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Determining the sites at which neuromodulators exert peripheral effects in the cardiac neuromuscular system of the American Lobster, *Homarus americanus*

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An Honors Project for the Program of Neuroscience

By Audrey Elizabeth Jordan

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Table of Contents

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Abstract:

Networks of neurons known as central pattern generators (CPGs) generate rhythmic patterns of output to drive behaviors like locomotion and respiration. These CPGs are relatively fixed networks of neurons that produce consistent, stereotypical patterns in the absence of other inputs. The heart contractions of the American lobster (*Homarus americanus*) are neurogenic and controlled by a CPG known as the cardiac ganglion. Neuromodulators (e.g. amines, amino acids, and neuropeptides) can enable flexibility in CPG motor output, thereby allowing organisms to adjust to changes in their environment or sensory input. Neuromodulators have been shown not only to exert effects on CPGs, but also to alter muscle contractions by acting on the neuromuscular junction and the muscle itself.

A tissue-specific transcriptome gleaned from the cardiac ganglion and cardiac muscles of the American lobster was used to predict sites and sources of a variety of crustacean neuromodulators. Using a bioinformatics workflow, putative neuropeptides and receptors were predicted utilizing the transcriptomes and then inferences were made about their potential modulatory effects on the periphery of the cardiac neuromuscular system. If corresponding receptors were predicted to be expressed in the cardiac muscle, then it was hypothesized that the neuropeptide had peripheral effects. Receptors determined to be located at the cardiac muscle included those for the following peptides and amines: C-type Allatostatin (AST-C), bursicon, DH31, DH44, myosuppressin, octopamine (β receptor), octopamine-tyramine combo, and serotonin.

One peptide that has been extensively studied and for which a cardiac muscle receptor was identified is myosuppressin. Myosuppressin has been shown to have modulatory effects at the cardiac neuromuscular system of the American lobster. In the whole heart preparation, myosuppressin was found to enhance the contraction force. In the isolated cardiac ganglion, myosuppressin increased burst duration and decreased cycle frequency and thus, the duty cycle of the action potential bursts. Myosuppressin also has modulatory effects on the periphery of cardiac neuromuscular system alone. It remains an open question of whether myosuppressin acts on the cardiac muscle directly, if it is exerting its effects at the neuromuscular junction (NMJ), or both.

To test this, I performed physiological experiments on the isolated NMJ. Myosuppressin did not modulate the amplitude of the excitatory junction potentials. Since I did not observe any effects at the NMJ, I next tested the effects of myosuppressin on the cardiac muscle. By isolating the cardiac muscle from cardiac ganglion CPG and then stimulating muscle contractions using L-glutamate, I showed that myosuppressin increased contraction amplitude. Therefore, these data suggest myosuppressin exerts its peripheral effects at the cardiac muscle and not the NMJ.

Chapter 1: Introduction

1.1-Central pattern generators

Organisms' ability to perform critical rhythmic behaviors that are necessary for survival, like locomotion and respiration, are driven by neural networks that generate rhythmic motor patterns. These networks of neurons are known as central pattern generators (CPGs). CPGs are relatively fixed networks of neurons that produce consistent, stereotypical patterns in the absence of other inputs.

The synaptic connections made between the neurons in a CPG can produce differing rhythmic activity based on which specific neurons are active. One common motif is the firing of pacemaker neurons that inhibit other network neurons and cause an oscillatory pattern (Marder et al., 2001; Smith et. al. 1991). This oscillatory theory explains the contraction and relaxation of muscles that produces rhythmic movement. The neurons in a motor CPG network innervate muscle and drive contractions. The network of neurons, motor efferents, and the innervated muscle comprise the CPG-effector system.

CPG-effector systems, which are present in in both vertebrates and invertebrates, produce rhythmic behaviors that need to be flexible to allow organisms to adjust to changes in the environment and sensory input (Dickinson, 2006). Neuromodulators like peptides and amines acting on the CPG-effector system enable flexibility in the motor outputs. In some cases, neuromodulators have been shown to activate the CPG circuit and alter muscle movements by acting directly on the peripheral effector system, which is composed of both the neuromuscular junction and the muscle (e.g. Bishop et al., 1984; Dickinson et al., 2015; Erxleben et al., 1995; Jorge-Rivera and Marder, 1996).

1.2-The lobster's heart as a CPG-effector system

The simplicity of invertebrate CPG-effector systems makes the American lobster *(Homarus americanus)* an optimal experimental model. The lobster's heart is part of an open circulatory system in which the hemolymph, which acts as the blood of the lobster, flows in through the ostia, dorsally and ventrally located on the heart, and is pumped out through the anterior and posterior arteries (Figure 1). Unlike the human heart, which can contract independent of any neural input (myogenic), the lobster cardiac neuromuscular system is neurogenic and therefore muscle contractions are generated by neuronal input (Cooke, 2002). This neural input comes from a cluster of neurons on the heart wall known as the cardiac ganglion. The cardiac ganglion is one of the CPGs found in the lobster. It is a network of nine neurons with four small, posterior pacemaker interneurons (Small Cells) and five large, anterior motor neurons (Large Cells) arranged in a Y shape (Figure 1) (Cooke, 2002). Axons extend beyond the ganglion, where they innervate and make synapses with the cardiac muscle (Yazawa et al., 1999).

The pacemaker interneurons spontaneously generate bursts of action potentials that drive the behavior of the motor neurons through both electrical and excitatory chemical synapses (Cooke, 2002). In Hartline's (1967) investigation of the neural activity at the cardiac ganglion, it was discovered that the soma of the motor neurons is electrically unexcitable; action potentials can only be initiated at the spike initiating zone located on the proximal axon. Driver potentials in this region provide the underlying depolarization within the cells that can bring the membrane potential over threshold at the spike initiating zone to cause a burst of sodium-based action potentials. Driver potentials are long, sustained potentials mediated by calcium currents and three different outward potassium currents: an early voltage-dependent A-current, a voltage dependent delayed outward K-current, and a smaller, slow outward C current (Tazaki and Cooke, 1986).

Since the five motor neurons are electrically coupled, they fire these bursts synchronously. The activity of the motor neurons acts on the cardiac muscle to cause a contraction in a unidirectional manner.

The CPG-effector system is a closed feedback system (Figure 2). The increased calcium concentration caused by enhanced muscle contraction results in the activation of a negative feedback pathway. Increased calcium elicits the release of nitric oxide, which in turn decreases the cycle frequency of contraction by acting on the cardiac ganglion (Mahadevan et al. 2004). The muscle stretch also activates mechanosensitive receptors that provide feedback to the cardiac ganglion and are thought to be a positive feedback pathway (Maynard, 1960). The dendrites, or collateral processes, of the pacemaker and motor neurons are key players in sending signals to the muscle fibers to activate this stretch feedback pathway (Hartline, 1979; Cooke, 2002; Yazawa et al., 1999). The intrinsic feedback pathways are an important aspect of the CPG-effector system in stabilizing the heart's activity.

Various neuropeptides and amines can modulate the CPG-effector system's contractile response and currents (Harris-Warrick et al, 1991). If neuromodulators are acting at any point in the CPG-effector system, their modulation could alter the activity of subsequent regions. However, the outputs are not always the same for each region within the CPG-effector system. For example, Fort et al. (2007) discovered that the neuromodulator CCAP exerts counteracting effects in the different regions of the cardiac neuromuscular system to ultimately stabilize the CPG-effector system. These effects of CCAP suggest that other neuromodulators could have similar effects.

By observing the different ways that neuromodulators regulate each region of the CPG-effector system, we can gain more insight into the intrinsic and extrinsic mechanisms that drive the changes in the rhythmic behaviors.

1.3- Physiology of the Neuromuscular Junction Physiology

The neuromuscular junction (NMJ) is the chemical synapse between the motor neuron and the muscle fiber (Worden, 1998). The presynaptic axon terminal of the NMJ is identified by a protein dense structure, which aids in the docking of transmitter loaded vesicles (Jahromi & Atwood, 1974). There are varying numbers of active zones on the presynaptic membrane, with some having no active zones at all (Levitan and Kaczmarek, 2015). The number of active zones available at the presynaptic cleft determine how much transmitter is released and the magnitude of the postsynaptic response. In crustaceans, the postsynaptic response to transmitter release is a depolarization of the muscle membrane potential known as an excitatory junction potential (EJP).

In vertebrates, the well-known transmitter that stimulates EJPs is acetylcholine; however, in crustaceans, glutamate serves as the neurotransmitter for many NMJs to drive muscle contractions. Glutamate rapidly increases sodium currents, causing a rapid depolarization in the muscle followed by a steadier repolarization (Jan & Jan, 1976; Titlow & Robin, 2018). The EJP amplitude is determined by a variety of factors, including the amount of transmitter released from the presynaptic cell, the density of receptors on the postsynaptic membrane, the resistance of the postsynaptic membrane, and the presence of recirculating modulators. The amplitude can also vary based on the type of muscle response (e.g. spiking or graded muscle contractions) (Titlow & Robin, 2018).

When the neuron experiences repetitive stimuli, there is often an increase in transmitter release, which is hypothesized to cause facilitation. Facilitation is thought to occur when repeated action potentials result in calcium build-up at release sites, which does not have enough time to return to lower, unstimulated levels before the next stimulus (Levitan and Kaczmarek, 2015). Thus, there is residual calcium in the presynaptic cell. The extra calcium then acts on a neuronal calcium sensor protein (CaS), which enhances the activity of the calcium channels and causes more calcium to enter the synaptic membrane with every action potential. Each subsequent EJP at the NMJ is more enhanced than the last until the CaS reaches a point of saturation or the stimulus ceases (Figure 3).

1.4-Muscle Physiology: Cardiac Striated Muscle

The cardiac muscle of the American lobster is striated muscle. Crustacean cardiac striated muscles are non-propagating fibers, so neural input controls the force of contraction (Millar et al. 2005). Muscle contractions are graded.

Neuromodulators have been shown to alter muscle activity by modulating calcium dynamics (Levitan and Kaczmarek, 2015). Contractions are controlled by levels of calcium within the muscle fibers. When the muscle fibers are depolarized by CPG-generated action potentials, calcium is released from sarcoplasmic reticulum. The sarcoplasmic reticulum sequesters calcium within the muscle fiber, limiting the amount of free calcium within the cell. Once released, free calcium binds to the contractile protein and elicits the contraction.

Neuromodulators acting on the cardiac neuromuscular system could influence any step of this muscle contraction, some of the most obvious being the neurotransmitter release and calcium dynamics in the muscle.

1.5- Peptidergic Modulation

A well-studied group of neuromodulators is the neuropeptides. Peptides are chains of amino acids that are covalently bound. Neuropeptides are encoded as chains of amino acids that have signal sequences at their (N)-terminus and are known as preprohormones (Christie et al. 2010). Once synthesized, the preprohormones go through post translational processing, where enzymes cleave the peptide at specific sites, making smaller chains of peptides. Many of these peptides then undergo post-translational modifications, which are known to alter the peptide structure, making the peptide biologically active and stabilizing it for cellular interactions and neural output. Common structural changes in crustaceans can include disulfide bridges between cysteines residues, tyrosine sulfation, and C- terminal amidation (Christie et al. 2010).

These neuropeptides can modulate the cardiac neuromuscular system at both an intrinsic and extrinsic level (Katz, 1995). In *H. americanus*, intrinsic neuromodulators are synthesized and released at the cardiac ganglion, then they act directly on the cardiac ganglion to control their own modulation. Extrinsic modulators can be released: locally and/or hormonally. Hormonally released extrinsic modulators are synthesized outside the cardiac neuromuscular system and released into the hemolymph to travel through the circulatory system to reach the target cells. The hormonally released neuromodulators can act on multiple target CPGs. Locally released extrinsic modulators are synthesized and released in other regions of the nervous system (e.g. thoracic ganglion) that have nerves going into the cardiac ganglion, where they are released at the nerve terminals in the cardiac ganglion. Additionally, these modulators act on receptors in peripheral regions and not at the cardiac ganglion.

By knowing the sites and sources of modulation, predictions can be made about whether the neuromodulator modulates at the axon terminal, postsynaptic site, or the cardiac muscle. Modulators acting at the axon terminal in the effector system have receptors located at the

presynaptic membrane of the NMJ and will be referred to as presynaptic modulators. Presynaptic modulators can alter the calcium influx, the number of active zones, and the extent to which the muscle depolarizes (Levitan and Kaczmarek, 2015). While modulators acting at the postsynaptic site or muscle have receptors at the postsynaptic region of muscle and will be referred to as postsynaptic modulators. Postsynaptic modulators can affect the receptor availability, the muscle membrane resistance, and affinity of receptors. Neuromodulators could also regulate the muscle function directly, altering the calcium dynamics, including modulation of the calcium concentration that enters the muscle, the internal handling of calcium, or the affinity of troponin for calcium. Increasing the amount of calcium bound through any of those pathways would result in a larger contraction even with the same sized depolarization and/or amount of glutamate released (Levitan and Kaczmarek, 2015).

Tissue-specific transcriptomes (e.g. cardiac ganglion and cardiac muscle) can be used to make inferences about putative peptides' site(s) of action. However, it becomes difficult to determine a neuromodulator's specific actions if receptors are located at both cardiac ganglion and the cardiac muscle. If modulation is postsynaptic, it could be acting on either the cardiac muscle or the NMJ. Tissue-specific transcriptomes cannot be made for the NMJ, due to mRNA being located in the cell bodies and not the terminal; thus, bioinformatic cannot make predictions about receptors located at this region. Bioinformatics also cannot determine the pathways at which a neuromodulator alters the muscle contraction. Thus, to determine whether neuromodulators act at the NMJ or directly affect the muscle contraction, physiological experiments that isolate these regions are necessary. However, there are very few studies in which these experiments have been performed. One of these few studies was Wilkens et al.

(2005), who showed that proctolin exerts effects on the periphery. They performed physiological experiments that determined that proctolin exerted its effects on both the NMJ and the muscle.

1.6- Tissue-Specific Transcriptomics and Bioinformatics Utilized to Identify Putative Neuropeptides and Receptors

To determine whether specific neuropeptides are likely to act as intrinsic or extrinsic modulators in a CPG-effector system, tissue-specific transcriptomes have been analyzed. Transcriptomics is a method in which the first step is to extract messenger RNA (mRNA) from the tissue of interest. The mRNA holds the genetic information that leads to the formation of proteins like neuropeptides and receptors. The Dickinson lab has collaborated with researchers at the University of Hawaii at Manoa, who have used *in silico* transcriptomics to identify peptide sequences at a large scale (Christie et al., 2015). With this method, the Dickinson lab and collaborators were able to predict a variety of neuropeptides and receptors present within the motor and pacemaker cells of the cardiac ganglion, cardiac muscle, eyestalk, brain, and other tissues in the American lobster (Christie et al., 2015; Christie et al., 2017; Oliesky et al., 2020).

Using a bioinformatics workflow, putative neuropeptides or receptors can be predicted from transcriptomes. Bioinformatics can also be used to make inferences about the structural characteristics and location of the putative peptides and receptors. Through understanding the potential localization of neuropeptides' synthesis and release, predictions can be made about their potential modulatory roles. Predicting the location of receptors can indicate the sites of modulation for corresponding neuropeptides and whether they are intrinsic or extrinsic modulators. Even though bioinformatics is a useful tool for preliminary research, it is necessary to do physiological experiments to confirm these predictions.

1.7- Myosuppressin

Using physiological methods, many neuromodulators have been shown to affect the periphery; however, they have not been studied in detail. One such neuromodulator is the highly conserved peptide, myosuppressin. Myosuppressin, characterized by its C terminal motif-HVFLRFamide, is a well-studied neuropeptide in decapods and is a part of the FMRFamide-like peptide family (Stevens et al., 2009). Oliesky et al. (2020) identified five putative myosuppressin receptors in the brain-, eyestalk ganglia-, and cardiac ganglion-specific transcriptomes of *H. americanus*. The distribution of these five myosuppressin receptors differed among the pacemaker and motor neurons of the cardiac ganglion. Differing responses to myosuppressin were also observed when studying the pacemaker and motor neurons separately.

Myosuppressin characteristically drives inhibitory responses in the muscle of various arthropod species (Tanaka, 2016). However, in the cardiac neuromuscular system of the American lobster, myosuppressin often results in muscular excitation. In the isolated whole heart, for example, myosuppressin caused an increase the contraction amplitude (Figure 4). In an isolated cardiac ganglion preparation, myosuppressin resulted in an increase in burst duration and a decrease in cycle frequency of the action potential bursts (Stevens et al., 2009).

Stevens et al. (2009) also demonstrated that myosuppressin exerts modulatory effects at the periphery. To isolate the periphery for experimentation, they eliminated all endogenous cardiac ganglion activity, then stimulated the motor nerve to elicit transmitter release, causing a single contraction for each stimulating burst. Myosuppressin was then superfused over the lobster's heart, resulting in an increase in the amplitude of contraction from baseline (Figure 5). Although myosuppressin modulates the muscle contractions, it remains unclear whether the site of action is the NMJ, the muscle, or both.

The objective of these experiments was twofold. Firstly, I used bioinformatics to generate a list of potential neuromodulators that may affect the cardiac neuromuscular system. I determined whether they were predicted to be intrinsic or extrinsic modulators, and whether receptors were in the cardiac ganglion or the cardiac muscle. Based on these results, I selected a neuromodulator that was predicted to be present in both the cardiac ganglion and the cardiac muscle and physiologically known to exert effects at the cardiac ganglion and the periphery. Yet this selected neuromodulator's effects at the periphery (NMJ and/or the muscle) remained unknown. One such peptide that met these parameters was myosuppressin. Myosuppressin was predicted to have receptors located on the cardiac ganglion and the cardiac muscle. Based on this information and previous literature, it was predicted that myosuppressin exerted effects on both the NMJ and the cardiac muscle. Physiological experiments were performed to determine the site(s) of action at which myosuppressin exerts effects.

Chapter 2: Methods

2.1- Animals

Lobsters (*H. americanus*) were purchased from seafood retailers in Brunswick, ME, and were kept in a tank of recirculating seawater at 10-12 °C. They were fed scallops and shrimp once a week.

2.2- Bioinformatics

2.2.1- Tissue Specific Transcriptomics

The *H. americanus* tissue-specific transcriptomes were assembled by Dr. Patsy Dickinson's lab, along with collaborator Dr. Andrew Christie's lab. The mRNA was extracted from brain, eyestalk, cardiac ganglion, and cardiac muscle tissue (Christie et al., 2015; Christie et al., 2017). The mRNA reads were used to generate tissue-specific transcriptomes, which are publicly available on the Hawaii database (http://clc01.pbrc.hawaii.edu/cgi-bin/blast/blast.html). In order to predict the sites and sources of putative neuropeptides in the cardiac neuromuscular system, the transcriptomes of the cardiac ganglion and the cardiac muscle were analyzed.

2.2.2- Bioinformatics Workflow

Using a well-vetted bioinformatics workflow, specific neuropeptides and receptors were searched for using the transcriptome sequences. An established precursor sequence of the protein of interest was used as the query sequence. Precursor protein sequences were either extracted from the *H. americanus* transcriptome or a well-established *Drosophila melanogaster* transcriptome (Veenstra, 2016; https://www.uniprot.org/; http://flybase.org/blast/). Using the University of Hawaii Manoa BLAST software, the specific *H. americanus* tissue transcriptome assembly was blasted using a tblastn against the query sequence. The program produced Trinity numbers linked to aligning nucleotide sequences. The nucleotide sequence that corresponded to

the Trinity number was translated into an amino acid sequence using the program Expasy (https://web.expasy.org/translate). Expasy produces six possible open reading frames (three forward and three reverse). The longest sequence was selected because that is conceivably the sequence that translates into the protein of interest. The selected open reading frame sequence was aligned with its query sequence using the MAFFT alignment software (https://mafft.cbrc.jp/alignment/software/). The amino acid sequences that were identical was indicated by an asterisk ('*'). The percent identity was calculated based on the similarity in alignment. If there was a percent identity above 80 percent, the neuromodulator or receptor would be predicted to be synthesized or present in the tissue. Using reciprocal blast programs, the unknown proteins were blasted against known proteins using Flybase and NCBI Blast to compare and make predictions about the identity of the unknown protein (Christie et al., 2015). Using the program Flybase (http://flybase.org/blast/), the neuropeptide and receptor sequences were compared to *D. melanogaster* annotated proteins. Using NCBI Protein Blast (https://blast.ncbi.nlm.nih.gov/Blast.cgi), the proteins were blasted using a blastp and then compared to non-redundant arthropods proteins, which allowed for a larger scale search.

2.2.3- Neuropeptides

Preprohormones, once cleaved by enzymes, become smaller peptides that undergo post translational modifications that are known to cause changes in the peptide's modulatory effects. Enzyme cleavage sites were predicted based on the programs used (detailed below) and research in Christie et al. (2017), which analyzed the transcriptomes of the eyestalk ganglia of the American lobster. SignalP 5.0 (http://www.cbs.dtu.dk/services/SignalP/) and Neuropred (http://stagbeetle.animal.uiuc.edu/cgi-bin/neuropred.py) software predicted the signal peptide that promotes cleavage at that region. Using Expasy's Sulfinator program

(https://web.expasy.org/sulfinator/), sites of tyrosine sulfation within the protein sequences were predicted. “DiANNA” (http://clavius.bc.edu/~clotelab/DiANNA/) compares the putative peptide isoforms to the current sequence and helped predict the disulfide bond formation between cysteine residues. Other cleavage sites were manually predicted from previous research that predicted common sites of cleavage like X-X-K-R↓, R-X-X-R↓, R-X-X-X-X-R↓, and RR↓ (‘↓’ indicates the point of cleavage) (Veenstra, 2000).

2.2.4- Receptors

Using the following programs, the characteristics and location of putative receptors were predicted. The program WOLFpsort (https://wolfpsort.hgc.jp/) software was used to make inferences about the location of the receptor within the cell (Wu et al., 2015). Using the program Pfam (http://pfam.xfam.org/search/sequence), the specific structure of the receptor was predicted. Many of the receptors were identified as 7 transmembrane receptors, indicating that they are most likely G protein-coupled receptors (GPCRs). GPCRs usually signal a secondary messenger pathway to exert their effect. Further investigations into the GPCRs were done with the program TOPCONS (https://topcons.cbr.su.se/), which combines five topology methods (OCTOPUS, Philius, PolyPhobius, SCAMPI, and SPOCTOPUS). The topology of the receptors and the number of times the receptor passes through the cell membrane was estimated (Tsirigos et al., 2015).

