGFEFSS V PSLVGDEADD QRFISSNT HQFE DH FQWHPSPN FVRPIRNRT FTWEPSHKNG	T	FTPK FTFL ENPFFFLFPM TVEWMIFVWV VEFLLTN VEFLLTN
TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4_Hsap_NP_003297.1 TRPC4_Mmus_NP_058680.1 TRP_Spur XP_793901 TRP_Cint XP_002134651.2 TRP_Skow_XP_002733765.1 TRP_Lflor_emb CAA1261.1 TRP_B10_XP_002611405.1 TRP_Movec1_XP_001637374.1	YNEDKK-NTM YNEDKK-NTM IDRSDL-NRQ YDDDPDVDQR LHQTSR-DGR KEEKKISELR LERRQV-RPA SLDQRM-HDR IRF	GPALERIDYL GPALERIDYL GPPPTIVEWM AEVPKPTEWL HTQFNWCEVF GREPNFIBVL GSPATIVELM EPVPNTVEWM GPTPSLTESA KFLFNFSDIL RKMPSGLEWL	LILMIIGMI LILMIIGMI ILFMVLGFI ILFMVLGFI ILHGMAMELM IMLYIACLL ILGYVIGHI ICYVIGHI IFVMVLGMI LVIVVI ITIMIFGI IFSMILGVA	EIPPTTMLYS	TME I PTAFTD	DEFTTSGETP

Cca7050 Cca21784 Ava16635_4 Ava9904_1 Ava6620_1	EFS DRI DIA DIA	KPFMTKIBWI EAILDGLLLV LNPCBWI NDPLLIIBLI FVTFDVI	TLAYVLALL- FFIFVFGLI- FIVWSLTYI- VWVWTFTII- YFLYMVAYI-			
TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4_Hsap_NP_003297.1 TRPC4_Mus_NP_05860.1 TRP_Spur_XP_793901 TRP_Cint_XP_002124651.2 TRP_skow_XP_002733765.1 TRP_Lflor_emb[CAA11261.1 TRP_Bflo_XP_002611405.1 TRP_Bflo_XP_002611405.1 TRP_Nec4_XP_0016470409 TRP_Nvec1_XP_001637374.1	VTVTDPATTM		RIERLHKDVM	SDIK SDIK SDIK SDIK SDIK SDIK SDIK SDIK		YECLEDFL YECLEDFL DGCLQDYI DGCLQDYI DGCQDYI DGCPRNYI ECLKAYI MQGALEYI QGALEYI 
Cca21784 Ava16635_4 Ava9904_1 Ava6620_1		L L M LDEVFQ	YRFLIEDKTK	QIR EVR GKHIKHNQYI	SFL OLFAGNGRVM OLLHEKGSLL RIL	REGFHFYF RLERRFYF KRVSAYL NRIRGYI NSALFEYL
TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4_Hsap_NP_003297.1 TRPC4_Mmus_NP_058680.1 TRP_Spur_XP_793901 TRP_Cint_XP_002124651.2 TRP_skow_XP_002733765.1 TRP_Lflor_emb CAA11261.1 TRP_Bflox_XP_00211405.1	EESRNQLSFV EESRNQLSFV HDWMNLMDFV HDWNNLMDFV KSQLTLMDER IQLMNVLDFF RQWNWLDFT HDMNIMDLV SDQMNVMDFI	MNSEY MNSEY MNSEY MAKIE MLLIL LSEY TNSEY MNSEY	LATFAL LATISL LATISL AESEAA ITSFAS LCTISL WATFTL VATIAL	KVVAHNKFH- KVVAHNKFH- KIVAFVKYS- AVAAPVVSGG SFISHRNSWI RFTAWWLKKS RLLAWLQVRR RVVSYIKFKD	RRGKKAAAGT AQQRWDEIFK GT ERAE	ATNT ENATFVECDH
TRP4 Sman xP 002576849.1 TRP.Nvec4 XP 001640409 TRP Nvec1 XP 001640409 Cca7050 Cca21784 Ava16635_4 Ava904_1 Ava620_1	RLKGNSIWLL SQWWNLVTLA SSGNNMDIG TRLGHKTNCI SGLDYKMDIS NDRWNQFDTA SSANNIJLA SSGNNIJLA	YNLCYKKGVL MLGTF MVFLL IITMF FALFF LILTF LAIGF	WKTKRSURQI IISGI LGAFV 	KIVFYNEP WVAGSALS WTIIFIV RLIVIYS RAIAYFT RLIPQVPLS KLGCDCS-A RISVFII		
- TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_003297.1 TRPC4_Hsap_NP_003297.1 TRPC4_Mmus_NP_058680.1 TRP_Spux XP_793901 TRP_Cint XP_002124651.2 TRP_skow_XP_00213765.1 TRP_Lflor_emb CAA11261.1 TRP_Bflo_XP_002611405.1 TRP_Nvec1_XP_001637374.1 Cca7050 - Cca21784 Ava16635_4 Ava9004_1 Ava620_1	MSGNITLFGQ		DFADR ALNPB ALNPB TRTGR CYYSYKHADS PST7DEVQP -LNPYAFEER GIHPR QIHPR VSKEG DFDSN VSKEG DFDSN 	KDMDAFHBTL KDMDAFHBTL ESMDWHBTL ESMDWHBTL ESMDWHBTL ANNSAYDGIL ANNYCSDGOL ATWPCDDTI KHMDAYDENI STØQADHFTL SLAESYRFIL AKLAHDVLLS KVESPNDVLR TDNLVL TDNLVL GGENARNLNV	VRegupar VRegupar VRalipar VRalipar ISegupar ISegupar VRegupar IRegupar VRegupar VRegupar ISegupar VSegupar VSegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar ISegupar	ANVISYLRIF ANVISYLRIF ANIFSSLRIF AVISFISL GIVISTRIFI GIVISTRIFI ANIFSSLRIF ANIFSSLRIF ANIFSSLRIF GVILAFI GVILAFI STISTRIV GVILAFI TVLACVIVI IGFVILFRIF FGVFLYMSFF
TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4 Hsap_NP_003297.1 TRPC4 Mmus_NP_05860.1 TRP_Spur_XP_793901 TRP_Cint_XP_002124651.2 TRP_Skow_XP_002733765.1 TRP_Lflor_emb CAA11261.1 TRP_Bflo_XP_002611405.1 TRP_Nvec1_XP_001640409 TRP_Nvec1_XP_001637374.1 Cca7050 Cca21784 Ava6635_4 Ava6904_I Ava6904_I Ava660_1	FMYTTSSIIG FMYTTSSIIG SLFTANSHIG CYTVMNRHVG YILEVNEKFG YIFQANFVIG YLFQANFVIG VYFTYSPOIG NAVQVNSTIG YLVFYSPOIG QYLRYHRVIG RYLSWHPVIG QYLVIIKDSYG QYLVIRGIG	PLQISMEOML PLQISMEOML PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL PLQISLEANL	QDFCKFLCMF QDFCKFLCMF LDILKFLFIY FDICKFLFIY FDICKFLFY FDICKFLFY SDIVKFLSVY FDIVKFLSVY KDICKFLSVY KDICKFLLF VFCCFAFIS QNMACFVVL EFILFIVIL KNLCSFLLFV KNLKFLVFF	LLVD FSFTIG LLVD FSFTIG CLVDLAFANG CFWFAFSIG FWFFAFSIG FWFFSFACG FLVDFSFACG FLVDFAFANG FLVDFAFANG FLVDFAFANG FLVDFAFASG FLVDFAFASG MVFTAFAAG LIFFUAYCVA LIFFUAYCVA LIFFUAYCVA VLVSLGFGII	LTOLYDKGYT LTOLYDKGYT LNOLYFY-YE MNOLYGY-YS LFNDYSY-YR LNOLYWY-YG LNLYWY-YG LNUYF-YN LNOLYF-YN RRYSSO-Y WTMTWSSE VNIYGA LYNYRG SQTLYPNLP WQAVVASDTL EVTUTSTNQ-	SKEQ SKEQ ETKG YITR SSSP ALRA MMNGSLQTDG KNRA WAGK WAGK RDDP YEDF YEDF

TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4_Hsap_NP_003297.1 TRPC4_Mmus_NP_058680.1 TRP_Spur_XP_93901 TRP_Cint XP_002124651.2 TRP_skow_XP_002733765.1 TRP_Lflor_emb CAA11261.1 TRP_Bflo_XP_00251405.1 TRP_Mvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 TRP_Nvec4_XP_001640409 Cca21784 Ava6635_4 Ava9904_1 Ava6620_1	KDCVGIF KDCVGIF LTCKGIR LSCKGIR VICDTNN WISQDAD EECE	AGIT TLEEGQKDVY DIDAILD AVNKTEANNT VFNETVRANA		THRFI-CTC THRFI-CTC ASSNF-ETL ASSNF-ETL ASSNF-ETL ASTIE-ETF ASLSD-RSM SBANF-EIL YSTNF-EIV YSTNF-EIV YSTNF-EIV YSTNF-EIV GESMQ-SSA SYAFVFGNIF AQFIF-TIF GWNLWR-ILL	FALEWYIESI FALEWYIESI GSLEWSIFGL QSLEWSIFGL STLEWALFGL ITLEWANFGL GTLWANFGL QSLEWALFGL QSLEWANFGL QSLEWANFGL QSLEWALFGL QSLEWALFGL ASLEWALFGL ASLEWALFGL FRPYMOLFGE FSPYYQIEGE	AHVAIFYTRF AHVAIFYTRV IMYYTNV IMYYTNV DYRCVEV VGTDVIKI VTVEHAHL VDTSINI TDFSINI TDFSINI GEDTINV IDVSIN GEDTINV IDVGDISN FFBEHQA FFIPQLGT FFGANIRT
TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4_Msap_NP_003297.1 TRPC4_Mmus_NP_058680.1 TRP_Spur XP_793901 TRP_Cint XP_002134651.2 TRP_Skow_XP_002733765.1 TRP_Lflor_emb CAA1261.1 TRP_Bflo_XP_002611405.1 TRP_Mvc1_XP_00160409 TRP_Nvcc1_XP_001637374.1 Cca21784 Ava16635_4 Ava904_1 Ava620_1	SY 	-GELLOS 	SSNF		QTTNPLLEFD	VGAVI VGAVI VGATM VGLIL 
TRPC1_Hisap_NP_003295.1 TRPC1_Husp_NP_003297.1 TRPC4_Mnus_NP_058680.1 TRPC4_Mnus_NP_058680.1 TRP_Cint XP_002124651.2 TRP_Skow_XP_002733765.1 TRP_Lflor_emb[CAAll261.1 TRP_Bflo_XP_002611405.1 TRP_Bflo_XP_002611405.1 TRP_Nvec4_XP_001640409 TRP_Nvec1_XP_001640409 Cca21784 Ava16635_4 Ava904_1 Ava6620_1	VETNINVUVI FETNINVISLU FETNINVISLU FETNINVISLU FETNINVISLU VAAHUVIAIU FEGSUMIII FEGSUMIII FEGSUMIII FETNIASII ALENIASIU NAVWIJSSU LUVWIJESNU LIILQLIANV	VIRKIUAMI VIINKIAMM VIINMIAMM VIINMIAMM VIINMIAMM VIINMIAMM VIINMIAMM VIINMIAMM VIINMIAMM VIINMIAMM VIINMIAMM VIINMIAMM ILINMIAKF IINNIAKF IINNIAKF	HKSGCLAANH NNSYCLAADH NNSYCLAADH NNSYCLAADH NNSYCLAADH NNSYCLAADH NNSYCLAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH NNSYCHAADH 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KLMSYDEG KLMSYDEG KLMSYDEG KLMSYDD STAR KLMSYDD STAR KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYDD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD KLMSYD K	-CTLPPEPNI -GTLPTPFNV -GTLPTPFNV -STLPVPFNL -STLPPPFNI -STLPPPFNI -GTLPPPFNI -STLPPPFNI 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TRPC1_Hsap_NP_003295.1 TRPC1_Mmus_NP_035773.1 TRPC4_Msap_NP_003297.1 TRPC4_Mmus_NP_058680.1 TRP_Spur_XP_793901 TRP_Cint_XP_002124651.2 TRP_Skow_XP_002733765.1 TRP_Lflo_Te_mb[CAll261.1 TRP_Bflo_XP_002611405.1 TRP4_Sman_XP_002576849.1 TRP4_Nuex_XP_002576849.1	IESPKTI IPSPKTI IPSPKSL IPSPKSL IESPKSM LTIPQCIHDG IISPKSM IESPKSF WEPPKFF	-CYMISSL -CYMISSL -WYLIKWI -WYLVKWI -UYLFRWL VTYIFKLT -VCFFKAI -TNMMTLF -WYTIMWVKN	-SKWICSHTS -SKWICSHTS -WTHLCKKKM -WTHLCKKKM -RGKLGSEKH -RKELYKKTR -QRIMCGSCE -KSLILSHTA SCSEICNFR-	KGKVKRQNSL KGKVKRQNSL RRKPESFGTI RQEIRDRNKA RASSSQRR KTKSRPQRQS EQKQAKWTNV KKOLNRMRSI	KEWRN KEWRN GVRTQHRRAA GRRAA KME DHHR LEGTI RSTV GKMTA	LKQ LKQ DNL DNL KKTELRK KKTHLNSDGV KNIN VKL
TRP_Nvec1_XP_001637374.1 Cca7050 Cca21784 Ava16635_4 Ava9904_1 Ava6620_1	LESIASI LETEXYI LHUTVDI LNEIVDL LVILYRV LSHIRKL LVYLFRT	-AYQLSEI -INFF -VRLI LEFLFRK -VERLYLL -VKRLYLL -VKFLYGK -FGICKTV	-QEMVRGKKS -RRPNLEAAM CNRYRVNSTV CAVRIFRKNI -CQDFFKEHE	RESIKRTNIS WMSLIPLTV KSKDRGNNE- YKEDMKNFH- ETMEDEFQRD	INE TPE THFNRAKVYP	VYFGHHNENG