2.3 Physiological Experiments

2.3.1- Lobster Heart Dissection and Experimental Set Up

For physiological experimentation, the lobsters were anesthetized in ice for ~30 minutes. The heart, which is located anterior to the tail and dorsally situated, was removed from the body and detached from the carapace. The heart remained attached to the hypodermis and was placed

in a bath of physiological lobster saline (composition in mM: 479.12 NaCl, 12.74 KCl, 13.67 CaCl2, 20.00 MgSO4, 3.91 Na2SO4, 11.45 Trizma base, and 4.82 maleic acid; pH 7.45). Under a dissecting microscope, the heart was opened to visualize the intact cardiac ganglion and the muscle fibers.

A Rabbit peristaltic pump (Gilson, Middleton, WI) was used to superfuse saline over the cardiac neuromuscular system at a rate of approximately 5ml/min. A Peltier temperature regulator (CL-100 bipolar temperature controller and SC-20 solution heater/cooler; Warner Instruments, Hampden, CT) was used to cool the saline. Due to the lobster's thermal sensitivity, it was critical that the saline temperature was maintained at 10-10.5^{o}C to keep the cardiac ganglion activity stable (Johnson et al., 1991; Tang et al., 2010; Oellermann et al., 2020).

2.3.2- Myosuppressin Preparation

Myosuppressin (pQDLDHVFLRFamide; MW = 1272.46 g/mol) was synthesized by GenScript Corporation (Piscataway, NJ) and was stored as a stock solution at 10^{-3}M and stored at -20^{o}C. Myosuppressin is relatively insoluble in water, so to make the stock solution, it was dissolved in DMSO (15%) and deionized water. For experiments, stock solutions were diluted in lobster saline to 10^{-7}M.

2.3.3- The neuromuscular junction

To visualize the activity at the NMJ, the EJPs were recorded using a microelectrode filled with squid cytoplasmic fill (20 mM NaCl, 15 mM Na_2SO_4, 10 mM Hepes, 400 mM potassium gluconate, 10 mM $MgCl_2$) (Hooper et al., 2015). The electrode was inserted into a single muscle fiber. The intracellular activity was monitored by using an AxoClamp 2B amplifer (Axon Instruments, Molecular Devices, LLC., San Jose, CA).

However, before inserting the microelectrode, the cardiac ganglion was removed to eliminate spontaneous EJPs (Figure 6A). The motor nerve ending was then stimulated using a model 2100 Isolated Pulse Stimulator (A-M System, Sequim, WA) to elicit a contraction of the muscle fibers in which it innervates. The intracellular electrode was then inserted into one of those muscle fibers. The resting membrane potentials of the muscle fibers were between -30 and -70 mV.

To evoke EJPs, the motor nerve ending was stimulated with three stimulating pulses, resulting in three EJPs (Figure 6B). Each stimulation had a duration of 5×10^{-4} seconds and an inter-pulse period of 0.4 seconds. Because each motor nerve required a different threshold voltage to reliably generate an EJP, a range of voltages were required across preparations (2-7 V). Every 10 seconds, the three stimuli were delivered using a burst width of 1.1 seconds. Once the preparation was stable for experimentation, myosuppressin was superfused over each preparation for 20 minutes (Stevens et al., 2009). To ensure that the preparation's activity returned to baseline, a 40-minute saline wash was imposed.

2.3.4- Investigating the role of the cardiac muscle

To determine whether myosuppressin exerts an effect directly on the muscle, the cardiac muscle contractions were measured in the absences of neuronal input using methods that were adapted from Maguire (2019). The heart of the lobster was opened to visualize the cardiac muscle and cardiac ganglion. A bundle of healthy cardiac muscle was located (either the left or right longitudinal cardiac muscle), and hooks were glued perpendicular to each end of the bundle using GluTure topical tissue adhesive (Zoetis Inc., Kalamazoo, MI) (Figure 7). For gluing, the muscle fiber bundle was dried so that there was no physiological saline in the region that was to be glued. Glue was allowed to dry to the muscle for 30 seconds before reapplying saline. A hook

attached to a force transducer was perpendicularly placed gently on the center of the bundle. The SI-H optical force transducer (WPI Inc., Sarasota, FL) measured the extent to which the muscle contracted. The force transducer was calibrated to measure the force of contraction in grams.

Since the cardiac ganglion drives the contraction of the cardiac muscle, the cardiac ganglion was completely removed from the preparation. Thus, the muscle fibers were isolated from any stimulus and source of drive, while also completely bypassing the NMJ so that the muscle activity could be independently measured.

Normally the NMJ releases the excitatory neurotransmitter glutamate onto the muscle to cause a contraction (Delgado et al., 2000). Since the activity from the NMJ was eliminated, the muscle was artificially stimulated using a Picospritzer II (General Valve Corporations, Fairfield, NJ) to puff glutamate at 10^{-4}M from an electrode (Glass, Standard, 1.0 MM x .5) cut with a tip of about 15μm (Figure 7). The puff (pressure of 20psi and duration of 200ms) was administered on a singular muscle fiber to induce contraction of that fiber (Aonuma et al., 1998).

Desensitization of the muscle from glutamate was observed when an alternative method was initially used. Here, glutamate (10^{-3} M) was superfused over the muscle for 15-30 seconds every three minutes (based on methods in Lingle (1980)). However, there was a clear decrease in the muscle contraction with every superfusion, which was predicted to be attributed to the muscle desensitization to glutamate (Titlow & Robin, 2018). This issue was resolved by transitioning to the puffing method and using a lower concentration of glutamate.

Once the muscle showed a clear response to the glutamate, glutamate puffs were repeatedly delivered every 100 seconds using a Grass S88 Stimulator (Grass Inst. Co., Quincey, MA), to avoid the desensitization of the muscle fiber. When the muscle was stabilized, myosuppressin (10^{-7} M) was superfused over the muscle for 20 minutes, to record its response on

the cardiac muscle. After myosuppressin, the preparation underwent a 40-minute-long saline wash to ensure that all the myosuppressin was eliminated from the preparation before continuing experimentation. During the saline wash, glutamate was still repeatedly puffed. Only preparations in which responses returned approximately to baseline were analyzed.

As a control, lobster saline was puffed onto the muscle to ensure that the mechanical force of the puff application did not cause a muscle contraction.

2.3.5- Data Recording and Analysis

Analogue signals were digitalized at 10kHz using a Micro 1401 (CED, Milton, Cambridge, UK) and recorded on Spike 2v7 (software; CED, Milton, Cambridge, UK).

Neuromuscular Junction

The amplitudes of the three stimulated EJPs (EJP 1, EJP 2, EJP 3) were measured by using the "peak finder" function and the "minimum value" function in Spike 2. Since the EJPs showed facilitation, I analyzed them as three separate groups: EJP 1, 2, and 3 in each condition (e.g. saline control, myosuppressin, and wash).

For each heart preparation (N=6), amplitudes of the twelve sets of three stimulated EJPs from 1-120 seconds prior to myosuppressin superfusion were averaged, as were the amplitudes of the twelve EJP sets recorded 600-720 seconds after that start of myosuppressin superfusion.

Cardiac Muscle

The glutamate-evoked contraction amplitude was measured using a custom script that found the maximum value of the force (in grams) after each glutamate puff. To analyze the contraction change between saline and myosuppressin, the amplitudes of four stimulated contractions, elicited 300-700 seconds before the onset of myosuppressin superfusion, were

measured, as were contractions stimulated from 600-1000 seconds after the onset of myosuppressin superfusion (N=5).

2.3.6- Neuromuscular Junction and Cardiac Muscle: Statistical Analysis

Prism v7.0 was used for statistical analysis and graphing (GraphPad Software, Inc., San Diego, California). Using a paired t-test, the significance between saline and myosuppressin was determined, with the significant value being less than 0.05.

Chapter 3: Results

3.1- Bioinformatics

Using the bioinformatics workflow, the sites and sources of modulation of a variety of neuropeptides and their corresponding receptors were predicted.

3.1.1- Neuropeptides in the Cardiac Ganglion

Using the "cardiac ganglion combo" transcriptome, which includes both the pacemaker interneurons and the motor neurons, twenty-five neuropeptides were analyzed to determine their expression in the cardiac ganglion (Table 1). Of the neuropeptides searched for, sequences encoding RNA were identified in the cardiac ganglion transcriptome for the following: C-type allatostatin (AST-C), myosuppressin, proctolin, red pigment concentrating hormone (RPCH), and tachykinin (CabTRP) (Table 2)**.** These neuropeptides are predicted to be synthesized and released from the neurons within the cardiac ganglion.

3.1.2- Receptors in the Cardiac Ganglion and Cardiac Muscle

Using the cardiac ganglion combo transcriptome, twenty-three receptors were analyzed to determine their expression in the cardiac ganglion (Table 3). In the cardiac ganglion combo transcriptome, of the receptors analyzed, sequences encoding RNA were present for those of the following neuropeptides and amines: adipokinetic hormone-corazonin-like peptide **(**ACP), AST-C, buscicon, CCAP, diuretic hormone 31 (DH31), diuretic hormone 44 (DH44), myosuppressin, octopamine (β receptor), proctolin, pyrokinin, and serotonin (Table 4). All eleven receptors were identified as 7 transmembrane receptors and were predicted to be GPCRs.

Using the cardiac muscle transcriptome, twenty-two receptors were analyzed to determine their expression in the cardiac muscle (Table 3). The receptors sequences encoding RNA in the cardiac muscle transcriptome were present for those of the following neuropeptides

and amines: AST-C, bursicon, DH31, DH44, myosuppressin, octopamine β, and serotonin (Table 5). All seven receptors were predicted to be 7 transmembrane GPCRs.

Since there can be multiple receptors for each neuropeptide, the specific receptor variants are listed in Table 4 and 5. The percent identities to the query sequences for each present neuropeptide and receptor identified in these transcriptomes are also indicated in Tables 2, 4, and 5.

3.1.3- Intrinsic and extrinsic modulation

From the bioinformatics workflow, AST-C and myosuppressin were predicted to be intrinsic modulators. AST-C and myosuppressin were also predicted to be the only two (of those analyzed) that might function as locally released extrinsic modulators. This suggests that many of the other neuromodulators analyzed that have receptors located in the cardiac neuromuscular system are released and synthesized in other systems of the lobster, such as the paracardial organ or the eyestalk. However, since transcriptomes are often incomplete, it is possible that this transcriptome did not include the sequences that are linked with the putative proteins of interest.

3.1.4- Myosuppressin

Five protein sequences that appear to be homologous to myosuppressin receptors (MSR-I, II, III, IV, V) in other systems have been identified in the lobster nervous system (Oliesky et al., 2020). For MSR IV, three variants were identified. MSR II-IV (all variants) were found in the cardiac ganglion. I further investigated the MSRs and corroborated the results reported in Oliesky et al. (2020), identifying MSR II-IV (all variants) in the cardiac ganglion. The MSRs that were identified by Oliesky et al. (2020) had a partial or full alignment with the query sequences with a 100 percent identity. In the present study, only MSR IV (variant 1 and 2) was

identified in the cardiac muscle, with both variants being partial sequences. Both variants showed 100 percent identity with the query sequences.

3.2- Physiological Experiments

3.2.1- Myosuppressin does not act at the neuromuscular junction

Since MSRs were predicted to be present in both cardiac ganglion and cardiac muscle tissue, it was hypothesized that these receptors may be expressed at the presynaptic and/or postsynaptic terminal of the NMJ, where myosuppressin binding could result in enhanced EJP amplitude. Figure 8 shows that the mean EJP amplitudes recorded in control saline and during the superfusion of 10^{-7}M myosuppressin did not differ for any of the three consecutively stimulated EJPs (paired t-test, $p < 0.05$; N=6). These data suggest that myosuppressin does not act at the NMJ.

3.2.2- Myosuppressin Cardiac Muscle Results

Since MSRs were predicted to be present in cardiac muscle tissue, it was hypothesized that these receptors may be expressed at the muscle, where myosuppressin binding could result in altered muscle contraction. To test this, I applied myosuppressin at a concentration of 10^{-7}M over the muscle while recording from a single fiber. Figure 9 shows that myosuppressin induced an increase in glutamate-evoked contractions of the cardiac muscle. Peak contraction amplitude occurred around 600 seconds after myosuppressin was applied and then during the saline wash the amplitude decreased steadily. There was an increase in the mean amplitude of the glutamate-evoked contractions when myosuppressin (10^{-7}M) was superfused compared to control saline (paired t-test, $p < 0.05$; N=5) (Figure 10). These data suggest that myosuppressin is acting at the cardiac muscle.

Chapter 4: Discussion

A number of neuromodulators have been shown to exert effects on the lobster cardiac neuromuscular system; of these, several have been found to exert effects on the NMJ and/or the cardiac muscle (e.g. Wilkens et al., 2005; Dickinson et al., 2015). One of these neuromodulators is proctolin, which is known to modulate both the NMJ and the muscle (Wilkens et al., 2005). Surprisingly, in my investigation of the cardiac muscle transcriptome, RNA encoding the proctolin receptor was not found. However, that does not mean proctolin cannot act at the muscle, as shown in Wilkens et al. (2005). Instead, it suggests that the cardiac muscle transcriptome is incomplete. Since both myosuppressin and proctolin enhance contractions of the intact heart, it may be possible that they use analogous mechanisms, in which case we might expect them to exert effects at the periphery similarly. Interestingly, while myosuppressin did not appear to modulate at the NMJ, I show that myosuppressin exerts effects directly on the cardiac muscle. However, since there was a small sample size for analyzing the effects of myosuppressin on both the NMJ and the cardiac muscle, these are preliminary results that can be further studied using the same methodology.

4.1- Proctolin modulates the NMJ via altered membrane resistance and regulates the cardiac muscle via L-type Ca^{2+} channels

Proctolin was found to cause an increase in the muscle membrane resistance at the postsynaptic membrane, leading to an increase in EJP amplitude (Erxleben et al., 1995). Conversely, my results which indicate that myosuppressin does not modulate the EJPs and, thus, it seems unlikely to alter muscle resistance. Muscle membrane resistance was not measured in this experiment. However, there was no obvious, observable change in membrane potential when myosuppressin was applied (data not shown).

To examine the effect of myosuppressin on calcium dynamics in the muscle, one can measure changes in the Ca^{2+} concentration, using a fluorescent calcium indicator similar to methods used in Wilkens et al. (2005). They show that the extent to which the cardiac muscle contracted with proctolin was proportional to an increase in Ca^{2+}. These data suggest that proctolin affects the Ca^{2+} dynamics; however, the mechanism of action remains unclear.

This method would inform us about whether Ca^{2+} does play a role in modulation. Wilkens et al. (2005) shows that the cardiac muscle had an enhanced muscle force during proctolin application, results that are similar to the effect myosuppressin had on the cardiac muscle. There are at least two processes that could underlie this phenomenon: modulation of T-type Voltage gated Ca^{2+} channels or Ca^{2+} release from L-type Ca^{2+} channels in the sarcoplasmic reticulum (SR). Proctolin does not affect the T-type Ca^{2+} channels. In the presence of T-type Ca^{2+} blockers (nifedipine, verapamil, and Cd^{2+}), proctolin still enhanced contraction, showing the T-type Ca^{2+} receptors are not sufficient to drive the proctolin-induced increase in contraction. However, with ryanodine, which is a L-type Ca^{2+} blocker, they found that contraction was suppressed even with application of proctolin, suggesting that proctolin needs the sequestered Ca^{2+} from the SR to cause enhanced contraction. Moreover, when they applied proctolin and caffeine, which elicits Ca^{2+} release from the SR, there was a faster and stronger proctolin-induced contraction in comparison to when caffeine was not present. This suggests that the Ca^{2+} release from L-type Ca^{2+} channels mediate the effect of proctolin on the muscle. Performing a similar experiment using myosuppressin would aid in determining whether Ca^{2+} dynamics are altered by activation of myosuppressin receptors in the cardiac muscle of the lobster.

Myosuppressin receptor IV (variants 1 and 2) was predicted to be located at the cardiac muscle. Pfam and Topcons predicted these variants to be GPCRs based on their characteristic 7

transmembrane structure. Many GPCRs activate secondary messenger pathways that can alter calcium dynamics within the muscle, which would allow them to modulate the contraction. In vertebrate cardiac muscle, the cAMP pathway usually elicits muscle contraction (Kuo & Ehrlich, 2015). Myosuppressin GPCRs are not well understood. However, in *Drosophila*, proctolin GPCRs were found to modulate cardiac muscle contraction through activation of both cAMP and IP_3 pathways (Hiripi et al., 1979; Lange, 1988; Hinton & Osborne, 1996; Baines et al., 1990). Both pathways activate the release of Ca^{2+} from the SR, which supports evidence that proctolin mediates sequestered Ca^{2+} release as observed by Wilkens et al. (2005).

As mentioned, myosuppressin could be eliciting a variety of different mechanisms, including activation of secondary messengers, altered calcium dynamics in the muscle, or both. Another possibility is that myosuppressin could indirectly mediate ion channels through activating the G-protein. However, this is unlikely, since there was no obvious change in the membrane potential with myosuppressin (data not shown). Membrane potential was not measured in this experiment, so future research could be done looking at this parameter for more insight on the G-protein pathway. Myosuppressin could also affect a combination of these mechanisms listed and that combination could result in the response seen at the cardiac muscle.

4.2- Myosuppressin is a FMRFamide-like peptide

Myosuppressin is part of the larger FMRFamide-like peptide (FLP) family. Myosuppressin has been shown to have inhibitory effects, however, in the American lobster, myosuppressin drives responses with an excitatory component in the cardiac neuromuscular system of the American lobster (Tanaka, 2016; Stevens et al. 2009). Activated FRMFamide GPCRs have been studied in the cardiac muscle of the squid (*Loligo forbesii*) and were found to alter calcium in the cardiac muscle (Chrachri et al., 2000). In the squid, there are two types of

cardiac muscle—type I, which is a smooth surfaced membrane while type II has a more invaginated surfaced membrane. FLPs act on the L-type Ca^{2+} channels, but not on T-type Ca^{2+} channels in both muscle types. Interestingly, the two muscle types responded to FLP differently. In type I cardiac muscle, FLP suppressed the L-type Ca^{2+} channels through a GPCR pathway and, in type II muscles, FLP caused a calcium current influx, which was not triggered by a GPRC (Chrachri et al., 2000). Since myosuppressin shares similar structural elements to FLPs and is known to cause increased contractile responses in the cardiac muscle, the altered Ca^{2+} dynamics caused by myosuppressin may be similar to that seen from FLP acting on the type II muscle. However, the myosuppressin receptor has also been predicted to be a GPCR, thus resembling the pathway that resulted in the suppression of contraction seen in type I muscle. Information about the membrane surface structure of the cardiac muscle in the American lobster is not known, so it is unclear whether the muscle would resemble type I or II squid cardiac muscle more closely. Moreover, FLPs have differing effects on the varying cardiac muscle due to the complexity of downstream receptor pathways. Experiments are needed to confirm myosuppressin receptors as GCPRs, through observing expression of common secondary messengers like cAMP and IP_3. Furthermore, studying the structure of the cardiac muscle in the American lobster would contribute to the understanding of its commonalities with squid cardiac muscle.

4.3- Differing Effects of Neuromodulators Based on Receptor Variants and Distribution

It is possible that the multiple myosuppressin receptors could exert different effects through varying G-protein or other signaling pathways. For instance, in the stomatogastric nervous system of *Cancer borealis*, serotonin released from the same presynaptic neuron drove different responses in three postsynaptic neurons: LG, MCN1 axon terminals, and DG (Delong et

al., 2009; Kiehn et al., 1992; Powell et al. 2020). It is hypothesized that the serotoninergic-mediated responses were distinct based on the types of 5-HT receptors expressed by these neurons. It has also been hypothesized that the distribution of those different receptors in the tissue lead to unique responses in different cells. Oliesky et al. (2020) found that myosuppressin, when acting on the pacemaker interneurons and the motor neurons separately, produced differing responses. They hypothesized that this could be attributed to the varying distribution of the myosuppressin receptors I-V, alongside the hypothesis that the receptors also exert different effects.

4.4- Myosuppressin may alter the neuromuscular transform

Because the cardiac neuromuscular system of the lobster is subject to stretch-induced positive-feedback and the nitric oxide negative-feedback, understanding more about how myosuppressin modulates contractions would provide further insight into how the heartbeat is regulated in these animals. For instance, we know that modulation of the cardiac ganglion output alters the heart contraction amplitude through the non-linear neuromuscular transform (NMT) (Williams, 2013). The NMT is the activity that results from specific motor neuronal patterns transforming into muscle contractions. Mapping the NMT activity allows inferences to be made about whether there is facilitation or defacilitation of muscle contractions, providing information that can help us understand how modulators exert their effects. William et al. (2013) mapped the NMT activity by observing how the contraction amplitude depended on duty cycle and burst frequency. Although the NMT is non-linear, the cardiac muscle showed stronger contractions with decreased cycle frequency and duty cycle. Myosuppressin is known to increase the burst duration while decreasing the duty cycle and cycle frequency of action potential bursts in the isolated cardiac ganglion (Stevens et al., 2009). Based on Williams et al. (2013), the burst

activity of myosuppressin would increase contraction amplitude. This trend has been specifically attributed to facilitation of contractions due to the decreased duty cycle for contraction (Williams, 2013; Stevens et al., 2009). Through understanding the relationship between the neural circuits and the motor outputs, there can be a greater understanding of how these complex pattern generators are modulated.

4.5- Other Neuromodulators' Effects on the Periphery of the Cardiac Neuromuscular System

AST-C is one of the neuromodulators that has been analyzed in an isolated periphery (Wiwatpanit et al., 2012). There are four receptors that have been predicted to be in the cardiac neuromuscular system based on homologous sequences to AST-C receptors in other systems. Of those four, receptor 1 and 2 have been shown to be functional, while receptor 3 and 4 have been found to be non-functional (Walsh, 2017; J. Joe Hull, personal communication). In my investigation of the cardiac muscle, I predicted that receptor 1 and 2 were expressed in cardiac muscle (Table 5). Interestingly, Wiwatpanit et al. (2012) found that AST-C did not alter activity at the NMJ or cardiac muscle. These results reveal that receptors predicted to be expressed at the cardiac muscle using bioinformatics, does not necessarily mean that they modulate the heartbeat. These receptors could act in other ways such as, regulating metabolism or mediating another system that cannot be physiologically recorded at present. The receptors could also be expressed conditionally or be non-functional in the cardiac muscle.

Little is known concerning the mechanisms by which other neuromodulators actually modulate the NMJ or muscle fibers. GYS and SGRN are two peptides that have been studied in the American lobster; both were found to cause an increase in contraction amplitude at the periphery, but it is still unknown whether they exert effects at the NMJ and/or the cardiac muscle (Dickinson et al., 2015). Other neuropeptides that have been found to have enhancing effects on

the cardiac neuromuscular system by increasing both the amplitude and frequency of the heart contraction in whole heart preparations, include DH31, sulkakinin, octopamine, and to a lesser extent tyramine (Christie et al., 2010; Dickinson et al., 2007; unpublished data by Anthony Yanez). My data show that both DH31 and octopamine are predicted to have receptors located in the cardiac muscle. In future research, similar methodology to the myosuppressin experiments described here could be used to discover if GYS and/or SGRN modulate the periphery through the NMJ, muscle, or both. Additionally, other modulators such as DH31, octopamine, sulkakinin, and tyramine could be investigated in this way. Using the CPG-effector system to study the mechanisms of modulation will give us a greater understanding of neuronal circuits at large and can provide insight into how lesser known circuits operate.

Chapter 5: Figures and Tables

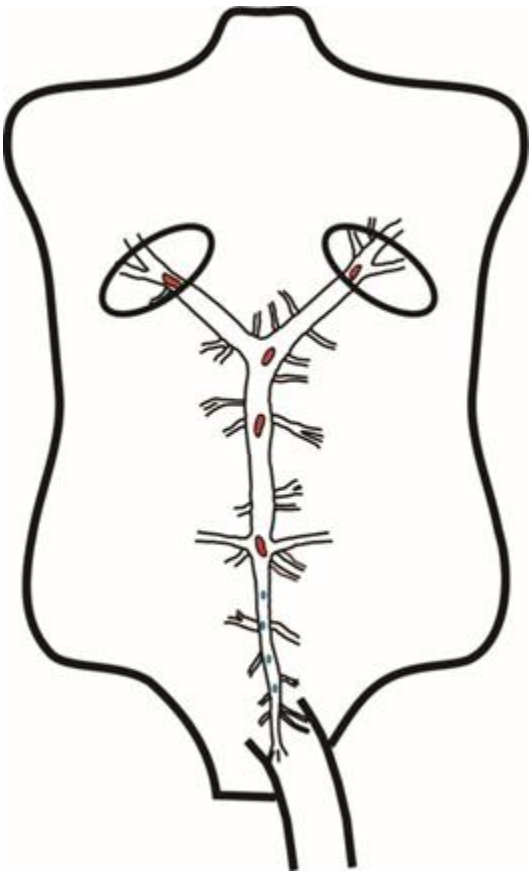

Figure 1. **A ventral view of the cardiac neuromuscular system of the lobster.** The Y shape of the cardiac ganglion is illustrated, with the motor neurons in red and the pacemaker interneurons in green. The two ovals over the two branches of the "Y" are the ostia where hemolymph enters the heart. The arteries are located at the posterior and anterior end of the system (Dickinson et al., 2016).

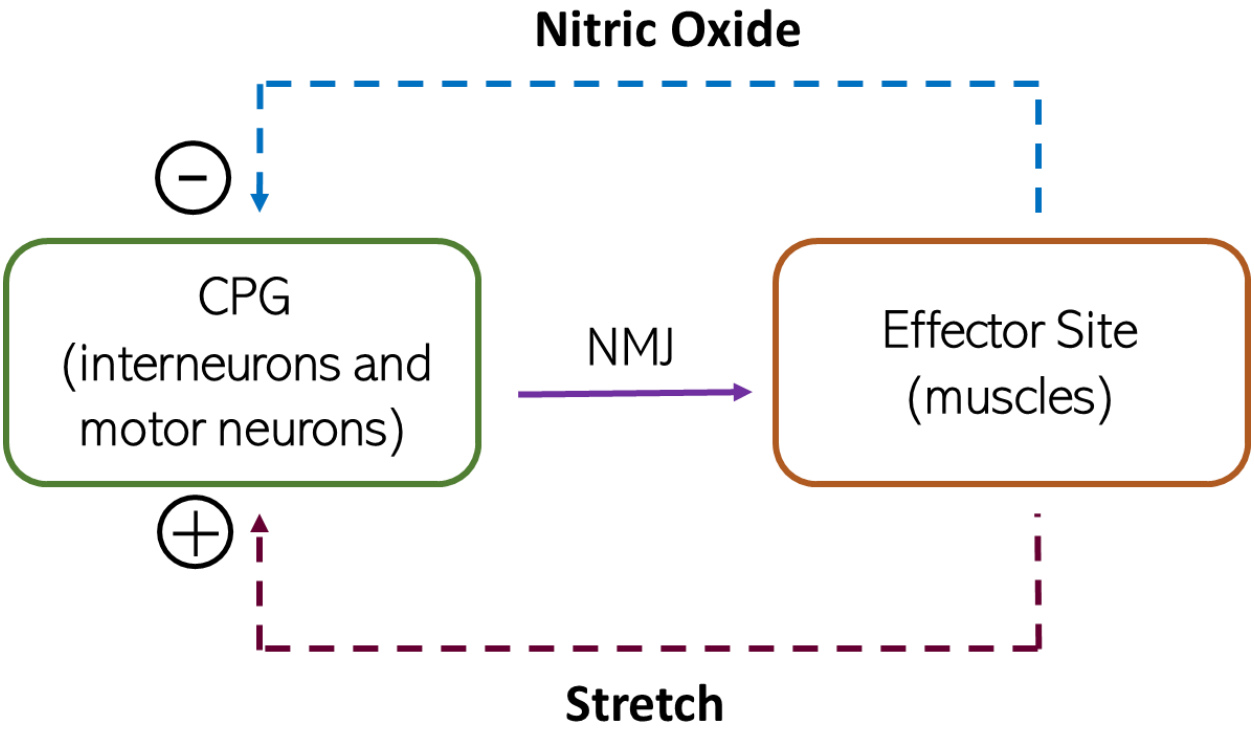

Figure 2. **A schematic diagram of the CPG-effector system and its closed feedback system.** The nitric oxide response is a negative feedback pathway while a stretch sensitive response is a positive feedback pathway. Neuromodulators that modulate at the level of the CPG, NMJ, or effector site can in turn modulate other regions within the CPG-effector system.

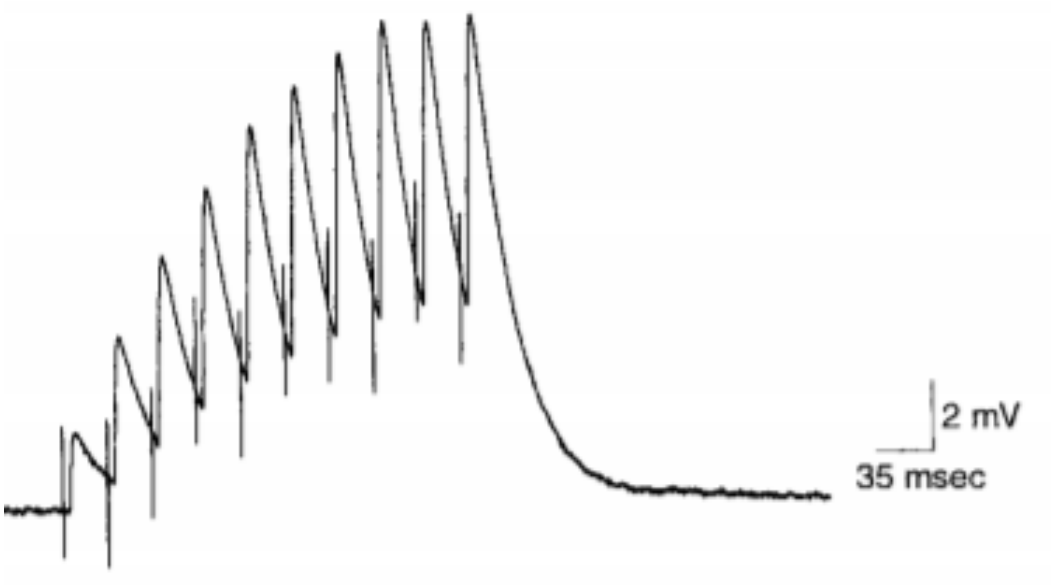

Figure 3. **Example of the facilitation of EJPs.** A nerve was stimulated with ten identical pulses at 40Hz, resulting in a facilitation of the EJPs (Crider & Cooper, 2000).

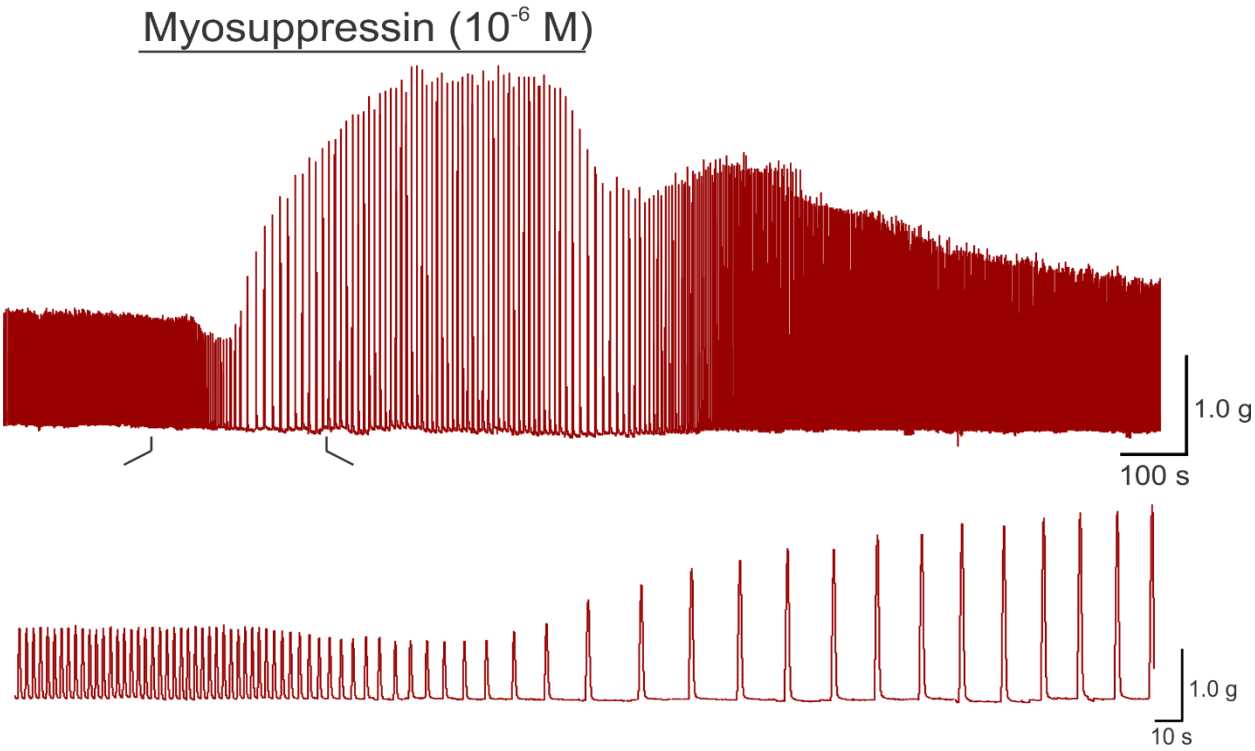

Figure 4. **Myosuppressin increases amplitude and decreases frequency of the muscle contraction in the whole heart of the American lobster**. An example of a whole heart recording with myosuppressin at 10^{-6}M (application illustrated by the black line). The recording measures force in grams on the y-axis and time in seconds on the x-axis (Stevens et al. 2009).

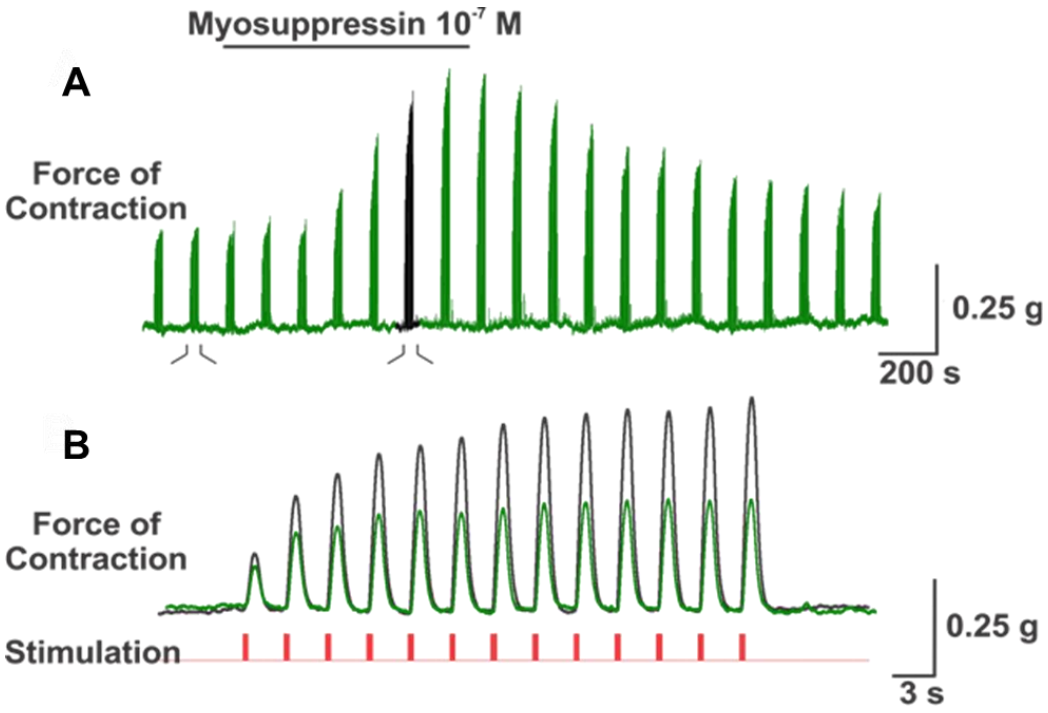

Figure 5. **Myosuppressin caused an increase in contraction more than double the contraction at baseline in the periphery of the cardiac neuromuscular system of the American lobster.** (A) An example recording of the heart's contractile force at just the periphery. The periphery was isolated through removing the cardiac ganglion and then the motor nerve was stimulated thirteen times at 60Hz with 300ms bursts. (B) With a higher speed recording, there is a visible increase in the contractile force with myosuppressin (black) compared to baseline (green) from the start stimulation (orange) to the end of the thirteen bursts. The recording measures force in grams on the y axis and time in seconds on the x axis (Stevens et al., 2009).

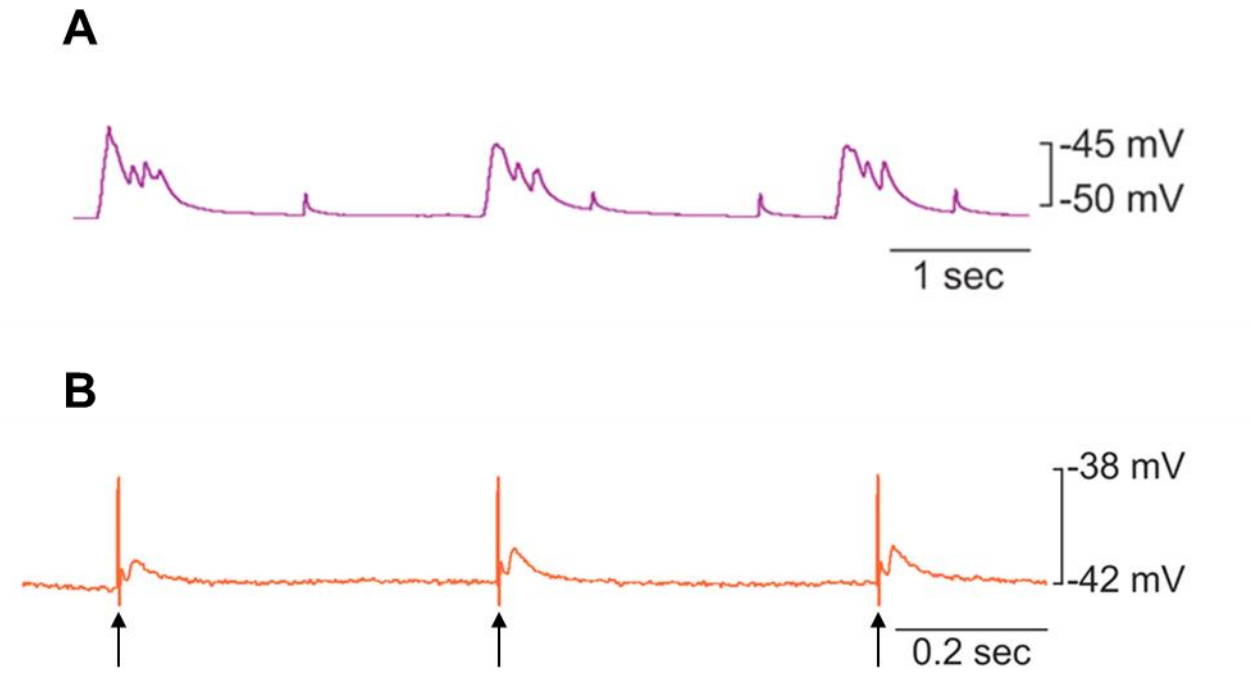

Figure 6. **Comparing endogenous EJPs to stimulated EJPs**. (A) Spontaneous excitatory junction potentials (EJPs) are a result of bursts of action potentials coming from the intact cardiac ganglion. (B) Recording of excitatory junction potentials (EJPs) at the neuromuscular junction (NMJ) when the cardiac ganglion was removed, so the neural activity at the NMJ was isolated. Each EJP results from a single stimulus to the motor nerve—indicated by the black arrows (note the stimulus artifact before each EJP). Note the differing time scales for A and B.

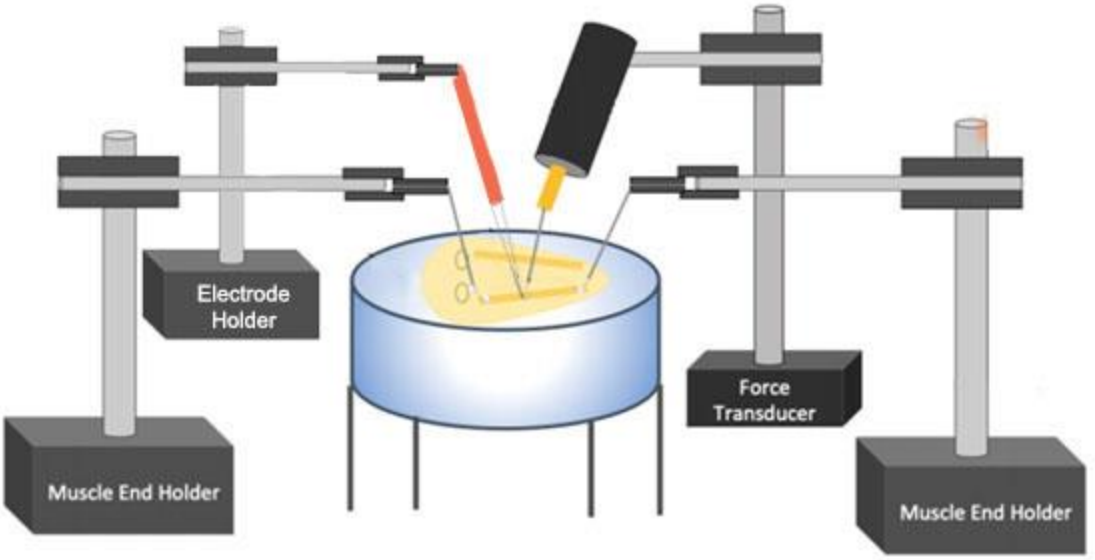

Figure 7. **Experimental set up for measuring glutamate-evoked contractions from the cardiac muscle (an experiment model modified from Matthew Maguire's thesis (2019)).** The muscle end holders have hooks, which held the cardiac muscle bundle in place. The white patches where the hooks meet the muscle are representative of the GluTru that helped in holding the muscle in place. The force transducer then placed on the center of the muscle bundle, which measured the contraction force of the cardiac muscle. The glass microelectrode, represented by the clear triangle attached to the salmon colored electrode holder, was filled with glutamate and puffed onto the muscle fiber that was being measured by the force transducer. Note the removed cardiac ganglion, which would normally reside in between the left and right longitudinal muscle.