TRP_Spur XP_793901	EKEQQ	YRE IMGK <mark>I</mark> VK	RY IFDAKRDE	DENNQEQW	VNRLKQDISG	FKYDMFEALT
TRP_Cint XP_002124651.2	RMSMH	HINVMTRIVK	RYVLRAQVEE	AGGSNTSEAD	LQEIKHDISS	LRYDVIGGLT
TRP Lflor embl(CAA11261 1	KREIR	YOYVIRNUIS	RYIMNKORPO	K-DEMVSODD	INELKODIST	FREDLLTILS
TRP Bflo XP 002611405.1	RKDMA	YKDVIONIVR	RYIANEIRDR	ESSEGLCEDD	INELKODISS	FRYMLALL-
TRP4_Sman_XP_002576849.1	NKSTQ	SKPLFSDIKQ	PVHRKI	TTSTGINKSD	FNKTLLPSST	SIGGIIGPV-
TRP_Nvec4_XP_001640409						
TRP_Nvec1_XP_001637374.1						
Cca21784	PRFFA	OKELIOTIKR	KFERF	CMESPSTKSD	MRKUSFOLHE	T.K
Ava16635 4	HKEKE	KEKILFDFEK	RCVLACNFNL	EOTNEL	NLDKRITE	VDNRLKNT
Ava9904 1	RKNAE	RWKWTKDIQQ	QGLNRWESKR	LSEQEE	SVRNLL <mark>S</mark> N	VETKLEDVYR
Ava6620_1	FADEYWRNRE	KIRIKGN <mark>I</mark> Q-	LKKRQKQV	EYLTQKSQEQ	SLHRKYTVKY	FYFNFTGVRR
TRPC1_Hsap_NP_003295.1	FRTSKYAMFY	PRN				
TRPC1_Mmus_NP_035773.1	FRTSKYAMFY	PRN				
TRPC4 Hsap_NP_003297.1	-RGSKLSTIQ	SANASKES	SNSADSDEKS	DSEGNS	KD	KKKNFSLFDL
TRP Spur XP 793901	CMDKKMSEME	ORIEDGGVKE	PGTOMFHEME	DVVKRPLYOP	DSM	OSVISGCSDI.
TRP Cint XP 002124651.2	RWDSKIEELF	NSLEKOKTEE	GOIQISTAVA	QIERKS	KN	ERLAPPVLDA
TRP_Skow_XP_002733765.1	-KKEQMRGTS	QIENVKHEII	GELRGISGAP	ENESTTIVGA	PRRSLSTVNP	PSFISQSFDK
TRP_Lfloremb CAA11261.1	DNGFETPTVH	Q-AKTSSRLD	RMWKNLSAAT	EGQTETLMEE	AGLDEE	
TRP_Bflo_XP_002611405.1	-KSDGGEGGP	DSLQDERP	SRRKRRTGKY	SLEALS	QP	RSRSMNNLDR
TRP4_Sman_XP_0025/6849.1	-DNPAFENEE	VIVNKTSI	SSSVDLDGKK	QGKSTTVLDQ	KTSVSDVTSQ	QLNPNFIPCT
TRP_Nvec1_XP_001637374.1						
Cca7050						
Cca21784						
Ava16635_4		QHLIVTLT	NKVDSLVRST	GSFE	SE	QDFFSLQGDT
Ava9904_1	NCHTLLDHMG	SDEPLLTMMT	SEIREVRRQL	ADFGVH	SF	QNYLLILHLV
AV46620_1	KGVKSVNLFF	CAIPFNLX				
TRPC1 Hsap NP 003295.1						
TRPC1_Mmus_NP_035773.1						
TRPC4 Hsap_NP_003297.1	TTLIHPRSAA	IASERHNISN	GSALVVQE	PPREKQRKVN	FVT	
TRPC4_Mmus_NP_058680.1	TTLIHPRSAA	IASERHNLSN	GSALVVQE	PPREKQRKVN	FVA	
TRP_Spur_XP_/93901 TRP_Cint_XP_002124651_2	TEINK	SKGSNNADNS	PILDDGLSDP	STKNRRQPKS	TSMPCNIAGY	LIPPDWERNE
TRP_Skow_XP_002733765.1	SELESLKDDL	THTIRSEIKE	ELOESLER			
TRP Lflor emb CAA11261.1						
TRP_Bflo_XP_002611405.1	LEE-HPAVDE	TDSAKACLSR	PLAAAAVRSV	FPVLEQRQRN	-VM	
TRP4_Sman_XP_002576849.1	SAVVCEETIT	NNTDQNTVEK	QLQQSKLKQP	PSQLSIETKT	PSM	
TRP_Nvec4_XP_001640409						
Cca7050						
Cca21784						
Ava16635_4	MGSMHGRRIL	IRYFNNVSIL	QLFISPLSYT	TSPVLYQERL	NIF	FILC
Ava9904_1	IKHITRST	HFKITGLLLL	PLYIYTVYSC	TSPLCYFPKT	FIFVVTIQYF	PINICLFLFC
Ava6620_1						
TRPC1_Hsap_NP_003295.1						
TRPC1_Mmus_NP_035773.1						
TRPC4 Hsap_NP_003297.1		DIKNFGLF	HRRSKQNAAE	QNANQIFSVS	EEVARQQAAG	PLERNIQLES
TRP Spur XP 793901	PILEMDEDPD	VPILGGPPRK	ESKKRRFSAN	HMMNHIGSRH	LKRKKSHTKN	TTRV
TRP Cint XP 002124651.2						
TRP_Skow_XP_002733765.1			ALNSAAQE	SSVNGLLPTS	SDLYHTHLYT	QL
TRP_Lfloremb CAA11261.1						
TRP_Bf10_XP_002611405.1	N	GQVAGAADR'I	WSRGNPGGGL	QDGNPLLLQT DUD DVIEQUE	ERVSSMG	RISRTFVTLA
TRP Nvec4 XP 001640409	NIIKNDK		NEIRSQIVRQ	DHADKIESVE	NEA15QLF5D	
TRP Nvec1 XP 001637374.1						
Cca7050						
Cca21784						
Ava16635_4	MKVSEDLVVL	SR				
Ava6620 1	SSRMIYD	2MILCCA				
11120020_1						
TRPC1_Hsap_NP_003295.1						
TRPC1_Mmus_NP_035773.1						
TRPC4 Hsap_NP_003297.1	RGLASRGDLS	IPGLSEQCVL	VDHRERNTDT	LGLQVGKRVC	P-FKSEKVVV	EDTVPIIPKE
TRPC4_MMUS_NP_058680.1 TRP_Spur_XP_793901	KGLASKGDRS	IFGLNEQCVL	VDHRERNTDT	Tetőneksác	STEKSEKVVV	FDIALDE
TRP Cint XP 002124651.2						
TRP_Skow_XP_002733765.1						
TRP_Lflor_emb CAA11261.1						
TRP_Bflo_XP_002611405.1	SPVLGRRRRQ	QRKGLDE	EEDTE	LGAMSRTNRN	FANENDMGSV	FTCAPITEID