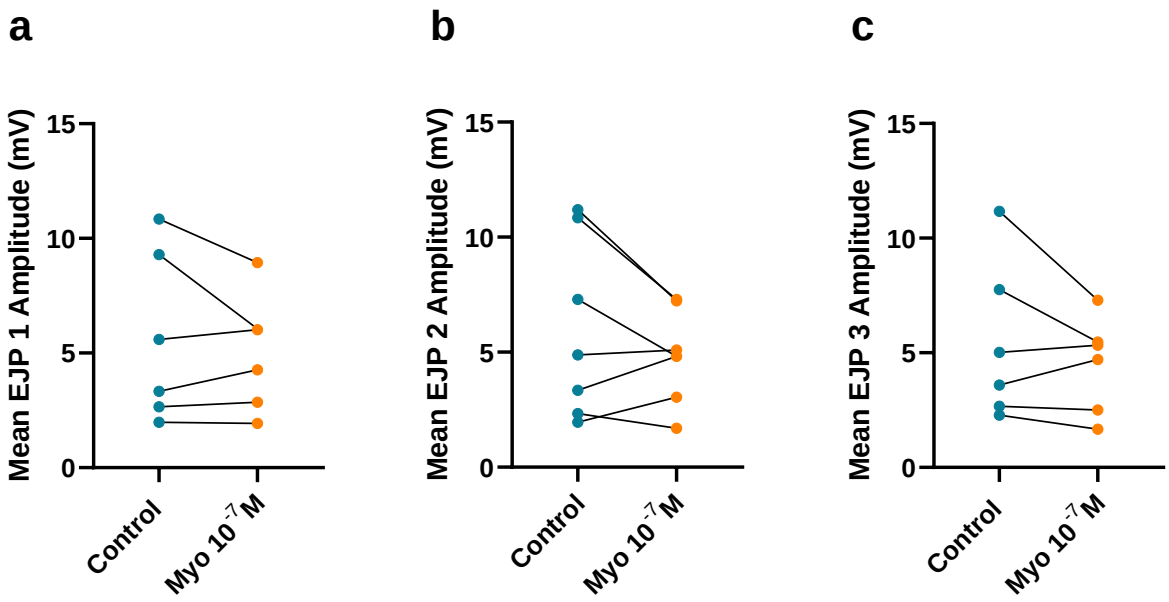

Figure 8. **Myosuppressin caused no significant change in EJP amplitude at the neuromuscular junction in the heart of the American lobster**. The mean amplitude of stimulated (a) EJP 1, (b) EJP 2, and (c) EJP 3 was calculated from the saline control (teal; EJP 1 (5.62 ± 3.69), EJP 2 (5.11 ± 3.42), EJP 3 (5.41 ± 3.45)) and the application of 10^{-7}M myosuppressin (orange; EJP 1 (5.01 ± 2.54), EJP 2 (4.46 ± 1.91), EJP 3 (4.50 ± 2.06)). There was no significant difference in the amplitude of EJPs between control and myosuppressin ($p > 0.05$, paired t-test; N= 6).

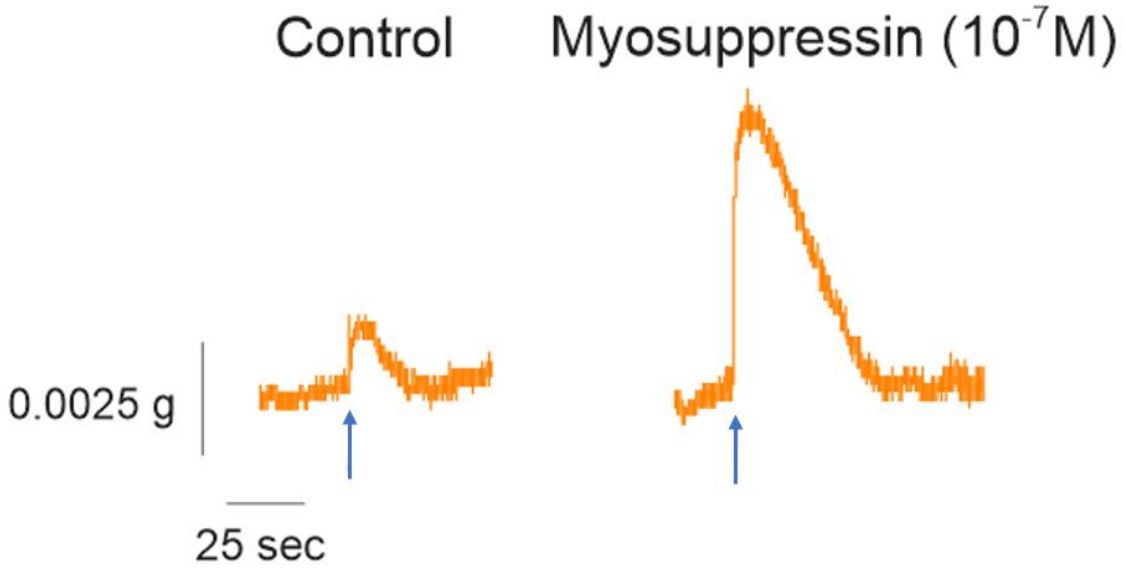

Figure 9. **Myosuppressin resulted in an increase in the amplitude of glutamate-evoked contractions when the endogenous cardiac ganglion activity was eliminated**. Both contractions were stimulated by a glutamate (10^{-4}M) puff, the time of these puffs is indicated by the blue arrows. The recording measures the force in grams (g) on the y-axis and time in seconds on the x-axis.

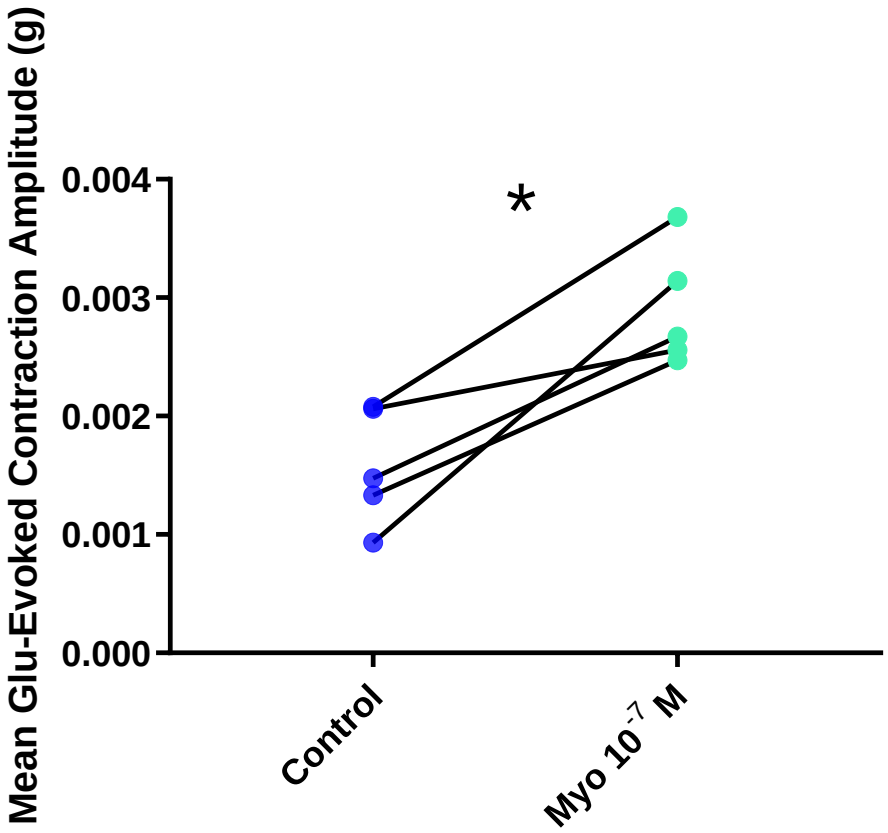

Figure 10. **Myosuppressin increased glutamate-evoked contraction amplitude in the isolated cardiac muscle**. The mean glutamate-evoked contraction amplitude from the isolated cardiac muscle in control saline (blue; 0.00158 ± 0.00049) and in myosuppressin 10^{-7}M (green; 0.002 ± 0.00050). Contraction amplitude to myosuppressin application in response to glutamate puff (paired t-test, $p < 0.05$; N= 5).

Neuropeptides	CG
ACP	-
AST-A	-
AST-B	-^
AST-C	+
Bursicon A	-
Bursicon B	-
CabTRP	+
CCAP	-
CCHamide 2	-
Corazoin	-
DH31	-*
DH44	-*
EFLamide	-
Elevenin	-
FMRFamide	-
MIH	-
Myosuppressin	+
Proctolin	+
Pyrokinin	-
Relaxin	-
RPCH	+
SIFamide	-*
Sulfakinin	-
Trissen	-
Vasopressin	-

Table 1**. Summary of the predictions made about whether the neuropeptide is synthesized and released in the cardiac ganglion using the *H. americanus* cardiac ganglion combo transcriptome.** Those neuropeptides that were predicted to be synthesized and released at the cardiac ganglion are indicated by '+,' while those that were not are indicated by '-.'

* - Alignment was inconclusive

^ - Alignment was too small

Neuropeptide	Trinity Number	Completeness of transcript	Percent Identity
AST-C	TR71619|c0_g1_i1	Partial	91.4
CabTRP	TR91706|c0_g1_i2	Partial	100
	TR91706|c0_g1_i1	Partial	100
Myosuppressin	TR26925|c0_g1_i3	Full	100
	TR26925|c0_g1_i2	Full	100
	TR26925|c0_g1_i1	Full	100
Proctolin	TR46909|c0_g1_i2	Full	100
	TR46909|c0_g1_i1	Full	100
RPCH	TR68520|c0_g1_i1	Full	100

Table 2. **Compiled data about the putative neuropeptides predicted to be synthesized and released in the cardiac ganglion.** Predictions were based on the neuropeptide's sequence alignment to their query sequence. The trinity number is an identifier for a nucleotide sequence in the cardiac ganglion combo transcriptome of *H. americanus.* The trinity numbers that are grouped by color are identical protein sequences. Percent identity was calculated by the number of matching amino acids over the number of total amino acids (that overlapped with the putative peptide sequence).

Receptor	CM	CG
ACP	-	+
AST-A	-	-
AST-C	+	+
Bursicon	+	+
CCAP	-	+
CCHamide	-*	-*
Corazoin	-	-
DH31	+	+
DH44	+	+
EFLamide	0	-
FMRFamide	-	-
Myosuppressin	+	+
Proctolin	-*	+
Pyrokinin	-	+
RPCH	-	-
SIFamide	-	-
Sulfakinin	-	-
Tackykinin	-	-
Amines		
Dopamine	-	0
Octopamine	0	-*
Octopamine β	+	+
OctTyr Combo	-	-
Serotonin	+	+
Tyramine	-*	-*

Table 3. **Summary of the presence of predicted receptors in the cardiac ganglion (CG) and the cardiac muscle (CM) using the tissue-specific transcriptomes of *H. americanus***. Those receptors that were predicted to be located at the cardiac ganglion/muscle are indicated by '+,' while those that were not are indicated by '-.'

* - Alignment was inconclusive

0- Not searched for in the transcriptome

Receptor	Variant	Trinity Number	Completeness of transcript	Percent Identity
ACP	Receptor 1	TR2344|c2_g3_i1	Partial	100
	Receptor 1	TR2344|c2_g3_i2	Partial	100
AST-C	Receptor 2	TR8916|c1_g2_i4	Full	100
	Receptor 2	TR8916|c1_g2_i2	Full	100
	Receptor 2	TR8916|c1_g2_i1	Full	100
	Receptor 4	TR56862|c4_g5_i1	Full	100
	Receptor 4	TR56862|c4_g4_i1	Full	100
	Receptor 4	TR56862|c4_g3_i1	Full	100
	Receptor 4	TR56862|c4_g2_i1	Full	100
	Receptor 4	TR56862|c4_g1_i1	Full	100
Bursicon	Receptor 1	TR45425|c0_g1_i1	Partial	100
	Receptor 1	TR68968|c0_g1_i1	Partial	100
CCAP	Receptor 1	TR86078|c0_g1_i1	Partial	100
	Receptor 1	TR3748|c0_g1_i1	Partial	100
DH31	Receptor 1	TR7828|c0_g1_i1	Full	99.6
	Receptor 1	TR7828|c0_g1_i2	Partial	99.7
DH44	Receptor 1	TR7124|c0_g1_i1	Partial	100
	Receptor 1	TR52110|c0_g1_i1	Partial	100
	Receptor 2	TR17601|c0_g1_i1	Partial	100
	Receptor 2	TR50316|c0_g1_i1	Partial	100
	Receptor 2	TR18146|c0_g1_i1	Partial	100
Myosuppressin	Receptor 2	TR22607|c0_g1_i3	Full	100
	Receptor 2	TR22607|c0_g1_i1	Partial	100
	Receptor 3	TR27825|c0_g1_i1	Partial	100
	Receptor 4 V1	TR38943|c0_g1_i4	Full	100
	Receptor 4 V1	TR38943|c0_g1_i3	Full	100
	Receptor 4 V1	TR38943|c0_g1_i1	Full	100
	Receptor 4 V2,3	TR38943|c0_g1_i4	Partial	100
	Receptor 4 V2,3	TR38943|c0_g1_i3	Partial	100
	Receptor 4 V2,3	TR38943|c0_g1_i1	Partial	100
Proctolin	Receptor 1	TR31134|c0_g2_i4	Full	99.8
	Receptor 1	TR31134|c0_g2_i3	Full	99.8
	Receptor 1	TR31134|c0_g2_i2	Full	99.8
	Receptor 1	TR31134|c0_g2_i1	Full	99.8
	Receptor 1	TR31134|c0_g2_i5	Partial	99.7
	Receptor 2	TR388|c0_g1_i2	Partial	100
	Receptor 2	TR388|c0_g1_i3	Partial	100
	Receptor 2	TR388|c0_g1_i1	Partial	100
Pyrokinin	Receptor 1	TR19456|c0_g1_i1	Partial	100
Amines				
Octopamine β	Receptor 2	TR29189|c0_g1_i1	Partial	100

	Receptor 2	TR7749|c0_g1_i1	Partial	100
Serotonin	Type 7 Receptor	TR30021|c1_g2_i2	Full	100
	Type 7 Receptor	TR30021|c1_g2_i1	Full	100

Table 4. **Compiled data about the receptors predicted to be expressed in the cardiac ganglion, including the variants of the receptors**. The trinity number is an identifier for a nucleotide sequence in the cardiac ganglion combo transcriptome of *H. americanus*. The trinity numbers that are grouped by color are identical protein sequences. Percent identity was calculated by the number of matching amino acids over the number of total amino acids (that overlapped with the putative receptor sequence).

Receptor	Variant	Trinity Number	Completeness of transcript	Percent Identity
AST-C	Receptor 1	TR42870|c0_g1_i1	Partial	83.4
	Receptor 2	TR42870|c0_g1_i1	Partial	100
Bursicon	Receptor 1	TR22406|c0_g1_i1	Partial	100
	Receptor 1	TR27789|c0_g1_i1	Partial	100
DH31	Receptor 2	TR48162|c0_g1_i2	Partial	100
	Receptor 2	TR48162|c0_g1_i1	Partial	99.1
DH44	Receptor 1	TR32466|c0_g1_i1	Partial	100
Myosuppressin	Receptor 4 Variant 1	TR17352|c0_g1_i1	Partial	100
	Receptor 4 Variant 2	TR17352|c0_g1_i1	Partial	100
Amines				
Octopamine β	Receptor 2	TR42209|c0_g1_i1	Partial	100
	Receptor 2	TR34866|c0_g1_i1	Partial	100
Serotonin	Type 7 Receptor	TR54400|c0_g1_i1	Partial	98.7
	Type 7 Receptor	TR40843|c0_g1_i1	Partial	100
	Type 7 Receptor	TR14406|c0_g1_i2	Partial	100
	Type 7 Receptor	TR14406|c0_g1_i1	Partial	100

Table 5. **Compiled data about the receptors predicted to be expressed in the cardiac muscle, including the variants of the receptors**. The trinity number is an identifier for a nucleotide sequence in the cardiac muscle transcriptome of *H. americanus.* The trinity numbers that are grouped by color are identical protein sequences. Percent identity was calculated by the number of matching amino acids over the number of total amino acids (that overlapped with the putative receptor sequence).

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Index

Query sequence and Putative Neuropeptide Alignments: Cardiac Ganglion Neuropeptides

AST-C

TR71619|c0_g1_i1

```
AST-C           MMPCPGHLIVALTLVLALTHALPAKEGPEAQKEVSSGHDGGRLTKRAAPASDTSQEELAA
TR71619|c0_g1_i ------------------------------------------------------------


AST-C           LKDLILSRLAAELEDSYQDLPSFKRDLLKAGIDMQEDDEGDDEGRREVKKKRMFAPLSGL
TR71619|c0_g1_i -----------------------------------------------------MFVPLSGL
                                                                     **.*****

AST-C           PGNLRTIKRQIRYHQCYFNPISCFRRK
TR71619|c0_g1_i PGELPTIKRQIRYHQCYFNPISCFRRK
                **:* **********************
```

CabTRP

TR91706|c0_g1_i2, TR91706|c0_g1_i1

```
CabTRP          MVRACTWAVLLGVVVVMGVVSAAGEGQDTPQDRERRAPSGFLGMRGKKDASTALDDNTAA
TR91706|c0_g1_i MVRACTWAVLLGVVVVMGVVSAAGEGQDTPQDRERRAPSGFLGMRGKKDASTALDDNTAA
                ************************************************************

CabTRP          SEYSSLPDPYPLYGLRDNNLPMLFAVPWKTKKAPSGFLGMRGKKSDEEVFSDATADNDLE
TR91706|c0_g1_i SEYSSLPDPYPLYGLRDNNLPMLFAVPWKTKKAPSGFLETRGKKSDEEVFSDATADNDLE
                ************************************  ********************

CabTRP          ILLKRAPSGFLGMRGKKAPSGFLGMRGKKAPSGFLGMRGKKYYXXXXXXXXXXXXSSRSE
TR91706|c0_g1_i ILLKRAPSGFLGMRGKKAPSGFLGMRGKKAPSGFLGMRGKKYYD--------------DD
                ******************************************               .:

CabTRP          LPLDFWVCVARRLITVRTPTRR
TR91706|c0_g1_i SDMDAYI---------------
                  :* ::
```

Myosuppressin

TR26925|c0_g1_i3, TR26925|c0_g1_i2, TR26925|c0_g1_i1

```
Myosuppressin   MVFRSCSWSCLLVVGVVVVMGVCVGVGETMPPPICLSQQVPLSPFAKKLCSALINISEFS
TR26925|c0_g1_i MVFRSCSWSCLLVVGVVVVMGVCVGVGETMPPPICLSQQVPLSPFAKKLCSALINISEFS
                ************************************************************

Myosuppressin   RAMEEYLGAQAIERSMPVNEPEVKRQDLDHVFLRFGRSQQ
TR26925|c0_g1_i RAMEEYLGAQAIERSMPVNEPEVKRQDLDHVFLRFGRSQQ
                *****************************************
```

Proctolin

TR46909|c0_g1_i2, TR46909|c0_g1_i1

```
Proctolin       MTRTGLVVVVALVVLAAALTQARYLPTRADDTRLDEIRELLREMLERTAEGANSRISGSG
TR46909|c0_g1_i MTRTGLVVVVALVVLAAALTQARYLPTRADDTRLDEIRELLREMLERTAEGANSRISGSG
                ************************************************************

Proctolin       YDKRFMYKRSVPEEGAAEMVQPALNLPQ
TR46909|c0_g1_i YDKRFMYKRSVPEEGAAEMVQPALNLPQ
                ****************************
```

RPCH

TR68520|c0_g1_i1

```
RPCH            MVRAGCALMLVVVVFASCVSAQLNFSPGWGKRAAAASGTDPAAASLHPAPPAVLTAASGA
TR68520|c0_g1_i MVRAGCALMLVVVVFASCVSAQLNFSPGWGKRAAAASGTDPAAASLHPAPPAVLTAASGA
                ************************************************************

RPCH            NAGDSCGTIPVSAVMHIYRLIRTEAARLIQCQEEEYMG
TR68520|c0_g1_i NAGDSCGTIPVSAVMHIYRLIRTEAARLIQCQEEEYMG
                ***************************************
```

Query sequence and Putative Receptor Alignments: Cardiac Ganglion Combo Receptors

ACP

TR2344|c2_g3_i1

```
ACP             -----------DRYFAVLHPLKVNDAQRRGKIMLFFAWLISAVISLPQSVIFNVQPHPDY
TR2344|c2_g3_i1 MSSMVLVCISLDRYFAVLHPLKVNDAQRRGKIMLFFAWLISAVISLPQSVIFNVQPHPDY
                          **************************************************

ACP             PEFYQCVTFGFFNANNSGQMMYTIFCISFLYFIPLSIIIIAYTRIILEISRKSKDTQHDY
TR2344|c2_g3_i1 PEFYQCVTFGFFNANNSGQMMYTIFCISFLYFIPLSIIIIAYTRIILEISRKSKDTQHDY
                ************************************************************

ACP             TREERYHGRLQLRRSNMSNIERARTRTLRMTFIIVMAFIWCWTPYALATLWNFIDPKTFY
TR2344|c2_g3_i1 TREERYHGRLQLRRSNMSNIERARTRTLRMTFIIVMAFIWCWTPYALATLWNFIDPKTFY
                ************************************************************

ACP             SMNKHLQDILFIIGVSNSVVNPIIYGRYSISCCRDVWTKSGEFCCYCCWCWCCSCASHQR
TR2344|c2_g3_i1 SMNKHLQDILFIIGVSNSVVNPIIYGRYSISCCRDVWTKSGEFCCYCCWCWCCSCASHQR
                ************************************************************

ACP             LGSVPPTNINSCKSNGHCH----------------------------VRSLLIEWNRSSQ
TR2344|c2_g3_i1 LGSVPPTNINSCKSNGHCHVPSANTRSTIYNNSTRDRRVVGVMLQVKVRSLLIEWNRSSQ
                ******************                             **************

ACP             KSLAAPEGGE-----------------------------------------------------
TR2344|c2_g3_i1 KSLAAPEGGEMVPMVPLGVPVSLQQKLPTPVATNSASSPMTASRAFSRRPPLMETHQEED
                **********

ACP             -------------------------------------------
TR2344|c2_g3_i1 NDEVSSGYSSSHAHFFRSYHDLTTCSERPLRTQVWENHHSC
```

TR2344|c2_g3_i2

```
ACP             -----------DRYFAVLHPLKVNDAQRRGKIMLFFAWLISAVISLPQSVIFNVQPHPDY
TR2344|c2_g3_i2 MSSMVLVCISLDRYFAVLHPLKVNDAQRRGKIMLFFAWLISAVISLPQSVIFNVQPHPDY
                           **************************************************

ACP             PEFYQCVTFGFFNANNSGQMMYTIFCISFLYFIPLSIIIIAYTRIILEISRKSKDTQHDY
TR2344|c2_g3_i2 PEFYQCVTFGFFNANNSGQMMYTIFCISFLYFIPLSIIIIAYTRIILEISRKSKDTQHDY
                ************************************************************

ACP             TREERYHGRLQLRRSNMSNIERARTRTLRMTFIIVMAFIWCWTPYALATLWNFIDPKTFY
TR2344|c2_g3_i2 TREERYHGRLQLRRSNMSNIERARTRTLRMTFIIVMAFIWCWTPYALATLWNFIDPKTFY
                ************************************************************

ACP             SMNKHLQDILFIIGVSNSVVNPIIYGRYSISCCRDVWTKSGEFCCYCCWCWCCSCASHQR
TR2344|c2_g3_i2 SMNKHLQDILFIIGVSNSVVNPIIYGRYSISCCRDVWTKSGEFCCYCCWCWCCSCASHQR
                ************************************************************

ACP             LGSVPPTNINSCKSNGHCHVRSLLIEWNRSSQKSLAAPEGGE
TR2344|c2_g3_i2 LGSVPPTNINSCKSNGHCHGKS-----------EVPTDRVEP
                ******************* :*           .:.: .
```

AST-C

Receptor 2

TR8916|c1_g2_i4, TR8916|c1_g2_i2, TR8916|c1_g2_i1

```
AST-C           MENDTLSEPEDTIPLNCSYLLYGDLYNRSDFLNESNCTLGLFTGGKNEMSIAAIVITQMF
TR8916|c1_g2_i4 MENDTLSEPEDTIPLNCSYLLYGDLYNRSDFLNESNCTLGLFTGGKNEMSIAAIVITQMF
                ************************************************************

AST-C           YAITCLVGLCGNTLVIYVVTRFSKMQTVTNLYILNLAIADELFVVGIPFLMTTSMLRYWP
TR8916|c1_g2_i4 YAITCLVGLCGNTLVIYVVTRFSKMQTVTNLYILNLAIADELFVVGIPFLMTTSMLRYWP
                ************************************************************

AST-C           FGSIMCKLYMITTSLNQFTSSLFLTIMSADRYIAVCHPISSPRFRTPMISKLVSLTAWTL
TR8916|c1_g2_i4 FGSIMCKLYMITTSLNQFTSSLFLTIMSADRYIAVCHPISSPRFRTPMISKLVSLTAWTL
                ************************************************************

AST-C           SALMIVPVFMYSNTLQDNGLDNCNIFWPESQGVRGEIAFIRYSFALAFGIPLTLIFIFYS
TR8916|c1_g2_i4 SALMIVPVFMYSNTLQDNGLDNCNIFWPESQGVRGEIAFIRYSFALAFGIPLTLIFIFYS
                ************************************************************

AST-C           LVLHKLKSVGPKSKSKEKKKSRQKVTRLVLTVITVYVICWLPYWVLQLTLILSTPKQGHS
TR8916|c1_g2_i4 LVLHKLKSVGPKSKSKEKKKSRQKVTRLVLTVITVYVICWLPYWVLQLTLILSTPKQGHS
                ************************************************************

AST-C           NFMVVLFMISSCLSYINSALNPILYAFLSDNFKKSFMKACTCAARMEVNNALRPENSMFP
TR8916|c1_g2_i4 NFMVVLFMISSCLSYINSALNPILYAFLSDNFKKSFMKACTCAARMEVNNALRPENSMFP
                ************************************************************

AST-C           LRQRGTSAKSRMTRRDRESGEGTTSQCGLSKEPSTAVTTTNARPNLSNNSGSSGDELTVR
TR8916|c1_g2_i4 LRQRGTSAKSRMTRRDRESGEGTTSQCGLSKEPSTAVTTTNARPNLSNNSGSSGDELTVR
                ************************************************************

AST-C           NGRSPGPRLPDLIQ
TR8916|c1_g2_i4 NGRSPGPRLPDLIQ
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Receptor 4

TR56862|c4_g5_i1, TR56862|c4_g4_i1, TR56862|c4_g3_i1, TR56862|c4_g2_i1, TR56862|c4_g1_i1

```
AST-C           MTSPDLYGDPGKVSNCSLMCQECQGREESSWEAVMTALVTKEAGVMAVLCGAGLVTNTLA
TR56862|c4_g5_i MTSPDLYGDPGKVSNCSLMCQECQGREESSWEAVMTALVTKEAGVMAVLCGAGLVTNTLA
                ************************************************************

AST-C           VSLMVASITHLHHTSWYLINRAIADMLFLLTVPVDAGTHLQDSWLYGSVMCQMRSTVAIM
TR56862|c4_g5_i VSLMVASITHLHHTSWYLINRAIADMLFLLTVPVDAGTHLQDSWLYGSVMCQMRSTVAIM
                ************************************************************

AST-C           APLLSSVFLVAISSSWYLDACKPNLDAKYRSILLKVVSAVCWFGCIVFTIPTFLQSEVFM
TR56862|c4_g5_i APLLSSVFLVAISSSWYLDACKPNLDAKYRSILLKVVSAVCWFGCIVFTIPTFLQSEVFM
                ************************************************************

AST-C           EVSRVRFHCVSLPLSEDTILGQVLRLEIIFLVFAIPFVISWVFVSLVHQVHKNQTNVLPQ
TR56862|c4_g5_i EVSRVRFHCVSLPLSEDTILGQVLRLEIIFLVFAIPFVISWVFVSLVHQVHKNQTNVLPQ
                ************************************************************

AST-C           PSTSEAAPSQPGPKLPYRLLITLLVAFTGCQGPYWLVYLVRELLRHVEFSAGAMMMFPVT
TR56862|c4_g5_i PSTSEAAPSQPGPKLPYRLLITLLVAFTGCQGPYWLVYLVRELLRHVEFSAGAMMMFPVT
                ************************************************************

AST-C           MCLPALNAAINPLLCIYFLRDLRKDKPKVNKTHQPEMIALFTL
TR56862|c4_g5_i MCLPALNAAINPLLCIYFLRDLRKDKPKVNKTHQPEMIALFTL
                *********************************************
```

Bursicon

Receptor 1

TR45425|c0_g1_i1

```
Bursicon          MRDSGDAGGPAGGGRGSLAPLLLPLCLLLLLLAPAVSACPTACTCEAVPPRRSSALSRRS
TR45425|c0_g1_i MRDSGDAGGPAGGGRGSLAPLLLPLCLLLLLLAPAVSACPTACTCEAVPPRRSSALSRRS
                ************************************************************

Bursicon          VWAAKTEVPAAHNTNNVTLVCRDAGLMAPPDLVALNGLDPATVSKMDLSKNGITELHEYS
TR45425|c0_g1_i VWAAKTEVPAAHNTNNVTLVCRDAGLMAPPDLVALNGLDPATVSKMDLSKNGITELHEYS
                ************************************************************

Bursicon          FSLYPSLHTLKVCGNRLTTIAAGAFQDIPLRVLVLDNNKLSELVADSLPASLREISLERN
TR45425|c0_g1_i FSLYPSLHTLKVCGNRLTTIAAGAFQDIPLRVLVLDNNKLSELVADSLPASLREISLERN
                ************************************************************

Bursicon          TFTSIPPSLTALHGLQFLNLARNRLTALKDGDLRGLHNLQRLSLHQNRISTVESRALAPL
TR45425|c0_g1_i TFTSIPPSLTALHGLQFLNLARNRLTALKDGDLRGLHNLQRLSLHQNRISTVESRALAPL
                ************************************************************

Bursicon          RNLEKLDLEVNTLTEVPTAVTRCLKLKELLLGSNRLTYVGEDSFKGLARLQDVALWPNQL
TR45425|c0_g1_i RNLEKLDLEVNTLTEVPTAVTRCLKLKELLLGSNRLTYVGEDSFKGLARLQDVALWPNQL
                ************************************************************

Bursicon          LTIHQRAFSNLPSLTKLILKEMKQLQEFPDLNGTSSLELIRIDRAALTAVPENLCSVAPK
TR45425|c0_g1_i LTIHQRAFSNLPSLTKLILKEMKQLQEFPDLNGTSSLELIRIDRAALTAVPENLCSVAPK
                ************************************************************

Bursicon          LRSLNLQRNSISEMPDLNRCRQLRLIDLSHNNISSLPAATFSSLSFLQDLLLQGNRVHTI
TR45425|c0_g1_i LRSLNLQRNSISEMPDLNR----------------------------------------
                ******************

Bursicon          HNNTFNGLEKLQVLQLEDNLITSIHQDAFLPLVSLEDINLGNNSFPELPAQGLEHVVSIK
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon          VHNNRHLRVFPGPESFPMVRALTLSYAYHCCPFLRLEDHTEAPQIIEEVIYSGDGFKGLD
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon          PTIWNVSSVWPETAGLRTNFAAIWANLAADFPPANTDLVDTTSLDLGEATAATHTLPLLP
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon          RHQVLCNPEPGPFMPCEDLFDWWTLRCGVWIVFLLALLGNGAVVVVLVFARAKMDVPRFL
TR45425|c0_g1_i ------------------------------------------------------------
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Bursicon        VTNLAFADFFMGLYLGFLAVVDASTLGEFRMYAIPWQTSVGCQVAGFLGVLSCELSVYTL
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon        TVITMERNYAITHAMHLNKRLSLRHAAYIMVLGWLFACTMALLPLIGVSDYRKFAVCLPI
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon        ETKGAGLGYVVFLMFINGVAFLILMGCYLKIYCAIRGSQAWNSNDSRIAKRMALLVFTDF
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon        ICWAPIAFFSLTAAFGLQLISLKEAKVFTVFILPFNSCCNPFLYALLTKQFKKDCVMLCK
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon        TIEESRVTRGIGRCRHSSNFSNRQTPANTNSALENSSRQDNQLCRCQNKTQESQKLHHRL
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon        RISALKYLFCHKDTEGLNSTSDFSYQPTKSAVKSKRHTSVSSETYSSSWSDTWRRGHAAM
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon        SLRILDRRHHNSWYLSRKPSQESNLSSSRNDSSATTASTSTWRISRSSVSSDISSSGSRG
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon        VGKSDVAPTLRLGSLRERRGECHIQIPTRQITHHHQALLVRQQSGASGQRSAPITSAVRI
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon        KPRLQRQSAIERETYIPNKAAGGQNEITCPLHQRSDNLSCVYEQESYEEEDHEASKDYLN
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon        PRCPMAGLTVTFIPRKLSTISSHSVSVVRDAEGDEPAVGPCVDVHSSSDPFPMSNCDFSR
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon        GGKCVSLTLLPQSSSQTSPSRFPSDGHLPRSPRCTELLYFTNLAAPALIVPSTEQNAESP
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon        PKDLDATPKNHYGQAILIHSQPRSPQSLEHDECMESTALMDDDCYGDDEVFEEENKSRER
TR45425|c0_g1_i ------------------------------------------------------------


Bursicon        PLETHFPLDDPPGETRPLI
TR45425|c0_g1_i -------------------
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TR68968|c0_g1_i1

```
Bursicon        MRDSGDAGGPAGGGRGSLAPLLLPLCLLLLLLAPAVSACPTACTCEAVPPRRSSALSRRS
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        VWAAKTEVPAAHNTNNVTLVCRDAGLMAPPDLVALNGLDPATVSKMDLSKNGITELHEYS
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        FSLYPSLHTLKVCGNRLTTIAAGAFQDIPLRVLVLDNNKLSELVADSLPASLREISLERN
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        TFTSIPPSLTALHGLQFLNLARNRLTALKDGDLRGLHNLQRLSLHQNRISTVESRALAPL
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        RNLEKLDLEVNTLTEVPTAVTRCLKLKELLLGSNRLTYVGEDSFKGLARLQDVALWPNQL
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        LTIHQRAFSNLPSLTKLILKEMKQLQEFPDLNGTSSLELIRIDRAALTAVPENLCSVAPK
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        LRSLNLQRNSISEMPDLNRCRQLRLIDLSHNNISSLPAATFSSLSFLQDLLLQGNRVHTI
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        HNNTFNGLEKLQVLQLEDNLITSIHQDAFLPLVSLEDINLGNNSFPELPAQGLEHVVSIK
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        VHNNRHLRVFPGPESFPMVRALTLSYAYHCCPFLRLEDHTEAPQIIEEVIYSGDGFKGLD
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        PTIWNVSSVWPETAGLRTNFAAIWANLAADFPPANTDLVDTTSLDLGEATAATHTLPLLP
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        RHQVLCNPEPGPFMPCEDLFDWWTLRCGVWIVFLLALLGNGAVVVVLVFARAKMDVPRFL
TR68968|c0_g1_i ------------MPCEDLFDWWTLRCGVWIVFLLALLGNGAVVVVLVFARAKMDVPRFL
                            **********************************************


Bursicon        VTNLAFADFFMGLYLGFLAVVDASTLGEFRMYAIPWQTSVGCQVAGFLGVLSCELSVYTL
TR68968|c0_g1_i VTNLAFADFFMGLYLGFLAVVDASTLGEFRMYAIPWQTSVGCQVAGFLGVLSCELSVYTL
                ************************************************************


Bursicon        TVITMERNYAITHAMHLNKRLSLRHAAYIMVLGWLFACTMALLPLIGVSDYRKFAVCLPI
TR68968|c0_g1_i TVITMERNYAITHAMHLNKRLSLRHAAYIMVLGWLFACTMALLPLIGVSDYRKFAVCLPI
                ************************************************************


Bursicon        ETKGAGLGYVVFLMFINGVAFLILMGCYLKIYCAIRGSQAWNSNDSRIAKRMALLVFTDF
TR68968|c0_g1_i ETKGAGLGYVVFLMFINGVAFLILMGCYLKIYCAIRGSQAWNSNDS--------------
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Bursicon        ICWAPIAFFSLTAAFGLQLISLKEAKVFTVFILPFNSCCNPFLYALLTKQFKKDCVMLCK
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        TIEESRVTRGIGRCRHSSNFSNRQTPANTNSALENSSRQDNQLCRCQNKTQESQKLHHRL
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        RISALKYLFCHKDTEGLNSTSDFSYQPTKSAVKSKRHTSVSSETYSSSWSDTWRRGHAAM
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        SLRILDRRHHNSWYLSRKPSQESNLSSSRNDSSATTASTSTWRISRSSVSSDISSSGSRG
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        VGKSDVAPTLRLGSLRERRGECHIQIPTRQITHHHQALLVRQQSGASGQRSAPITSAVRI
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        KPRLQRQSAIERETYIPNKAAGGQNEITCPLHQRSDNLSCVYEQESYEEEDHEASKDYLN
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        PRCPMAGLTVTFIPRKLSTISSHSVSVVRDAEGDEPAVGPCVDVHSSSDPFPMSNCDFSR
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        GGKCVSLTLLPQSSSQTSPSRFPSDGHLPRSPRCTELLYFTNLAAPALIVPSTEQNAESP
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        PKDLDATPKNHYGQAILIHSQPRSPQSLEHDECMESTALMDDDCYGDDEVFEEENKSRER
TR68968|c0_g1_i ------------------------------------------------------------


Bursicon        PLETHFPLDDPPGETRPLI
TR68968|c0_g1_i -------------------
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CCAP

Receptor 1

TR86078|c0_g1_i1

```
CCAP            MKSTIMAGKVEKSPYNQTVTVDSQSQLSEGVDSKTKSNHNSLYVLEDAFIEVNCSDFMDL
TR86078|c0_g1_i MKSTIMAGKVEKSPYNQTVTVDSQSQLSEGVDSKTKSNHNSLYVLEDAFIEVNCSDFMDL
                ************************************************************

CCAP            AAANGTCGNYTITSNVTNTTTTAGDSYYFYETEQFTVLWILFISIVVGNVAVIAALMLSK
TR86078|c0_g1_i AAANGTCGNYTITSNVTNTTTTAGDSYYFYETEQFTVLWILFISIVVGNVAVIAALMLSK
                ************************************************************

CCAP            TRKSRTNFFIMHLALADLSVGLISVLTDIIWKTTLSWNAGNIGCKAVRYAQVLVTYSSTY
TR86078|c0_g1_i TRKSRTNFFIMHLALADLSVGLISVLTDIIWKTTLSWNAGNIGCKAVRYAQ---------
                ************************************************

CCAP            VLVALSIDRYDAITHPMNFSGSWRRARRLVVVAWLLSAVFASPSLGFFRETSIDGVLQCW
TR86078|c0_g1_i ----------------GGGPGGW-----------------------------------
                             . .*.*

CCAP            IDFSEAWQWKLYMTLVALTVFVFPTIIITACYAIIVYTIWSKSKIMTVNSKALGSKNGEK
TR86078|c0_g1_i ------WWW-----------------------------------------LG------
                      * *                                         **

CCAP            RVTSGEDDSRRASSRGLIPKAKIKTVKMTLVIVFVFILCWSPYIVFDLLQVYGYVPQTPT
TR86078|c0_g1_i ------------------------------------------------------------


CCAP            NVAVATLIQSLAPLNSAANPIIYCLFSTHICRNLRRIPVVDWVVRQVFPCLECAQQPVEN
TR86078|c0_g1_i ----------------------YCQ----------------------PC--SPHQALDS
                                      **                      **  ..:*.::.

CCAP            RGAFHRYGTEYTTVSDASSRRHTLTSV
TR86078|c0_g1_i SGRLLLMASSSAGLT--SQRRGSGSSI
                 * :   .:. : ::  *.** : :*:
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TR3748|c0_g1_i1

```
CCAP            MKSTIMAGKVEKSPYNQTVTVDSQSQLSEGVDSKTKSNHNSLYVLEDAFIEVNCSDFMDL
TR3748|c0_g1_i1 ------------------------------------------------------------


CCAP            AAANGTCGNYTITSNVTNTTTTAGDSYYFYETEQFTVLWILFISIVVGNVAVIAALMLSK
TR3748|c0_g1_i1 ------------------------------------------------------------


CCAP            TRKSRTNFFIMHLALADLSVGLISVLTDIIWKTTLSWNAGNIGCKAVRYAQVLVTYSSTY
TR3748|c0_g1_i1 ------------------------------------------------------------


CCAP            VLVALSIDRYDAITHPMNFSGSWRRARRLVVVAWLLSAVFASPSLGFFRETSIDGVLQCW
TR3748|c0_g1_i1 ------------------------------------------------------------


CCAP            IDFSEAWQWKLYMTLVALTVFVFPTIIITACYAIIVYTIWSKSKIMTVNSKALGSKNGEK
TR3748|c0_g1_i1 ------------------------------------------------------------


CCAP            RVTSGEDDSRRASSRGLIPKAKIKTVKMTLVIVFVFILCWSPYIVFDLLQVYGYVPQTPT
TR3748|c0_g1_i1 ---------------------------MTLVIVFVFILCWSPYIVFDLLQVYGYVPQTPT
                                          ********************************

CCAP            NVAVATLIQSLAPLNSAANPIIYCLFSTHICRNLRRIPVVDWVVRQVFPCLECAQQPVEN
TR3748|c0_g1_i1 NVAVATLIQSLAPLNSAANPIIYCLFSTHICRNLRRIPVVDWVVRQVFPCLECAQQPVEN
                ************************************************************

CCAP            RGAFHRYGTEYTTVSDASSRRHTLTSV
TR3748|c0_g1_i1 RGAFHRYGTEYT---------------
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```

DH31

Receptor 1

TR7828|c0_g1_i1

```
DH31            MKCGAGSVCRLLYLMLLLWTTDGSSRSTTTQESLHRGFLLDDT-INDPGASSGDDHRLGL
TR7828|c0_g1_i1 MKCGAGSVCRLLYLMLLLWTTDGSSRSTTTQESLHRGFLLDDTFINDPGASSGDDHRLGL
                ****************************************** ****************

DH31            PGKYDLDLEYPEDDLHDLGKDTRERYILSDYQRDDLRLRESQQTLYKEYLKRASYRRSAE
TR7828|c0_g1_i1 PGKYDLDLEYPEDDLHDLGKDTRERYILSDYQRDDLRLRESQQTLYKEYLKRASYRSSAE
                ********************************************************* ***

DH31            LVPRTREEREGGDYTKHTTHDKQNTSVVSGNTQLQEKVVQEEEEAPADPLDDKNSAVGEE
TR7828|c0_g1_i1 LVPRTREEREGGDYTKHTTHDKQNTSVVSGNTQVQEKVVQEEEEAPADPLDDKNSAVGEE
                **********************************:***************************

DH31            SKTAGPLEEKEAGGGKVVDGDLHERMILSAGRPLCRSKEKYLPPDMYNADACALCYFHIV
TR7828|c0_g1_i1 SKTAGPLEEKEAGGGKVVDGDLHERMILSAGRPLCRSKEKYLPPDMYNADACALCYFHIV
                ************************************************************

DH31            NRELFNTKWITLEVQKAVEEEDVTYNVSVLLNPMNFSQLEEAVVTSEAVLASFKGEVGPS
TR7828|c0_g1_i1 NRELFNTKWITLEVQKAVEEEDVTYNVSVLLNPMNFSQLEEAVVTSEAVLASFKGEVGPS
                ************************************************************

DH31            KWRSCCEAAVQCCDQMLTASWPTGHCPNTWDGWQCWSATPRDTEAMRPCPSYIYYGREPS
TR7828|c0_g1_i1 KWRSCCEAAVQCCDQMLTASWPTGHCPNTWDGWQCWSATPRDTEAMRPCPSYIYYGREPS
                ************************************************************

DH31            CAKQATKKCETDGMWFRRTGSGQEWSNYSSCSVEHNIHRRLYVHIAAYSVSVAALLPALC
TR7828|c0_g1_i1 CAKQATKKCETDGMWFRRTGSGQEWSNYSSCSVEHNIHRRLYVHIAAYSVSVAALLPALC
                ************************************************************

DH31            IFLSYKQLRVHRITLHKHLFLSLLLEAVGVITFRFLQLYKKDLINQNLTWCVTLNLLTKY
TR7828|c0_g1_i1 IFLSYKQLRVHRITLHKHLFLSLLLEAVGVITFRFLQLYKKDLINQNLTWCVTLNLLTKY
                ************************************************************

DH31            TSLSNYMWYLCEGFYLHKLLASAFAEQNSLVIFYLIGWGFPLVPLTVYSVVRGLRDDNTD
TR7828|c0_g1_i1 TSLSNYMWYLCEGFYLHKLLASAFAEQNSLVIFYLIGWGFPLVPLTVYSVVRGLRDDNTD
                ************************************************************

DH31            CWIMPNESLDWIINLPPLLAILINIIFVVNIIRILVSKVRATNGNEPSQYRKAVRATMMV
TR7828|c0_g1_i1 CWIMPNESLDWIINLPPLLAILINIIFVVNIIRILVSKVRATNGNEPSQYRKAVRATMMV
                ************************************************************