TRP4_Sman_XP_002576849.1 TRP_Nvec4_XP_001640409 TRP_Nvec1_XP_001637374.1 Cca7050 Cca21784 Ava16635_4 Ava9904_1 Ava6620_1	HCKLNKISHH	PMDECSQMKN	QRSDLV	       	
TRPC1_Hsap_NP_003295.1					
TRPC1 Mmus NP 035773.1					
TRPC4 Hsap NP 003297.1	KHAKEEDSS	DYDLNLPDTV	THEDYVTTRL		
TRPC4 Mmus NP 058680.1	KHAHEEDSS	DYDLSPTDTA	AHEDYVTTRL		
TRP Spur XP 793901					
TRP_Cint XP_002124651.2					
TRP_Skow_XP_002733765.1					
TRP_Lfloremb CAA11261.1					
TRP Bflo XP 002611405.1	DSAEEEASHD	EENSSSESAS	RHE VV		
TRP4 Sman XP 002576849.1					
TRP Nvec4 XP 001640409					
TRP_Nvec1_XP_001637374.1					
Cca7050					
Cca21784					
Ava16635_4					
Ava9904_1					
Ava6620_ 1					

Supplementary Figure S4 Full alignment of sequences in Figure 5c.

# A1.6 Movie: Cilia in the osculum of a live sponge, *Ephydatia muelleri*, labeled using FM1-43.

High-frequency time-lapse microscopy (images taken at 50 millisecond intervals with exposure of 50 milliseconds) indicates that the cilia are non-motile and only vibrate in the flow that passes out the osculum. (to view the movie visit http://www.biomedcentral.com/1471-2148/14/3/additional)

## Appendix Two

### Supplementary material for Chapter Three



#### A2.1 Volume flow rates and oxygen removal in five species of demosponges.

To better understand the relationship between volume flow rate and oxygen removal, Figure 3-3 was re-plotted without the axes log transformed. a) Sponge pumping volume (L hr⁻¹ g DW sponge⁻¹) and oxygen removal (µmol hr⁻¹ g DW sponge⁻¹) were recorded over a five-minute period and plotted for one individual of each of five species of demosponges. Oxygen removal increased as the pumping volume increased both within an individual and between species, with the exception of *Cliona delitrix* (red). This same trend can be seen in b) when the mean oxygen removal and pumping volume over a 5 minute period is plotted for multiple individuals of each species (*Callyspongia* n=11; *Cliona* n=8; *Haliclona* n=10; *Neopetrosia* n=7; *Tethya* n=8).

## Appendix Three

# Automated image analysis for quantifying behaviour in the sponge

#### **A3.1 Introduction**

Advances in optical underwater imaging techniques over the past 50 years have allowed biologists to gain new insights into seafloor processes and ecosystem dynamics (Solan et al., 2003), but the voluminous data collected are often difficult to analyze. SCUBA depth limitations, boat access, costs of equipment, and limitations on the time spent underwater, all make underwater photography a useful, non-destructive tool for observing processes that occur on the seafloor. Images can be stored indefinitely and can be re-analysed at any time for new questions. Underwater time-lapse or video data can also provide information on otherwise cryptic behaviour, such as animals that behave differently when humans are around or behaviours too slow for humans to observe in real-time.

Here, I use examples of behaviour carried out *in situ* and *in vitro* by sponges (Porifera) to describe an efficient and simple method for quantifying behaviour and detecting events in time-lapse videos using the mathematical software MATLAB (v.R2013b; Mathworks). Sponges are good examples of sessile animals that are difficult to understand in real time, but which react to stimuli in the environment by changing their shape. I use this image analysis method to describe a range of behaviours carried out by sponges over minutes to hours, imaged *in vitro* and *in situ*. The primary aim is to demonstrate the utility of automated analysis of images in describing the variety of behaviours of animals such as sponges. Use of these automated approaches however, has highlighted the interesting differences in behaviour of sponges, and allows us to better understand the different stimuli that sponges respond to.

#### A3.2 Materials and Methods

MATLAB (v.R2013b; Mathworks) is a cross-platform (Windows, Mac, Linux) technical language software that is used across a wide range of disciplines for numerical computation, data analysis and visualization, and programming. Using the Image Processing Toolkit, it can read a diverse set of image and video formats and is capable of a high-level of image processing and analysis including a variety of image segmentation techniques (Gonzales et al., 2009). Although the use of MATLAB requires scripted input, there are many built-in tools as well as tools available for download online that use a Graphical User Interface (GUI), making it more user-friendly than traditional programming languages. Matlab is especially useful if the images to be analyzed come together with large amounts of data from other instruments, which also require Matlab analysis.

The simplest method to divide a digital image into its pixel components for analysis (called segmentation) uses a tool called thresholding (Arifin and Asano, 2006). The purpose of thresholding is to separate objects from their background by creating a binary image in which the subject is one colour of pixels (usually white, greyscale value = 255) and the background another colour (usually black, greyscale value = 0). The size of the objects can then easily be assessed based on the sum of white vs. black pixels in the binary image. Thresholding can therefore be used in any image set in which contrast exists between the object and the background. The optimal threshold value chosen to differentiate foreground and background can either be done manually by the user or automatically using a set of algorithms. Here, we used the well-known Otsu's method of automatic thresholding (Otsu, 1979) that selects an optimal value based on discriminant analysis. Thresholding can be sensitive to noise in the image, potentially introducing artefacts during analysis due to changes in illumination, focus, or movement of an object over the course of the experiment. Therefore, any images associated with outliers on the graph should be assessed for changes in illumination, focus, or object movement.

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### A3.3 MATLAB Script

A script for analysing time-lapse videos in MATLAB is provided here to allow researchers the ability to use the powerful image analysis software in MATLAB without having to learn programming language. This script is then applied to three different scenarios in sponges: sponge behaviour *in vitro*, osculum contractions *in situ* in response to ambient currents, and contractions of sponges in response to sediment in tanks.

```
\$\$ Using thresholding to quantify animal behaviour - Batch
analysis of multiple images
% This script will run through multiple images in a folder and calculate the
% percent tissue in each, storing the results into an excel file
%% Load images
clear all;close all;clc;
%Get names of files
display('Select ALL of the files that you want to analyze in the folder')
[filenames,pathname] = uigetfile('*.tif', 'Select File(s)', 'multiselect',
'on');
%% Create Regions of Interest (ROI), select threshold value, and analyze
percent tissue
PctTissue = zeros(size(filenames)); % creates a matrix of zeros that is the
%same size as the number of images to analyze
%For loop that will go through every image and:
% 1) Crop out the region of interest
% 2) Convert the image to a binary B&W image according to a threshold level
% selected
% 3) Analyze the binary image so that the percent tissue (white) is recorded
for ii=1:length(filenames)
 fn=fullfile(pathname, filenames{ii});
 if ii==1 % For the first image only:
    temp=imread(fn); %Load the image
   display('Using the cursor, draw a rectangle to select an ROI')
   display('then double-click in the centre of the ROI selected')
    [crop, RECT]=imcrop(temp); % Opens the image to select
                  % a Region of Interest (ROI)
%Selection of an ROI is by clicking and dragging using the cursor.
%The size of the rectangle can then be re-sized or positioned as needed.
%Once the ROI is adequately placed, double-click in the centre to select %The coordinates of the ROI is saved as RECT
    figure, imshow(crop); %Show the cropped image
   imwrite(crop, 'select image name.tif'); % Save the cropped image
   threshval(ii) = grayThresh(crop(:,:,1));
   channelMask = im2bw(crop, threshval(ii));
    %%The # of White Pixels is the sum of all pixels (white pixel=1)
   numberOfWhitePixels=sum(channelMask(:));
    %%The # of Black Pixels are all remaining pixels (black pixels=0)
   numberOfBlackPixels=numel(channelMask)-numberOfWhitePixels;
    %%To calculate the percent of white pixels in the image:
   a=numberOfWhitePixels+numberOfBlackPixels;
   b=numberOfWhitePixels/a;
   PctTissue(ii) = b*100;
else %The same sequence will now run for every other image, using the
    %coordinates of the cropped image i=1 and the threshold value
```

```
%selected for i=1
    temp=imread(fn); % Loads the image
         crop=imcrop(temp, RECT); % Crops the image using the coordinates
         saved from image i=1
    threshval(ii) = graythresh(crop(:,:,1));
    channelMask = im2bw(crop, threshval(ii));
         numberOfWhitePixels=sum(channelMask(:));
         numberOfBlackPixels=numel(channelMask)-numberOfWhitePixels;
         a=numberOfWhitePixels+numberOfBlackPixels;
    b=numberOfWhitePixels/a;
    PctTissue(ii) = b*100;
     end
end
%% Look at some of the thresholded images
\% to ensure that the ROI and thresholded value chosen is measuring what you
% want it to
int=50;% spacing between thresholded images to save
t=10;% time interval between each photo of the time series
for j=1:int:size(filenames,2);
 fn=fullfile(pathname, filenames{j});
  temp=imread(fn); % Loads the image
  crop=imcrop(temp, RECT); % Crops the image using saved coordinates
  channelMask = im2bw(crop,threshval(j));
  figure, imshow(channelMask,[]);
  imwrite(channelMask,['select image name',num2str((j*t)-t),'.tif']);
         %Comment to not save the thresholded images
end
%% Save the results
%to combine data into one matrix, each column must be the same length.
%Repmat is used for all data that is only one value, to create columns
%that are all the same length
xcoord = repmat(RECT(:,1), size(PctTissue));
ycoord = repmat(RECT(:,2), size(PctTissue));
height = repmat(RECT(:,3), size(PctTissue));
length = repmat(RECT(:,4), size(PctTissue));
% To add a column of the time for each photo:
[t1,t2] =size(filenames); % t2 is the number of photos
time=(0:10:((t2*t)-t)); %Creates a time series starting at time '0'
     %and increasing by t (time between photos chosen on line 79)
% Store the results
result= ...
  [{'FILENAME', 'Time', 'Pct Tissue', 'Threshold Level', 'X Coordinate', 'Y
Coordinate', 'Height', 'Length', 'Date Analyzed'}; ...
 filenames', ...
  num2cell(time')...
 num2cell(PctTissue'), ...
  num2cell(threshval'),...
 num2cell(xcoord'),...
 num2cell(ycoord'),...
 num2cell(height'),...
 num2cell(length'),...
  repmat({datestr(now)}, size(PctTissue'))];
%%Save a .mat file to call on for later analysis or graphs
'variable name' = result;
%Use this line for the first time that the .mat file is created
save('filename.mat', 'variable name');
%To add a variable to an existing .mat file, uncomment the line below
%save('filename.mat','variable name, '-append');
```

```
%%Write to Excel
xlswrite('Filename.xls', result, 'Sheetname);
%For mac and linux users, xlswrite does not work properly and will default
%to write a .csv file. Try downloading the xlwrite function
%% Create a graph of the results
x=getcolumn(cell2mat(result(2:end,2:3)),1);
y=100-(getcolumn(cell2mat(result(2:end,2:3)),2));
yy=smooth(y,20);
roi=num2str(RECT);
name=filenames{1,1};
% Scatterplot with points
plot(x,y,'.')
hold on
set(findobj('type','axes'),'fontsize',16, 'fontname', 'Arial', 'fontweight',
'b')
xlabel('Time (s)');
ylabel('Canal space (%)');
plot(x, yy, '-');
title(char(name, 'ROI coordinates', roi));
hold off
응응
```