DH31            VPLFGLQYIVTIYRHQELGCDWHDIYQIFNNVIEGSTGAVVAIIFCYTNGEVRSLLKRSW
TR7828|c0_g1_i1 VPLFGLQYIVTIYRHQELGCDWHDIYQIFNNVIEGSTGAVVAIIFCYTNGEVRSLLKRSW
                ************************************************************

DH31            VRLQERRAPRGVRGPEKLRSRSLSTVQTTLLDPSPARRNSSIVSICANNQPFRRSNSGAN
TR7828|c0_g1_i1 VRLQERRAPRGVRGPEKLRSRSLSTVQTTLLDPSPARRNSSIVSICANNQPFRRSNSGAN
                ************************************************************

DH31            ASQLLSLRGSRTSITQQSQASTVDSGTAPITAPSRRSPKQIASKLGPGGSERFVSSKSPV
TR7828|c0_g1_i1 ASQLLSLRGSRTSITQQSQASTVDSGTAPITAPSRRSPKQIASKLGPGGSERFVSSKSPV
                ************************************************************
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DH31            HNLDSNPVSRSPSLLEEVEDEVKRSEKREKSPQPSAARLGGERVERHPVVLFRKDEAEPC
TR7828|c0_g1_i1 HNLDSNPVSRSPSLLEEVEDEVKRSEKREKSPQPSAARLGGERVERHPVVLFRKDEAEPC
                ************************************************************

DH31            VNINVNGQFCGLRTSVDQGYESSQTIAVLDE
TR7828|c0_g1_i1 VNINVNGQFCGLRTSVDQGYESSQTIAVLDE
                *******************************
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TR7828|c0_g1_i2

```
DH31            MKCGAGSVCRLLYLMLLLWTTDGSSRSTTTQESLHRGFLLDDTINDPGASSGDDHRLGLP
TR7828|c0_g1_i2 ------------------------------------------------------------


DH31            GKYDLDLEYPEDDLHDLGKDTRERYILSDYQRDDLRLRESQQTLYKEYLKRASYRRSAEL
TR7828|c0_g1_i2 ------------------------------------------------------------


DH31            VPRTREEREGGDYTKHTTHDKQNTSVVSGNTQLQEKVVQEEEEAPADPLDDKNSAVGEES
TR7828|c0_g1_i2 ------------------------------------------------------------


DH31            KTAGPLEEKEAGGGKVVDGDLHERMILSAGRPLCRSKEKYLPPDMYNADACALCYFHIVN
TR7828|c0_g1_i2 ------------------------------------------------------------


DH31            RELFNTKWITLEVQKAVEEEDVTYNVSVLLNPMNFSQLEEAVVTSEAVLASFKGEVGPSK
TR7828|c0_g1_i2 ------------------------------------------------------------


DH31            WRSCCEAAVQCCDQMLTASWPTGHCPNTWDGWQCWSATPRDTEAMRPCPSYIYYGREPSC
TR7828|c0_g1_i2 ------------------------------------------------------------


DH31            AKQATKKCETDGMWFRRTGSGQEWSNYSSCSVEHNIHRRLYVHIAAYSVSVAALLPALCI
TR7828|c0_g1_i2 ------------------------------------------------------------


DH31            FLSYKQLRVHRITLHKHLFLSLLLEAVGVITFRFLQLYKKDLINQNLTWCVTLNLLTKYT
TR7828|c0_g1_i2 ------------------------------------------------------------


DH31            SLSNYMWYLCEGFYLHKLLASAFAEQNSLVIFYLIGWGFPLVPLTVYSVVRGLRDDNTDC
TR7828|c0_g1_i2 -----MWYLCEGFYLHKLLASAFAEQNSLVIFYLIGWGFPLVPLTVYSVVRGLRDDNTDC
                     ************************************************************

DH31            WIMPNESLDWIINLPPLLAILINIIFVVNIIRILVSKVRATNGNEPSQYRKAVRATMMVV
TR7828|c0_g1_i2 WIMPNESLDWIINLPPLLAILINIIFVVNIIRILVSKVRATNGNEPSQYRKAVRATMMVV
                ************************************************************

DH31            PLFGLQYIVTIYRHQELGCDWHDIYQIFNNVIEGSTGAVVAIIFCYTNGEVRSLLKRSWV
TR7828|c0_g1_i2 PLFGLQYIVTIYRHQELGCDWHDIYQIFNNVIEGSTGAVVAIIFCYTNGEVRSLLKRSWV
                ************************************************************
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DH31            RLQERRAPRGVRGPEKLRSRSLSTVQTTLLDPSPARRNSSIVSICANNQPFRRSNSGANA
TR7828|c0_g1_i2 RLQERRAPRGVRGPEKLRSRSLSTVQTTLLDPSPARRNSSIVSICANNQPFRRSNSGANA
                ************************************************************

DH31            SQLLSLRGSRTSITQQSQASTVDSGTAPITAPSRRSPKQIASKLGPGGSERFVSSKSPVH
TR7828|c0_g1_i2 SQLLSLRGSRTSITQQSQASTVDSGTAPITAPSRRSPKQIASKLGPGGSERFVSSKSPVH
                ************************************************************

DH31            NLDSNPVSRSPSLLEEVEDEVKRSEKREKSPQPSAARLGGERVERHPVVLFRKDEAEPCV
TR7828|c0_g1_i2 NLDSNPVSRSPSLLEEVEDEVKRSEKREKSPQPSAARLGGERVERHPVVLFREDEAEP--
                ************************************************:*****

DH31            NINVNGQFCGLRTSVDQGYESSQTIAVLDE
TR7828|c0_g1_i2 -------------------------------
```

DH44

Receptor 1

TR7124|c0_g1_i1

```
DH44            MPSITAPTEFPSYSLSDPAETEEEDSDEIYITLWRKFMEQSALINATNGDHKMLQCFNMY
TR7124|c0_g1_i1 ------------------------------------------------------------

DH44            LNTTMDPESDPGACPVKFDGVSCWPETPPDTTRAIPCFNDFNGVHYEPSDYNATLYCYPN
TR7124|c0_g1_i1 ------------------------------------------------------------

DH44            GTWSKKSFYNFCLNAVTNNSEVQGSTVNTISTIFYIGNSVSLVAVTLALWIFISFKDLRC
TR7124|c0_g1_i1 ------------------------------------------------------------

DH44            LRNTIHTNLLFTYLLHNLFWIVYASVQTLVNVSVGCSFFVALNYFTLTNFMWMFVEGFYL
TR7124|c0_g1_i1 ------------------------------------------------------------

DH44            YMLVVKTFSVENIKLRVYTLIGWGVPVPIIISWVILKSQLATTHPAGMEGHELEGLVRNC
TR7124|c0_g1_i1 ------------------------------------------------------------

DH44            PLMPDSTVDWIQKIPVLFLLSTNLIFLTRIMWVLITKLRSANTVETQRYRKATKALLVLI
TR7124|c0_g1_i1 --MPDSTVDWIQKIPVLFLLSTNLIFLTRIMWVLITKLRSANTVETQRYRKATKALLVLI
                  ************************************************************

DH44            PLLGLTYMLLIALPQELEHVRAILLSTQGFWVALFYCFLNSEVQNSIRHHIERWKTARGL
TR7124|c0_g1_i1 PLLGLTYMLLIALPQELEHVRAILLSTQGFWVALFYCFLNSEVQNSIRHHIERWKTARGL
                ************************************************************

DH44            ADPRHASVRHGRDGSPRPKTDCSSYSRRLFGGKRESLCSEVTTMTTYVANGYNPVSTQTG
TR7124|c0_g1_i1 ADPRHASVRHGRDGSPRPKTDCSSYSRRLFGGKRESLCSEVTTMTTYVANGYNPVSTQTG
                ************************************************************

DH44            GPPQQQQSLLQPAPQQPPTATGQHLTYRNSNAGIAPNSGGDPDVKSTVKDSLL
TR7124|c0_g1_i1 GPPQQQQSLLQPAPQQPPTATGQHLTYRNSNAGIAPNSGGDPDVKSTVKDSLL
                ********************************************************
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TR52110|c0_g1_i1

```
DH44            MPSITAPTEFPSYSLSDPAETEEEDSDEIYITLWRKFMEQSALINATNGDHKMLQCFNMY
TR52110|c0_g1_i MPSITAPTEFPSYSLSDPAETEEEDSDEIYITLWRKFMEQSALINATNGDHKMLQCFNMY
                ************************************************************

DH44            LNTTMDPESDPGACPVKFDGVSCWPETPPDTTRAIPCFNDFNGVHYEPSDYNATLYCYPN
TR52110|c0_g1_i LNTTMDPESDPGACPVKFDGVSCWPETPPDTTRAIPCFNDFNGVHYEPSDYNATLYCYPN
                ************************************************************

DH44            GTWSKKSFYNFCLNAVTNNSEVQGSTVNTISTIFYIGNSVSLVAVTLALWIFISFKDLRC
TR52110|c0_g1_i GTW-------------------------------------------------------------
                ***

DH44            LRNTIHTNLLFTYLLHNLFWIVYASVQTLVNVSVGCSFFVALNYFTLTNFMWMFVEGFYL
TR52110|c0_g1_i -------------------------------------------------------------


DH44            YMLVVKTFSVENIKLRVYTLIGWGVPVPIIISWVILKSQLATTHPAGMEGHELEGLVRNC
TR52110|c0_g1_i -------------------------------------------------------------


DH44            PLMPDSTVDWIQKIPVLFLLSTNLIFLTRIMWVLITKLRSANTVETQRYRKATKALLVLI
TR52110|c0_g1_i -------------------------------------------------------------


DH44            PLLGLTYMLLIALPQELEHVRAILLSTQGFWVALFYCFLNSEVQNSIRHHIERWKTARGL
TR52110|c0_g1_i -------------------------------------------------------------


DH44            ADPRHASVRHGRDGSPRPKTDCSSYSRRLFGGKRESLCSEVTTMTTYVANGYNPVSTQTG
TR52110|c0_g1_i -------------------------------------------------------------


DH44            GPPQQQQSLLQPAPQQPPTATGQHLTYRNSNAGIAPNSGGDPDVKSTVKDSLL
TR52110|c0_g1_i ---------------------------------------------------------
```

Receptor 2

TR17601|c0_g1_i1

```
DH44            MFAMLSQGHLAALICLVAFMVTTAENGNIPDRGTEVNSGSPWSVSEKETQDTSWAPEGVD
TR17601|c0_g1_i ------------------------------------------------------------


DH44            LQDTSSLDDEGAEGGGAGLAIDLSLFDSINGSSGEFNESWPEHKQKLWLKQMLLRREGEC
TR17601|c0_g1_i -----------------------------------------------------MLLRREGEC
                                                                     *********

DH44            HLYQLLEANTTSSDLHQEGSWCPRVWDKMLCWAPTPPNTTITQPCPDYVPGLIAEARASR
TR17601|c0_g1_i HLYQLLEANTTSSDLHQEGSWCPRVWDKMLCWAPTPPNTTITQPCPDYVPGLIAEARASR
                ************************************************************

DH44            RCGDNGSWAGGQGLGWTNYTPCVGHVAHPTSITIRFTIIGEWLPTIKKMSVVGYSVSLAT
TR17601|c0_g1_i RCGDNGSWAGGQGLGWTNYTPCVGHVAHPTSITIRFT----------------------
                ************************************

DH44            LVISFIILASLRKLRCPRNLLHLHLFGSFMLRALVVLLKSSLLMDGIALPHNFHLQDGET
TR17601|c0_g1_i ------------------------------------------------------------


DH44            YYNDGSQTWACKLMICVWQYFILANYSWLLMEGLYLHSLIFMALFTDSSAITLYILLGWG
TR17601|c0_g1_i ------------------------------------------------------------


DH44            LPLGCVGIWATLRATLDDAHCWTVNNVQWIFWVCIRAPVAISNLINFFFFLNVVRVLVLK
TR17601|c0_g1_i ------------------------------------------------------------


DH44            LRSSISAESMKYRKLGKSTLVLVPLFGVHYFVLWSLSTSTNAYVEIVWLFLDQVFASFQG
TR17601|c0_g1_i ------------------------------------------------------------


DH44            FFVAVLYCLMNGEVRQELRKLYNRWYKGDPLVVTSHSTLVSHTKTYASRGRTSLHSIHSQ
TR17601|c0_g1_i ------------------------------------------------------------


DH44            AERRDRQTPSPQMLRSNGGDGQSSRPRTPSPSPTPILTPSYVSRQQSK
TR17601|c0_g1_i -------------------------------------------------
```

TR50316|c0_g1_i1

```
DH44            MFAMLSQGHLAALICLVAFMVTTAENGNIPDRGTEVNSGSPWSVSEKETQDTSWAPEGVD
TR50316|c0_g1_i ------------------------------------------------------------

DH44            LQDTSSLDDEGAEGGGAGLAIDLSLFDSINGSSGEFNESWPEHKQKLWLKQMLLRREGEC
TR50316|c0_g1_i ------------------------------------------------------------

DH44            HLYQLLEANTTSSDLHQEGSWCPRVWDKMLCWAPTPPNTTITQPCPDYVPGLIAEARASR
TR50316|c0_g1_i ------------------------------------------------------------

DH44            RCGDNGSWAGGQGLGWTNYTPCVGHVAHPTSITIRFTIIGEWLPTIKKMSVVGYSVSLAT
TR50316|c0_g1_i ------------------------------------------------------------

DH44            LVISFIILASLRKLRCPRNLLHLHLFGSFMLRALVVLLKSSLLMDGIALPHNFHLQDGET
TR50316|c0_g1_i ------------------------------------------------------------

DH44            YYNDGSQTWACKLMICVWQYFILANYSWLLMEGLYLHSLIFMALFTDSSAITLYILLGWG
TR50316|c0_g1_i ------------------------------------------------------------

DH44            LPLGCVGIWATLRATLDDAHCWTVNNVQWIFWVCIRAPVAISNLINFFFFLNVVRVLVLK
TR50316|c0_g1_i ------------------------------------------------------------

DH44            LRSSISAESMKYRKLGKSTLVLVPLFGVHYFVLWSLSTSTNAYVEIVWLFLDQVFASFQG
TR50316|c0_g1_i ------------------------------------------------------------

DH44            FFVAVLYCLMNGEVRQELRKLYNRWYKGDPLVVTSHSTLVSHTKTYASRGRTSLHSIHSQ
TR50316|c0_g1_i ---------MNGEVRQELRKLYNRWYKGDPLVVTSHSTLVSHTKTYASRGRTSLHSIHSQ
                         **************************************************

DH44            AERRDRQTPSPQMLRSNGGDGQSSRPRTPSPSPTPILTPSYVSRQQSK------------
TR50316|c0_g1_i AERRDRQTPSPQMLRSNGGDGQSSRPRTPSPSPTPILTPSYVSRQQSKVSNLFSLNIVMS
                **********************************************

DH44            -
TR50316|c0_g1_i V
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TR18146|c0_g1_i1

```
DH44            MFAMLSQGHLAALICLVAFMVTTAENGNIPDRGTEVNSGSPWSVSEKETQDTSWAPEGVD
TR18146|c0_g1_i ------------------------------------------------------------

DH44            LQDTSSLDDEGAEGGGAGLAIDLSLFDSINGSSGEFNESWPEHKQKLWLKQMLLRREGEC
TR18146|c0_g1_i ------------------------------------------------------------

DH44            HLYQLLEANTTSSDLHQEGSWCPRVWDKMLCWAPTPPNTTITQPCPDYVPGLIAEARASR
TR18146|c0_g1_i ------------------------------------------------------------

DH44            RCGDNGSWAGGQGLGWTNYTPCVGHVAHPTSITIRFTIIGEWLPTIKKMSVVGYSVSLAT
TR18146|c0_g1_i ------------------------------------------------------------

DH44            LVISFIILASLRKLRCPRNLLHLHLFGSFMLRALVVLLKSSLLMDGIALPHNFHLQDGET
TR18146|c0_g1_i ------------------------------------------------------------

DH44            YYNDGSQTWACKLMICVWQYFILANYSWLLMEGLYLHSLIFMALFTDSSAITLYILLGWG
TR18146|c0_g1_i -------------MICVWQYFILANYSWLLMEGLYLHSLIFMALFTDSSAITLYILLGWG
                             *********************************************

DH44            LPLGCVGIWATLRATLDDAHCWTVNNVQWIFWVCIRAPVAISNLINFFFFLNVVRVLVLK
TR18146|c0_g1_i LPLGCVGIWATLRATLDDAHCWTVNNVQWIFWVCIRAPVAISNLINFFFFLNVVRVLVLK
                ************************************************************

DH44            LRSSISAESMKYRKLGKSTLVLVPLFGVHYFVLWSLSTSTNAYVEIVWLFLDQVFASFQG
TR18146|c0_g1_i LRSSISA---------------------------------------------------------
                *******

DH44            FFVAVLYCLMNGEVRQELRKLYNRWYKGDPLVVTSHSTLVSHTKTYASRGRTSLHSIHSQ
TR18146|c0_g1_i ------------------------------------------------------------

DH44            AERRDRQTPSPQMLRSNGGDGQSSRPRTPSPSPTPILTPSYVSRQQSK
TR18146|c0_g1_i -------------------------------------------------
```

Myosuppressin

Receptor 2

TR22607|c0_g1_i3

```
Myosuppressin    MFSVNFSESVVPRMEKVMEAAGAPPHTAGPLTIIIPLLANLTATADLDYDWDYHNVTANT
TR22607|c0_g1_i MFSVNFSESVVPRMEKVMEAAGAPPHTAGPLTIIIPLLANLTATADLDYDWDYHNVTANT
                ************************************************************

Myosuppressin    TTQDSFNSSTADEYCSTEEWDDFRHSYQAVHGCMSLVVCVFGSVANVINMVVLTRRSMVS
TR22607|c0_g1_i TTQDSFNSSTADEYCSTEEWDDFRHSYQAVHGCMSLVVCVFGSVANVINMVVLTRRSMVS
                ************************************************************

Myosuppressin    PTNAILTGLAVTDLLVMVEYIPYTMHQYVWQGRSLASQYSWGWAVFVLFHAHFTHVFHTI
TR22607|c0_g1_i PTNAILTGLAVTDLLVMVEYIPYTMHQYVWQGRSLASQYSWGWAVFVLFHAHFTHVFHTI
                ************************************************************

Myosuppressin    SIWLTVTLAVWRYIAIAFPQNNTTWCSMQRTHTVIVAAFFCSVICNIPSYLNFTISQAEH
TR22607|c0_g1_i SIWLTVTLAVWRYIAIAFPQNNTTWCSMQRTHTVIVAAFFCSVICNIPSYLNFTISQAEH
                ************************************************************

Myosuppressin    EGQTLYIVGFSHLALAHGGFLKSINFWIYAVMLKLLPCSALTGLSFALIQELLRAGRRRA
TR22607|c0_g1_i EGQTLYIVGFSHLALAHGGFLKSINFWIYAVMLKLLPCSALTGLSFALIQELLRAGRRRA
                ************************************************************

Myosuppressin    QLMKRNSSGRAADAERQADRVTIMLLAILVLFLASEVPQGILGFLTVIPDSGFFPCYQKL
TR22607|c0_g1_i QLMKRNSSGRAADAERQADRVTIMLLAILVLFLASEVPQGILGFLTVIPDSGFFPCYQKL
                ************************************************************

Myosuppressin    GEIMDMLVLFNSAINFLLYCAMSKQFRDTFSELFKSCCVQWLAIRAPRLPPCWKAVPADA
TR22607|c0_g1_i GEIMDMLVLFNSAINFLLYCAMSKQFRDTFSELFKSCCVQWLAIRAPRLPPCWKAVPADA
                ************************************************************

Myosuppressin    PPIEVNNTCITHV
TR22607|c0_g1_i PPIEVNNTCITHV
                *************
```

TR22607|c0_g1_i1

```
Myosuppressin   MFSVNFSESVVPRMEKVMEAAGAPPHTAGPLTIIIPLLANLTATADLDYDWDYHNVTANT
TR22607|c0_g1_i -------------MEKVMEAAGAPPHTAGPLTIIIPLLANLTATADLDYDWDYHNVTANT
                ************************************************

Myosuppressin   TTQDSFNSSTADEYCSTEEWDDFRHSYQAVHGCMSLVVCVFGSVANVINMVVLTRRSMVS
TR22607|c0_g1_i TTQDSFNSSTADEYCSTEEWDDFRHSYQAVHGCMSLVVCVFGSVANVINMVVLTRRSMVS
                ************************************************************

Myosuppressin   PTNAILTGLAVTDLLVMVEYIPYTMHQYVWQGRSLASQYSWGWAVFVLFHAHFTHVFHTI
TR22607|c0_g1_i PTNAILTGLAVTDLLVMVEYIPYTMHQYVWQGRSLASQYSWGWAVFVLFHAHFTHVFHTI
                ************************************************************

Myosuppressin   SIWLTVTLAVWRYIAIAFPQNNTTWCSMQRTHTVIVAAFFCSVICNIPSYLNFTISQAEH
TR22607|c0_g1_i SIWLTVTLAVWRYIAIAFPQNNTTWCSMQRTHTVIVAAFFCSVICNIPSYLNFTISQAEH
                ************************************************************

Myosuppressin   EGQTLYIVGFSHLALAHGGFLKSINFWIYAVMLKLLPCSALTGLSFALIQELLRAGRRRA
TR22607|c0_g1_i EGQTLYIVGFSHLALAHGGFLKSINFWIYAVMLKLLPCSALTGLSFALIQELLRAGRRRA
                ************************************************************

Myosuppressin   QLMKRNSSGRAADAERQADRVTIMLLAILVLFLASEVPQGILGFLTVIPDSGFFPCYQKL
TR22607|c0_g1_i QLMKRNSSGRAADAERQADRVTIMLLAILVLFLASEVPQGILGFLTVIPDSGFFPCYQKL
                ************************************************************

Myosuppressin   GEIMDMLVLFNSAINFLLYCAMSKQFRDTFSELFKSCCVQWLAIRAPRLPPCWKAVPADA
TR22607|c0_g1_i GEIMDMLVLFNSAINFLLYCAMSKQFRDTFSELFKSCCVQWLAIRAPRLPPCWKAVPADA
                ************************************************************

Myosuppressin   PPIEVNNTCITHV
TR22607|c0_g1_i PPIEVNNTCITHV
                *************
```