For an RGB image, use the following script prior to running the batch analysis to select which color channel to use. Then replace the "1" in the graythresh tool with the color channel number ("1" for red, "2" for green, and "3" for blue).

```
%% First, open and explore representative image
% Read a single image
[filenames,pathname] = uigetfile('Select File');
imgName = fullfile(pathname, filenames);
rgbImg = imread(imgName);
%% Explore color channels with Explore RGB
exploreRGB(rgbImg); % On line 176 of exploreRGB.m script, comment it
out so that it does not provide an error message
% Extract out each color channel
fR=rgbImg(:,:,1); %Red
fG=rgbImg(:,:,2); %Green
fB=rgbImg(:,:,3); %Blue
histR=imhist(fR);
histG=imhist(fG);
histB=imhist(fB);
% Graph the histograms of each color channel
figure, plot(histR,'r')
hold on
set(gca, 'xtick', [0:50:255]);
plot(histG, 'g');
plot(histB, 'b');
legend('Red Channel', 'Green Channel', 'Blue Channel');
hold off
```
# A3.4 Assessment

#### A3.4.1 Sponge behaviour in vitro

Freshwater sponges can be triggered to inflate and contract their whole body in response to mechanical or chemical stimuli, in a process termed a 'sneeze' (Elliott and Leys, 2007; Elliott and Leys, 2010; Ludeman et al., 2014). This behaviour is a useful tool for understanding coordination systems in sponges, but it is quite slow (15-60 minutes long), and is most easily viewed using time-lapse imaging. As spaces in the sponge expand and then contract, dimensions of these spaces can be measured to quantify the behaviour. Not only are manual measurements time-consuming, but they reflect observer bias. The custom computer image analysis tool-set I have developed converts the time-lapse videos into quantitative data. This approach may not always provide equivalent results, as shown previously by Elliott and Leys (2010, fig 1). Therefore, to determine how faithfully this new tool-set could reproduce results obtained manually, I compared the results with those obtained previously for a series of experiments looking at the pharmacological effects on the 'sneeze' behaviour (Figure A3-1;(Ludeman et al., 2014).

Still images were captured in Northern Eclipse v.7 (Empix Imaging Inc., Mississauga, ON, Canada) using an Olympus SZX Stereoscope every 10 s for 50 min, or until the sponge had completed an inflation/contraction cycle. Images were collected in greyscale to minimize storage space. To determine whether this computer image analysis workflow could differentiate changes in the behaviour in response to treatments, we looked at the sneeze response when the sponges were treated with the non-selective calcium channel blocker Gadolinium chloride. 5  $\mu$ M Gadolinium chloride was added to a Petri dish with the freshwater sponge *Ephydatia muelleri*, and the sneeze response was triggered 2 hours later using 90  $\mu$ M of the neurotransmitter L-glutamate (n=3). The drug was then washed out with culture medium over 24 hours and the sneeze response triggered again (n=3).

During the 'sneeze' response, the excurrent canals stereotypically inflate and then contract. To measure the change in the excurrent canals over time, a region of interest (ROI) that contained many branching excurrent canals and surrounding tissue was selected



Figure A3-1 A comparison of manual and automated measurement of the sneeze response in *Ephydatia muelleri*. (A) The sneeze response in *Ephydatia muelleri* was captured by time-lapse photography and (B) using the computer image analysis technique developed in MATLAB a region of interest was selected and the images were then thresholded. (C) Manual measurements, as described in Chapter Two, were then compared to (D) the automated results calculated using the percent canal space (black pixels) in the thresholded images.

(Figure A3-1 a). As many of the images had unimodal histograms, we used Otsu's method for selecting the optimal threshold value to differentiate the canal from the sponge tissue (Figure A3-1 b), designated by the function 'graythresh' in MATLAB (Otsu, 1979). After segmentation the tissue surrounding the canals was classified as white pixels and the canals classified as black pixels. We graphed the percent of black pixels or area fraction over the series of images to look for a change in canal size over time.

Previously the canal diameters had been measured manually using the line tool in ImageJ (v1.43r; NIH) (Ludeman et al., 2014); but to reduce time taken, only every tenth image for the first 60 images, and then every 20th image were used. We used the data collected from those experiments for comparison with digital image analysis tools here.

Neither manual nor computer image analysis detected a 'sneeze' response in sponges exposed to Gadolinium (Figure A3-2 a,b). Once the drug had been washed out over 24hr, each method was able to detect an increase and then a decrease in canal space (Figure A3-2 a,b), which is highly correlated ( $r^2 = 0.899$ ; Figure A3-2 c).