Receptor 3

TR27825|c0_g1_i1

```
Myosuppressin   VVMVEYIPYTVHQYVWQGRPLTSQYSWGWAVFVLSHAHFAQVFHTISIWLTVTLAVWRYI
TR27825|c0_g1_i ------------------------------------------------------------


Myosuppressin   AIAFPQNNTTWCSMRRTHTVSIAAFFCSVICNIPNYLTFTISTIEHKGHTLYIVNVSHLA
TR27825|c0_g1_i ------------------------------------------------------------


Myosuppressin   LAHGMLLHSINFWIYAVILKLLPCGALTGLSYALIRELLRAARRRAQLMKNAAGRGADAE
TR27825|c0_g1_i ----MLLHSINFWIYAVILKLLPCGALTGLSYALIRELLRAARRRAQLMKNAAGRGADAE
                    ************************************************************

Myosuppressin   RQADRVTKMLLAILVLFLASEVPQGILGLLTVIPDSGFFPCYQKLGEIMDMLVLFNSAIN
TR27825|c0_g1_i RQADRVTKMLLAILVLFLASEVPQGILGLLTVIPDSGFFPCYQKLGEIMD----------
                ************************************************

Myosuppressin   FLLYCAMSQQFRDTFSELFKPCCMPVLGIRKPRLPSSWKTMSSADPGTESNNTCITHV
TR27825|c0_g1_i ------------------------------------------------------------
```

Receptor 4 Variant 1

TR38943|c0_g1_i4, TR38943|c0_g1_i3, TR38943|c0_g1_i1

```
Myosuppressin    MMTAGSGEMVHHLEELEAYIPREELASILPNLTKDQASYLLQLLPVLNNDTRFSVELPSP
TR38943|c0_g1_i MMTAGSGEMVHHLEELEAYIPREELASILPNLTKDQASYLLQLLPVLNNDTRFSVELPSP
                ************************************************************

Myosuppressin    SAIPTDHAFCDVGFRDGYKEVHGYLALMICLVGAFTNVLNMIILTRREMINSTNTILTGL
TR38943|c0_g1_i SAIPTDHAFCDVGFRDGYKEVHGYLALMICLVGAFTNVLNMIILTRREMINSTNTILTGL
                ************************************************************

Myosuppressin    AVADFLLLMEYSFYATSYIKGQESMFDSYFHSVFILFHAHYTQVTHTIAICLTITLAVWR
TR38943|c0_g1_i AVADFLLLMEYSFYATSYIKGQESMFDSYFHSVFILFHAHYTQVTHTIAICLTITLAVWR
                ************************************************************

Myosuppressin    YIAICKPHLNLFLCTLPRARLAVCIAYVVSPILSVPNYLMYSIHQRTDKHTNTSLYHVDF
TR38943|c0_g1_i YIAICKPHLNLFLCTLPRARLAVCIAYVVSPILSVPNYLMYSIHQRTDKHTNTSLYHVDF
                ************************************************************

Myosuppressin    SDRARASNGLLQSVHFWFYSVLIKILPCLLLTFFIYHIIRAMYTAKRRKENLIKMGTPSM
TR38943|c0_g1_i SDRARASNGLLQSVHFWFYSVLIKILPCLLLTFFIYHIIRAMYTAKRRKENLIKMGTPSM
                ************************************************************

Myosuppressin    ETERKLPRMEKMTEKTTRMLLTVLLLFLATELPQGILAFLSGVYGHSFFRQCYLHWGEVM
TR38943|c0_g1_i ETERKLPRMEKMTEKTTRMLLTVLLLFLATELPQGILAFLSGVYGHSFFRQCYLHWGEVM
                ************************************************************

Myosuppressin    DLLALINGAVNFLLYYIMSHQFRVTFRFLLSPPQPVNLSPRLPGETVSTQL
TR38943|c0_g1_i DLLALINGAVNFLLYYIMSHQFRVTFRFLLSPPQPVNLSPRLPGETVSTQL
                ****************************************************
```

Receptor 4 Variant 2

TR38943|c0_g1_i4, TR38943|c0_g1_i3, TR38943|c0_g1_i1

```
Myosuppressin    MMTAGSGEMVHHLEELEAYIPREELASILPNLTKDQASYLLQLLPVLNNDTRFSVELPSP
TR38943|c0_g1_i MMTAGSGEMVHHLEELEAYIPREELASILPNLTKDQASYLLQLLPVLNNDTRFSVELPSP
                ************************************************************

Myosuppressin    SAIPTDHAFCDVGFRDGYKEVHGYLALMICLVGAFTNVLNMIILTRREMINSTNTILTGL
TR38943|c0_g1_i SAIPTDHAFCDVGFRDGYKEVHGYLALMICLVGAFTNVLNMIILTRREMINSTNTILTGL
                ************************************************************

Myosuppressin    AVADFLLLMEYSFYATSYIKGQESMFDSYFHSVFILFHAHYTQVTHTIAICLTITLAVWR
TR38943|c0_g1_i AVADFLLLMEYSFYATSYIKGQESMFDSYFHSVFILFHAHYTQVTHTIAICLTITLAVWR
                ************************************************************

Myosuppressin    YIAICKPHLNLFLCTLPRARLAVCIAYVVSPILSVPNYLMYSIHQRTDKHTNTSLYHVDF
TR38943|c0_g1_i YIAICKPHLNLFLCTLPRARLAVCIAYVVSPILSVPNYLMYSIHQRTDKHTNTSLYHVDF
                ************************************************************

Myosuppressin    SDRARASNGLLQSVHFWFYSVLIKILPCLLLTFFIYHIIRAMYTAKRRKENLIKMGTPSM
TR38943|c0_g1_i SDRARASNGLLQSVHFWFYSVLIKILPCLLLTFFIYHIIRAMYTAKRRKENLIKMGTPSM
                ************************************************************

Myosuppressin    ETERKLPRMEKMTEKTTRMLLTVLLLFLATELPQGILAFLSGVYGHSFFRQCYLHWGEVM
TR38943|c0_g1_i ETERKLPRMEKMTEKTTRMLLTVLLLFLATELPQGILAFLSGVYGHSFFRQCYLHWGEVM
                ************************************************************

Myosuppressin    DLLALINGAVNFLLYYIMSHQFRVTFRFLL--------------QTVSTQL
TR38943|c0_g1_i DLLALINGAVNFLLYYIMSHQFRVTFRFLLSPPQPVNLSPRLPGETVSTQL
                ******************************              :******
```

Receptor 4 Variant 3

TR38943|c0_g1_i4, TR38943|c0_g1_i3, TR38943|c0_g1_i1

```
Myosuppressin   MMTAGSGEMVHHLEELEAYIPREELASILPNLTKDQASYLLQLLPVLNNDTRFSVELPSP
TR38943|c0_g1_i MMTAGSGEMVHHLEELEAYIPREELASILPNLTKDQASYLLQLLPVLNNDTRFSVELPSP
                ************************************************************

Myosuppressin   SAIPTDHAFCDVGFRDGYKEVHGYLALMICLVGAFTNVLNMIILTRREMINSTNTILTGL
TR38943|c0_g1_i SAIPTDHAFCDVGFRDGYKEVHGYLALMICLVGAFTNVLNMIILTRREMINSTNTILTGL
                ************************************************************

Myosuppressin   AVADFLLLMEYSFYATSYIKGQESMFDSYFHSVFILFHAHYTQVTHTIAICLTITLAVWR
TR38943|c0_g1_i AVADFLLLMEYSFYATSYIKGQESMFDSYFHSVFILFHAHYTQVTHTIAICLTITLAVWR
                ************************************************************

Myosuppressin   YIAICKPHLNLFLCTLPRARLAVCIAYVVSPILSVPNYLMYSIHQRTDKHTNTSLYHVDF
TR38943|c0_g1_i YIAICKPHLNLFLCTLPRARLAVCIAYVVSPILSVPNYLMYSIHQRTDKHTNTSLYHVDF
                ************************************************************

Myosuppressin   SDRARASNGLLQSVHFWFYSVLIKILPCLLLTFFIYHIIRAMYTAKRRKENLIKMGTPSM
TR38943|c0_g1_i SDRARASNGLLQSVHFWFYSVLIKILPCLLLTFFIYHIIRAMYTAKRRKENLIKMGTPSM
                ************************************************************

Myosuppressin   ET------------------------------------------------------------
TR38943|c0_g1_i ETERKLPRMEKMTEKTTRMLLTVLLLFLATELPQGILAFLSGVYGHSFFRQCYLHWGEVM
                **

Myosuppressin   ----------------------------------------------VSTQL
TR38943|c0_g1_i DLLALINGAVNFLLYYIMSHQFRVTFRFLLSPPQPVNLSPRLPGETVSTQL
                                                          *****
```

Proctolin

Receptor 1

TR31134|c0_g2_i4, TR31134|c0_g2_i3, TR31134|c0_g2_i2, TR31134|c0_g2_i1

```
Proctolin       MEVLEMFEWAPSGVINNSILLEDPNSTSVLLPYGHNTSLFNLDGDNYPYYPEDQNTSYIS
TR31134|c0_g2_i MEVLEMFEWAPSGVINNSILLEDPNSTSVLLPYGHNTSLFNLDSDNYPYYPEDQNTSYIS
                ****************************************.****************

Proctolin       VEHHVGPPDKSSIPSTTSSNYASYERFMDESRHWVQRVLVPLVMCVGLVGNAVSMVVLTR
TR31134|c0_g2_i VEHHVGPPDKSSIPSTTSSNYASYERFMDESRHWVQRVLVPLVMCVGLVGNAVSMVVLTR
                ************************************************************

Proctolin       RKMRSSTNNYLTALAISDLLYLVFVFSLSLQHHPDIKQPRHWFYWQYFRYGLWLTDASSS
TR31134|c0_g2_i RKMRSSTNNYLTALAISDLLYLVFVFSLSLQHHPDIKQPRHWFYWQYFRYGLWLTDASSS
                ************************************************************

Proctolin       TSIWITVTFTIERYIAVSHPIKGKVLCTVSRAKKVVTVVYFLCFALTATTPHEWVVVTKT
TR31134|c0_g2_i TSIWITVTFTIERYIAVSHPIKGKVLCTVSRAKKVVTVVYFLCFALTATTPHEWVVVTKT
                ************************************************************

Proctolin       RPDTHQPYLALDYSSLGQDSTYRHTYYWFTAVTFILLPLCLLAVFNFFLIQAVRTSKLHR
TR31134|c0_g2_i RPDTHQPYLALDYSSLGQDSTYRHTYYWFTAVTFILLPLCLLAVFNFFLIQAVRTSKLHR
                ************************************************************

Proctolin       RKMTLVSERDHYSHQQEYKITVMLIAVVILALVCQMPTAVLLLYSTVYEPPPKTKTYAIM
TR31134|c0_g2_i RKMTLVSERDHYSHQQEYKITVMLIAVVILALVCQMPTAVLLLYSTVYEPPPKTKTYAIM
                ************************************************************

Proctolin       RGLGNIFNLLNAVNAAANFILYCAFSDRYRRTFLMTFVPCMYHQQPLAHSFVTSVTVGGS
TR31134|c0_g2_i RGLGNIFNLLNAVNAAANFILYCAFSDRYRRTFLMTFVPCMYHQQPLAHSFVTSVTVGGS
                ************************************************************

Proctolin       GGGGCVGGRGSDTTSIKSVCRRVSKSSTPSPRPPRDHSPRLASGSFKENGVGSLDARVTL
TR31134|c0_g2_i GGGGCVGGRGSDTTSIKSVCRRVSKSSTPSPRPPRDHSPRLASGSFKENGVGSLDARVTL
                ************************************************************

Proctolin       QYGFGRSPRHLTLSPADAHPHVNNAHVRVNKHSHVSPISRNKRATQAFDNNINPGPSPEL
TR31134|c0_g2_i QYGFGRSPRHLTLSPADAHPHVNNAHVRVNKHSHVSPISRNKRATQAFDNNINPGPSPEL
                ************************************************************

Proctolin       KKVDVGNHCEVSDEKVDLEVRKKYKEDEGVIIIEKAPTPSSSVSSVEENNLLEFKFIDDE
TR31134|c0_g2_i KKVDVGNHCEVSDEKVDLEVRKKYKEDEGVIIIEKAPTPSSSVSSVEENNLLEFKFIDDE
                ************************************************************

Proctolin       SCETSQSSPTSTTRAGEDENGDADGHLPSITLQKGDDSHLVNTSPLTPPKSSDTTNESTI
TR31134|c0_g2_i SCETSQSSPTSTTRAGEDENGDADGHLPSITLQKGDDSHLVNTSPLTPPKSSDTTNESTI
                ************************************************************

Proctolin       HSPD
TR31134|c0_g2_i HSPD
                ****
```

TR31134|c0_g2_i5

```
Proctolin       MEVLEMFEWAPSGVINNSILLEDPNSTSVLLPYGHNTSLFNLDGDNYPYYPEDQNTSYIS
TR31134|c0_g2_i MEVLEMFEWAPSGVINNSILLEDPNSTSVLLPYGHNTSLFNLDADNYPYYPEDQNTSYIS
                ****************************************.****************

Proctolin       VEHHVGPPDKSSIPSTTSSNYASYERFMDESRHWVQRVLVPLVMCVGLVGNAVSMVVLTR
TR31134|c0_g2_i VEHHVGPPDKSSIPSTTSSNYASYERFMDESRHWVQRVLVPLVMCVGLVGNAVSMVVLTR
                ************************************************************

Proctolin       RKMRSSTNNYLTALAISDLLYLVFVFSLSLQHHPDIKQPRHWFYWQYFRYGLWLTDASSS
TR31134|c0_g2_i RKMRSSTNNYLTALAISDLLYLVFVFSLSLQHHPDIKQPRHWFYWQYFRYGLWLTDASSS
                ************************************************************

Proctolin       TSIWITVTFTIERYIAVSHPIKGKVLCTVSRAKKVVTVVYFLCFALTATTPHEWVVVTKT
TR31134|c0_g2_i TSIWITVTFTIERYIAVSHPIKGKVLCTVSRAKKVVTVVYFLCFALTATTPHEWVVVTKT
                ************************************************************

Proctolin       RPDTHQPYLALDYSSLGQDSTYRHTYYWFTAVTFILLPLCLLAVFNFFLIQAVRTSKLHR
TR31134|c0_g2_i RPDTHQPYLALDYSSLGQDSTYRHTYYWFTAVTFILLPLCLLAVFNFFLIQAVRTSKLHR
                ************************************************************

Proctolin       RKMTLVSERDHYSHQQEYKITVMLIAVVILALVCQMPTAVLLLYSTVYEPPPKTKTYAIM
TR31134|c0_g2_i RKMTLVSERDHYSHQQEYKITVMLIAVVILALVCQMPTAVLLLYSTVYEPPPKTKTYAIM
                ************************************************************

Proctolin       RGLGNIFNLLNAVNAAANFILYCAFSDRYRRTFLMTFVPCMYHQQPLAHSFVTSVTVGGS
TR31134|c0_g2_i RGLGNIFNLLNAVNAAANFILYCAFSDRVSN---QTFSP----------------------
                **************************  .    ** *

Proctolin       GGGGCVGGRGSDTTSIKSVCRRVSKSSTPSPRPPRDHSPRLASGSFKENGVGSLDARVTL
TR31134|c0_g2_i ------------------------------------------------------------


Proctolin       QYGFGRSPRHLTLSPADAHPHVNNAHVRVNKHSHVSPISRNKRATQAFDNNINPGPSPEL
TR31134|c0_g2_i ---------------------------VRIF------------------------------
                                          **:

Proctolin       KKVDVGNHCEVSDEKVDLEVRKKYKEDEGVIIIEKAPTPSSSVSSVEENNLLEFKFIDDE
TR31134|c0_g2_i ------------------------------------------------------------


Proctolin       SCETSQSSPTSTTRAGEDENGDADGHLPSITLQKGDDSHLVNTSPLTPPKSSDTTNESTI
TR31134|c0_g2_i ------------------------------------------------------------


Proctolin       HSPD
TR31134|c0_g2_i ----
```

Receptor 2

TR388|c0_g1_i2

```
Proctolin       -----------------LAPPTLQPPITTDPYGNFSYYYNSTDLEATEASEQEIVDISGY
TR388|c0_g1_i2  MLNISTAAPLLAAALTTLAPPTLQPPITTDPYGNFSYYYNSTDLEATEASEQEIVDISGY
                                 ****************************************

Proctolin       EAFLDISRYVVQRVLVPMVLVVGVVGNAVTIVVLTRRQMRSSTNNYLTALAISDLLYLVF
TR388|c0_g1_i2  EAFLDISRYVVQRVLVPMVLVVGVVGNAVTIVVLTRRQMRSSTNNYLTALAISDLLYLVF
                ************************************************************

Proctolin       IFSLSIRHHPGMSRPHHWFYWHYFRYALWLTDASSSTSIWLTVTFTIERYIAVCHPIKGK
TR388|c0_g1_i2  IFSLSIRHHPGMSRPHHWFYWHYFRYALWLTDASSSTSIWLTVTFTIERYIAVCHPIKGK
                ************************************************************

Proctolin       VFCTESRAKRVIVAVFILCFALTATTPHEWVINEVTDATGQARLVMNYSVLGSNATYKKV
TR388|c0_g1_i2  VFCTESRAKRVIVAVFILCFALTATTPHEWVINEVTDATGQARLVMNYSVLGSNATYKKV
                ************************************************************

Proctolin       FYWFTAVIFILLPLVLLAVFNSFLIHVVKLSRAQRRTMTNHRVERDNHSQSQENKITIML
TR388|c0_g1_i2  FYWFTAVIFILLPLVLLAVFNSFLIHVVKLSRAQRRTMTNHRVERDNHSQSQENKITIML
                ************************************************************

Proctolin       IAVVLLALVCQLPVAVLLLYTTVYVSEPHSNSQYVELSLGNIFNLLAAINAACNFVLYCA
TR388|c0_g1_i2  IAVVLLALVCQLPVAVLLLYTTVYVSEPHSNSQYVELSLGNIFNLLAAINAACNFVLYCA
                ************************************************************

Proctolin       MSDKYRRTFLRTFCSRWYRQPSPLHSWMATAYSNVEDGSPRFSRMSSMRMSRRSSYRHPR
TR388|c0_g1_i2  MSDKYRRTFLRTFCSRWYRQPSPLHSWMATAYSNVEDGSPRFSRMSSMRMSRRSSYRHPR
                ************************************************************

Proctolin       EKTAATTGTRV
TR388|c0_g1_i2  EKTAATTGTRV
                ***********
```

TR388|c0_g1_i3, TR388|c0_g1_i1

```
Proctolin       -----------------LAPPTLQPPITTDPYGNFSYYYNSTDLEATEASEQEIVDISGY
TR388|c0_g1_i3, MLNISTAAPLLAAALTTLAPPTLQPPITTDPYGNFSYYYNSTDLEATEASEQEIVDISGY
                          ******************************************

Proctolin       EAFLDISRYVVQRVLVPMVLVVGVVGNAVTIVVLTRRQMRSSTNNYLTALAISDLLYLVF
TR388|c0_g1_i3, EAFLDISRYVVQRVLVPMVLVVGVVGNAVTIVVLTRRQMRSSTNNYLTALAISDLLYLVF
                ************************************************************

Proctolin       IFSLSIRHHPGMSRPHHWFYWHYFRYALWLTDASSSTSIWLTVTFTIERYIAVCHPIKGK
TR388|c0_g1_i3, IFSLSIRHHPGMSRPHHWFYWHYFRYALWLTDASSSTSIWLTVTFTIERYIAVCHPIKGK
                ************************************************************

Proctolin       VFCTESRAKRVIVAVFILCFALTATTPHEWVINEVTDATGQARLVMNYSVLGSNATYKKV
TR388|c0_g1_i3, VFCTESRAKRVIVAVFILCFALTATTPHEWVINEVTDATGQARLVMNYSVLGSNATYKKV
                ************************************************************

Proctolin       FYWFTAVIFILLPLVLLAVFNSFLIHVVKLSRAQRRTMTNHRVERDNHSQSQENKITIML
TR388|c0_g1_i3, FYWFTAVIFILLPLVLLAVFNSFLIHVVKLSRAQRRTMTNHRVERDNHSQSQENKITIML
                ************************************************************

Proctolin       IAVVLLALVCQLPVAVLLLYTTVYVSEPHSNSQYVELSLGNIFNLLAAINAACNFVLYCA
TR388|c0_g1_i3, IAVVLLALVCQLPVAVLLLYTTVYVSEPHSNSQYVELSLGNIFNLLAAINAACNFVLYCA
                ************************************************************

Proctolin       MSDKYRRTFLRTFCSRWYRQPSPLHSWMATAYSNVEDGSPRFSRMSSMRMSRRSSYRHPR
TR388|c0_g1_i3, MSDKYRRTFLRTFCSRWYRQPSPLHSWMATAYSNVEDGSPRFSRMSSMRMSRRSSYSGSG
                ************************************************************  .

Proctolin       EKTAATTGTR----------------------------------------------------
TR388|c0_g1_i3, SPRGSPTHGRGLSGGRPGHYLTVPSPSHNPTPALLTPTKTALLHPVPDDVSRPLLKKTSS
                .  .:.*  *

Proctolin       ------------------------------------------------------------
TR388|c0_g1_i3, GKNGSDNGNAGVTSPAVTASAATLLNGSPNSQTPAPSAPPPGAASRFARRLSSLLPQRNN


Proctolin       ------------------------V
TR388|c0_g1_i3, TSTQLAGRHIVITCQQPSVDEQTAL
                                        :
```