#### A3.4.2 Osculum contractions in situ in response to ambient currents

Despite a wide understanding of the importance of water flow for sponges, very few studies have assessed behavioural responses in sponges to increased ambient currents. In 1971 Reiswig documented the correlation between wave strength and oscular openings in *Tethya crypta* by using time-lapse photography over many days along with velocity measurements. Concurrent measurements of ambient velocity, excurrent velocity, and osculum area, as done by Reiswig (1971), can provide powerful data to understand how sponges respond to water flow.

A GoPro Hero2 camera in underwater housing was mounted over the sponge *in situ* using an aluminium frame (see Chapter Three) off of STRI point in Bocas del Toro, Panama. The camera was positioned to capture changes in osculum sizes of the sponge *Cliona delitrix* during an experiment in which the ambient current speed was manipulated using an underwater aquarium pump. Images were captured in colour (RGB) every 30 sec at 5 MP resolution for approximately one hour. Acoustic Doppler velocimeters were set up





to record both ambient water velocity beside the sponge and excurrent water velocity exiting the sponge. The underwater pump was directed at the sponge and run through four settings (off, low, medium, and high) for 5 minutes each, three times through. The camera battery did not last the entire experiment, however, therefore only two runs were analyzed here. Refer to Chapter Three for a more detailed description of these methods.

To detect changes in osculum area over the course of the experiment, a region of interest and some surrounding tissue was selected in *Cliona delitrix* (Figure A3-3 a) The red colour level was selected for each of the images and thresholded using 'graythresh' in MATLAB. A ruler was placed next to the osculum in one of the images to convert the number of pixels to osculum area and used to calculate pumping volume from the excurrent velocity (Figure A3-3 b,c).

#### A3.4.3 Contractions of sponges in response to sediment in tanks

Sponges, as suspension feeders, are sensitive to sediment and other materials in the water column that can clog their filtration system. It has been shown that some sponges respond to sediment by carrying out slow, rhythmic contractions to help clear out debris (Nickel, 2004; Elliott and Leys, 2007; Ellwanger et al., 2007) People have also long noted that sponges contract their excurrent opening, or osculum, in response to various stimuli (Parker, 1910; McNair, 1923; Emson, 1966; Prosser, 1967). Changes in both osculum diameter and sponge volume can be readily captured using time-lapse imaging, and it is important to be able to quantify the extent of contraction.

A GoPro Hero2 camera was mounted over the sediment chamber and positioned to capture changes in the volume and changes in osculum sizes of the sponge *Suberites* sp. during the experiment. Images were captured in colour (RGB) every 30 sec at 5 MP resolution for approximately eight hours. A low concentration of sediment (~12mg/L) was added to the chamber for the first hour.

For the analysis of sponge volume, the green colour level was selected and two threshold levels were chosen using the 'multithresh' function in MATLAB. The pixel intensities between the two threshold levels were then converted to white pixels during



Figure A3-3 | The sponge *Cliona delitrix* contracts its osculum in response to increasing ambient flow rates. (A) Images of the sponge osculum were taken using time-lapse photography and (B) osculum size was determined using thresholding. (C) The osculum contracts with increasing ambient flow rates, resulting in a decrease in pumping volume and an increased in excurrent velocity.

segmentation to differentiate the sponge from the dark background and the light colored rocks (Figure A3-4 a,b). A region of interest of the osculum and some surrounding tissue area was selected to detect movement of the osculum during the course of imaging. The red colour level was chosen as it provided the best distinction between sponge and osculum. Only one threshold value was selected, and the sponge tissue was converted to white pixels during segmentation. The change in the number of black pixels was then analysed over time (Figure A3-4 c).

## A3.5 Discussion

Here we provide a tool for the analysis of behaviour of aquatic organisms using time-lapse photography and computer image analysis. This tool is appropriate for cryptic animal behaviour, for studying growth of sessile benthic animals, and to capture events in video imagery. The rapid analysis of video data allows more time to be spent on interpreting the data. The use of computer image analysis may also reveal events or changes that were otherwise undetected by observers, either due to cryptic changes or from the ability to analyse many more images than would have been measured manually. The accuracy of measurements obtained using this computer image analysis will depend on the quality of image as well as the regions of interest and thresholding levels chosen. Comparison with manual measurements for the sponge 'sneeze' response, however, suggests that the results should be accurate for most applications and can differentiate between treatments. Computer image analysis will never be able to replace the critical observer of an informed experimenter, and therefore careful visual checks throughout the analysis workflow will ensure accuracy and prevent artefacts from occurring during the measurements. Importantly, this computer image analysis workflow minimizes or prevents human observer bias when analysing behaviour in time-lapse videos.



Figure A3-4 | The sponge *Suberites sp.* responds to increased suspended sediment in a tank. (A) Time-lapse photography was used to image the sponge during one hour of sediment addition to a tank followed by eight hours of recovery. (B) A region of interest along the body wall was thresholded and analyzed, and shows an increase in body volume during sediment addition (shaded green) followed by a contraction event. During recovery the sponge underwent a second inflation and contraction response. (C) A region of interest around an osculum and surrounding tissue was thresholded and demonstrates an immediate contraction of the osculum with an increase in sediment, followed by multiple osculum contractions during the recovery stage.

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