Pyrokinin

Receptor 1

TR19456|c0_g1_i1

```
Pyrokinin       QTSTPRNTFKKSLQTSAPGMSSPSQPERGVVVNLTEEVLGAVMTGVNNGSGGTEVNDTFD
TR19456|c0_g1_i ------------MQDSA-----------------------------------------
                          :* **

Pyrokinin       EHEYISRELGPQRVSYNTLLPLTVVYCVIAVGGVVGNALTCLVVARNHSMRTSTNYYLVN
TR19456|c0_g1_i ------------------------------------------------------------


Pyrokinin       LAVADLLTLCLALPIEMYQMWVQYPWPWGDAACKIRAILPETLAHVSVLNILAVTGERYV
TR19456|c0_g1_i ----------------------------SAALQHRKV----------------------
                                          .** : * :

Pyrokinin       AITDPVYARTTHTLARTARVLPVIWIVALLAATPWGYYQQVNLLLGPFGSLPQSAWCAIP
TR19456|c0_g1_i ------------------------------------------------DLPN-------
                                                               .**:

Pyrokinin       YHDTSTSWSWLMWVSSVGAFILPMTILMTLYCKIGVVLSIDPPTRTPAAGAGAMHTRKVG
TR19456|c0_g1_i ------------------------------------------------------MKARRQV
                                                                     *::*:

Pyrokinin       IRMLVAVVVAFFVCWAPFHAQRLMFVIVTSYGKWTAH--LRSVNTKLY----YFTGICYY
TR19456|c0_g1_i VVMLATVTVFFFVSLFPFRVFTLWIV-------WTPEEVIKTLGALRYYSMLYTARVMQF
                : **.:*.* ***.  **:.  * :*       **..  :::::  *    * : :  :

Pyrokinin       LNSAVNPILYNLTSTKFREAFLKLLSNDRRRRHLSRQSTFNTTGTSMSNGRSGSSRTIPT
TR19456|c0_g1_i ANSAVNPILYNLTSTKFREAFLKLLSNDRRRRHLSRQSTFNTTGTSMSNGRSGSSRTIPT
                 ************************************************************

Pyrokinin       DLGSLKDATYPARVALAKCGRHASFDDFPAPRPNMARYGRQSSFAGTYCLPNSTNSNSNS
TR19456|c0_g1_i DLGSLKDATYPARVALAKCGRHASFDDFPAPRPNMARYGRQSSFAGTYCLPNSTNSNSNS
                ************************************************************

Pyrokinin       VACSRQNSRAGENGVLSPLEARRSVEGEKRHSGEGRRLLEGERQSSSAFNTDMIEEERSS
TR19456|c0_g1_i VACSRQNSRAGENGVLSPLEARRSVEGEKRHSGEGRRLLEGERQSSSAFNTDMIEEERSS
                ************************************************************

Pyrokinin       GGVSRLDSVRRDQQNKIATEMEKLLSDECLNTEAGDSKTMAGAPGDAVNEMNLKQGTGEC
TR19456|c0_g1_i GGVSRLDSVRRDQQNKIATEMEKLLSDECLNTEAGDSKTMAGAPGDAVNEMNLKQGTGEC
                ************************************************************

Pyrokinin       KVEVEFPSNNDGVTSQDPGERGTTGKQDIASSSKENGDKDTITNTDNGKSVQFCDGVSTE
TR19456|c0_g1_i KVEVEFPSNNDGVTSQDPGERGTTGKQDIASSSKENGDKDTITNTDNGKSVQFCDGVSTE
                ************************************************************

Pyrokinin       FSVV
TR19456|c0_g1_i FSVV
                ****
```

Amines

Octopamine Beta

Receptor 2

TR29189|c0_g1_i1

```
Octopamine      MQGETAIMGESGELSTNGTWVGDMWVTANTSVDGTVDSVSGPEWKDLTVGIVKGVCMAVI
TR29189|c0_g1_i ------------------------------------------------------------


Octopamine      IVCAVLGNLLVVVSVVRHRRLRIITNYFVVSLAIADILVALMAMPFNASVELTGRWLFSY
TR29189|c0_g1_i ------------------------------------------------------------


Octopamine      RMCDLWNSFDVFASTVSILHLCSISIDRYYAIVRPLEYPRLMTKGRAVIMLCHVWLAPLV
TR29189|c0_g1_i ----------------------------------------MTKGRAVIMLCHVWLAPLV
                                                         ******************

Octopamine      ISFLPIFMGWYTTEEHLAERAANPSRCIFEVNTTYAVVSSSISFWMPCSVMVYMYYRIYL
TR29189|c0_g1_i ISFLPIFMGWYTTEEHLAERAANPSRCIFEVNTTYAVVSSSISFWMPCSVMVYMYYRIYL
                ************************************************************

Octopamine      EAARQERIMHRNTRLSSASQAAVVVSNNSTNTTITTASAGTNGVGSDNAGSLGLGSGGSG
TR29189|c0_g1_i EAARQERIMHRNTRLSSASQAAVVVSNNSTNTTITTASAGTNGVGSDNAGSLGLGSGGSG
                ************************************************************

Octopamine      RRLMAHRPSSDTQEATPTKNNLIKLKRERKAARTLGIIMGAFIVCWLPFFTWYVTITLCG
TR29189|c0_g1_i RRLMAHRPSSDTQEATPTKNNLIKLKRERKAARTLGIIMGAFIVCWLPFFTWYVTITLCG
                ************************************************************

Octopamine      EACPCPEIIVSILFWIGYFNSMLNPAIYAYFNRDFREAFRRTLQCVFRCGRPVDPWRGQL
TR29189|c0_g1_i EACPCPEIIVSILFWIGYFNSMLNPAIYAYFNRDFREAFRR----------------------
                ****************************************

Octopamine      GPPYDSDLCLQHNGHSTIVKAKARRYSTECGV
TR29189|c0_g1_i --------------------------------
```

TR7749|c0_g1_i1

```
Octopamine      MQGETAIMGESGELSTNGTWVGDMWVTANTSVDGTVDSVSGPEWKDLTVGIVKGVCMAVI
TR7749|c0_g1_i1 MQGETAIMGESGELSTNGTWVGDMWVTANTSVDGTVDSVSGPEWKDLTVGIVKGVCMAVI
                ************************************************************

Octopamine      IVCAVLGNLLVVVSVVRHRRLRIITNYFVVSLAIADILVALMAMPFNASVELTGRWLFSY
TR7749|c0_g1_i1 IVCAVLGNLLVVVSVVRHRRLRIITNYFVVSLAIADILVALMAMPFNASVELTGRWLFSY
                ************************************************************

Octopamine      RMCDLWNSFDVFASTVSILHLCSISIDRYYAIVRPLEYPRLMTKGRAVIMLCHVWLAPLV
TR7749|c0_g1_i1 RMCDLWNSFDVFASTVSIL---------------------------------------
                *******************

Octopamine      ISFLPIFMGWYTTEEHLAERAANPSRCIFEVNTTYAVVSSSISFWMPCSVMVYMYYRIYL
TR7749|c0_g1_i1 ------------------------------------------------------------


Octopamine      EAARQERIMHRNTRLSSASQAAVVVSNNSTNTTITTASAGTNGVGSDNAGSLGLGSGGSG
TR7749|c0_g1_i1 ------------------------------------------------------------

                                        .

Octopamine      RRLMAHRPSSDTQEATPTKNNLIKLKRERKAARTLGIIMGAFIVCWLPFFTWYVTITLCG
TR7749|c0_g1_i1 ------------------------------------------------------------


Octopamine      EACPCPEIIVSILFWIGYFNSMLNPAIYAYFNRDFREAFRRTLQCVFRCGRPVDPWRGQL
TR7749|c0_g1_i1 ------------------------------------------------------------


Octopamine      GPPYDSDLCLQHNGHSTIVKAKARRYSTECGV
TR7749|c0_g1_i1 --------------------------------
```

Serotonin

Receptor Type 7

TR30021|c1_g2_i2, TR30021|c1_g2_i1

```
Serotonin       MLASAGVASPTPSLHPLFNISHAAKLILQPSEAAHTPAEGAQGPMVGTDSALVTVDPVNY
TR30021|c1_g2_i MLASAGVASPTPSLHPLFNISHAAKLILQPSEAAHTPAEGAQGPMVGTDSALVTVDPVNY
                ************************************************************

Serotonin       TVLGDGGVETGGSALYMLFTTVLVVLVLLMIIVGTVVGNLLVCVAVCLVRKLRRPYNYLL
TR30021|c1_g2_i TVLGDGGVETGGSALYMLFTTVLVVLVLLMIIVGTVVGNLLVCVAVCLVRKLRRPYNYLL
                ************************************************************

Serotonin       VSLAVSDLCVALLVMPMALLHELLGEWQFGQLACDVWVSFDVLSCTASILNLCMISVDRY
TR30021|c1_g2_i VSLAVSDLCVALLVMPMALLHELLGEWQFGQLACDVWVSFDVLSCTASILNLCMISVDRY
                ************************************************************

Serotonin       LAITRPLEYGVKRTPRRMVAYIAFVWLGAAFISVPPILILGNEHGDGSICEVCQNFWYQI
TR30021|c1_g2_i LAITRPLEYGVKRTPRRMVAYIAFVWLGAAFISVPPILILGNEHGDGSICEVCQNFWYQI
                ************************************************************

Serotonin       YATFGSFYIPLTVMVIVYYKIFCAAKRIVDEERKAQAHLRLVEEAEADARASTAVLGSYT
TR30021|c1_g2_i YATFGSFYIPLTVMVIVYYKIFCAAKRIVDEERKAQAHLRLVEEAEADARASTAVLGSYT
                ************************************************************

Serotonin       QLKPVSRYSVVEVNNGGVETRLAPEAPPLSSKDETGSLLGPDSPHHLEVPPRLVVCSSSV
TR30021|c1_g2_i QLKPVSRYSVVEVNNGGVETRLAPEAPPLSSKDETGSLLGPDSPHHLEVPPRLVVCSSSV
                ************************************************************

Serotonin       SSAASADSTTGSRWSLCETNGKAHPPNANAGARTPTQPQHGHNCYNACQSTNGSGTNGSP
TR30021|c1_g2_i SSAASADSTTGSRWSLCETNGKAHPPNANAGARTPTQPQHGHNCYNACQSTNGSGTNGSP
                ************************************************************

Serotonin       RKRSHPPKIKLKFALAKERKASTTLGIIMSAFVVCWLPFFVLALVRPFKKPSAIPAWISS
TR30021|c1_g2_i RKRSHPPKIKLKFALAKERKASTTLGIIMSAFVVCWLPFFVLALVRPFKKPSAIPAWISS
                ************************************************************

Serotonin       LFLWLGYANSLLNPIIYATLNKDFRKPFQEILCLRCASLNLLMREEFYHSQYGGPDTPTL
TR30021|c1_g2_i LFLWLGYANSLLNPIIYATLNKDFRKPFQEILCLRCASLNLLMREEFYHSQYGGPDTPTL
                ************************************************************

Serotonin       SAVRTHTHTNPRNSSEIHLAIADPREASISEEAHESKI
TR30021|c1_g2_i SAVRTHTHTNPRNSSEIHLAIADPREASISEEAHESKI
                ***************************************
```

Query sequence and Putative Receptor Alignments: Cardiac Muscle Receptors

AST-C

Receptor 1

TR42870|c0_g1_i1

```
AST-C           MNSNSTLYLDFDGNDSDSFPLNCSFLNMKDPDATSNCSLGVFTGEVSPIHVVASIIMQAC
TR42870|c0_g1_i ------------------------------------------------------------


AST-C           YAIAFLVGLCGNTLVIYVVTRFSKMQTVTNLYIVNLAIADELFVIGIPFLMITSVLGYWA
TR42870|c0_g1_i ------------------------MQTVTNLYILNLAIADELFVVGIPFLMTTSMLRYWP
                                         *********:**********:****** **:* **.

AST-C           FGSIMCKLYMITTSLNQFTSSLFLTIMSADRYIAVCHPISSTKFRTPMISKLVSLTAWTT
TR42870|c0_g1_i FGSIMCKLYMITTSLNQFTSSLFLTIMSADRYIAVCHPISSPRFRTPMISKLVSLTAWTL
                ****************************************.:*****************

AST-C           SALMIVPVFMYSNTLEVNDLINCNIFWPDSFGISGQFVFTLYSFILAFGIPLILIFIFYG
TR42870|c0_g1_i SALMIVPVFMYSNTLQDNGLDNCNIFWPESQGVRGEIAFIRYSFALAFGIPLTLIFIFYS
                ***************: *.* *******:* *: *::.*  *** ******* *******.

AST-C           LVLQKLKSVGPKSKSKEKKKSHRKVTKMVLTVITVYVMCWLPYWVLQLALIFSPPREGQS
TR42870|c0_g1_i LVLHKLKSVGPKSKSKEKKKSRQKVTRLVLTVITVYVICWLPYWVLQLTLILSTPKQGHS
                ***:*****************::***::*********:**********:**:*.*::*:*

AST-C           PFMVVLFLISSCLSYFNSAINPILYAFLSENFKKSFMKACICATRKDANNALAVENSVFP
TR42870|c0_g1_i NFMVVLFMISSCLSYINSA-----------------------------------------
                 ******:*******:***

AST-C           RRRGGSAKPKNAKAHEMESNDAYTTQCTRDEATTAITMTTRSTVSQMGRENGTEIPTTQL
TR42870|c0_g1_i ------------------------------------------------------------
```

Receptor 2

TR42870|c0_g1_i1

```
AST-C           MENDTLSEPEDTIPLNCSYLLYGDLYNRSDFLNESNCTLGLFTGGKNEMSIAAIVITQMF
TR42870|c0_g1_i ------------------------------------------------------------


AST-C           YAITCLVGLCGNTLVIYVVTRFSKMQTVTNLYILNLAIADELFVVGIPFLMTTSMLRYWP
TR42870|c0_g1_i ------------------------MQTVTNLYILNLAIADELFVVGIPFLMTTSMLRYWP
                                         ********************************

AST-C           FGSIMCKLYMITTSLNQFTSSLFLTIMSADRYIAVCHPISSPRFRTPMISKLVSLTAWTL
TR42870|c0_g1_i FGSIMCKLYMITTSLNQFTSSLFLTIMSADRYIAVCHPISSPRFRTPMISKLVSLTAWTL
                ************************************************************

AST-C           SALMIVPVFMYSNTLQDNGLDNCNIFWPESQGVRGEIAFIRYSFALAFGIPLTLIFIFYS
TR42870|c0_g1_i SALMIVPVFMYSNTLQDNGLDNCNIFWPESQGVRGEIAFIRYSFALAFGIPLTLIFIFYS
                ************************************************************

AST-C           LVLHKLKSVGPKSKSKEKKKSRQKVTRLVLTVITVYVICWLPYWVLQLTLILSTPKQGHS
TR42870|c0_g1_i LVLHKLKSVGPKSKSKEKKKSRQKVTRLVLTVITVYVICWLPYWVLQLTLILSTPKQGHS
                ************************************************************

AST-C           NFMVVLFMISSCLSYINSALNPILYAFLSDNFKKSFMKACTCAARMEVNNALRPENSMFP
TR42870|c0_g1_i NFMVVLFMISSCLSYINSA----------------------------------------
                ******************

AST-C           LRQRGTSAKSRMTRRDRESGEGTTSQCGLSKEPSTAVTTTNARPNLSNNSGSSGDELTVR
TR42870|c0_g1_i ------------------------------------------------------------


AST-C           NGRSPGPRLPDLIQ
TR42870|c0_g1_i --------------
```

Bursicon

Receptor 1

TR22406|c0_g1_i1

```
Bursicon          MRDSGDAGGPAGGGRGSLAPLLLPLCLLLLLLAPAVSACPTACTCEAVPPRRSSALSRRS
TR22406|c0_g1_i MRDSGDAGGPAGGGRGSLAPLLLPLCLLLLLLAPAVSACPTACTCEAVPPRRSSALSRRS
                ************************************************************

Bursicon          VWAAKTEVPAAHNTNNVTLVCRDAGLMAPPDLVALNGLDPATVSKMDLSKNGITELHEYS
TR22406|c0_g1_i VWAAKTEVPAAHNTNNVTLVCRDAGLMAPPDLVALNGLDPATVSKMDLSKNGITELHEYS
                ************************************************************

Bursicon          FSLYPSLHTLKVCGNRLTTIAAGAFQDIPLRVLVLDNNKLSELVADSLPASLREISLERN
TR22406|c0_g1_i FSLYPSLHTLKVCGNRLTTIAAGAFQDIPLRVLVLDNNKLSELVADSLPASLREISLERN
                ************************************************************

Bursicon          TFTSIPPSLTALHGLQFLNLARNRLTALKDGDLRGLHNLQRLSLHQNRISTVESRALAPL
TR22406|c0_g1_i TFTSIPPSLTALHGLQFLNLARNRLTALKDGDLRGLHNLQRLSLHQNRISTVESRALAPL
                ************************************************************

Bursicon          RNLEKLDLEVNTLTEVPTAVTRCLKLKELLLGSNRLTYVGEDSFKGLARLQDVALWPNQL
TR22406|c0_g1_i RNLEKLDLEVNTLTEVPTAVTRCLKLKELLLGSNRLTYVGEDSFKGLARLQDVALWPNQL
                ************************************************************

Bursicon          LTIHQRAFSNLPSLTKLILKEMKQLQEFPDLNGTSSLELIRIDRAALTAVPENLCSVAPK
TR22406|c0_g1_i LTIHQRAFSNLPSLTKLILKEMKQLQEFPDLNGTSSLELIRIDRAALTAVPENLCSVAPK
                ************************************************************

Bursicon          LRSLNLQRNSISEMPDLNRCRQLRLIDLSHNNISSLPAATFSSLSFLQDLLLQGNRVHTI
TR22406|c0_g1_i LRSLNLQRNSISEMPDLNRCRQLRLIDLSHNNISSLPAATFSSLSFLQDLLLQGNRVHTI
                ************************************************************

Bursicon          HNNTFNGLEKLQVLQLEDNLITSIHQDAFLPLVSLEDINLGNNSFPELPAQGLEHVVSIK
TR22406|c0_g1_i HNNTFNG-------------------------------------------------------
                *******

Bursicon          VHNNRHLRVFPGPESFPMVRALTLSYAYHCCPFLRLEDHTEAPQIIEEVIYSGDGFKGLD
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon          PTIWNVSSVWPETAGLRTNFAAIWANLAADFPPANTDLVDTTSLDLGEATAATHTLPLLP
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon          RHQVLCNPEPGPFMPCEDLFDWWTLRCGVWIVFLLALLGNGAVVVVLVFARAKMDVPRFL
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon          VTNLAFADFFMGLYLGFLAVVDASTLGEFRMYAIPWQTSVGCQVAGFLGVLSCELSVYTL
TR22406|c0_g1_i ------------------------------------------------------------
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Bursicon        VTNLAFADFFMGLYLGFLAVVDASTLGEFRMYAIPWQTSVGCQVAGFLGVLSCELSVYTL
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon        TVITMERNYAITHAMHLNKRLSLRHAAYIMVLGWLFACTMALLPLIGVSDYRKFAVCLPI
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon        ETKGAGLGYVVFLMFINGVAFLILMGCYLKIYCAIRGSQAWNSNDSRIAKRMALLVFTDF
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon        ICWAPIAFFSLTAAFGLQLISLKEAKVFTVFILPFNSCCNPFLYALLTKQFKKDCVMLCK
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon        TIEESRVTRGIGRCRHSSNFSNRQTPANTNSALENSSRQDNQLCRCQNKTQESQKLHHRL
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon        RISALKYLFCHKDTEGLNSTSDFSYQPTKSAVKSKRHTSVSSETYSSSWSDTWRRGHAAM
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon        SLRILDRRHHNSWYLSRKPSQESNLSSSRNDSSATTASTSTWRISRSSVSSDISSSGSRG
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon        VGKSDVAPTLRLGSLRERRGECHIQIPTRQITHHHQALLVRQQSGASGQRSAPITSAVRI
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon        KPRLQRQSAIERETYIPNKAAGGQNEITCPLHQRSDNLSCVYEQESYEEEDHEASKDYLN
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon        PRCPMAGLTVTFIPRKLSTISSHSVSVVRDAEGDEPAVGPCVDVHSSSDPFPMSNCDFSR
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon        GGKCVSLTLLPQSSSQTSPSRFPSDGHLPRSPRCTELLYFTNLAAPALIVPSTEQNAESP
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon        PKDLDATPKNHYGQAILIHSQPRSPQSLEHDECMESTALMDDDCYGDDEVFEEENKSRER
TR22406|c0_g1_i ------------------------------------------------------------


Bursicon        PLETHFPLDDPPGETRPLI
TR22406|c0_g1_i -------------------
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TR27789|c0_g1_i1

```
Bursicon        MRDSGDAGGPAGGGRGSLAPLLLPLCLLLLLLAPAVSACPTACTCEAVPPRRSSALSRRS
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        VWAAKTEVPAAHNTNNVTLVCRDAGLMAPPDLVALNGLDPATVSKMDLSKNGITELHEYS
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        FSLYPSLHTLKVCGNRLTTIAAGAFQDIPLRVLVLDNNKLSELVADSLPASLREISLERN
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        TFTSIPPSLTALHGLQFLNLARNRLTALKDGDLRGLHNLQRLSLHQNRISTVESRALAPL
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        RNLEKLDLEVNTLTEVPTAVTRCLKLKELLLGSNRLTYVGEDSFKGLARLQDVALWPNQL
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        LTIHQRAFSNLPSLTKLILKEMKQLQEFPDLNGTSSLELIRIDRAALTAVPENLCSVAPK
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        LRSLNLQRNSISEMPDLNRCRQLRLIDLSHNNISSLPAATFSSLSFLQDLLLQGNRVHTI
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        HNNTFNGLEKLQVLQLEDNLITSIHQDAFLPLVSLEDINLGNNSFPELPAQGLEHVVSIK
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        VHNNRHLRVFPGPESFPMVRALTLSYAYHCCPFLRLEDHTEAPQIIEEVIYSGDGFKGLD
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        PTIWNVSSVWPETAGLRTNFAAIWANLAADFPPANTDLVDTTSLDLGEATAATHTLPLLP
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        RHQVLCNPEPGPFMPCEDLFDWWTLRCGVWIVFLLALLGNGAVVVVLVFARAKMDVPRFL
TR27789|c0_g1_i ------------MPCEDLFDWWTLRCGVWIVFLLALLGNGAVVVVLVFARAKMDVPRFL
                            **********************************************

Bursicon        VTNLAFADFFMGLYLGFLAVVDASTLGEFRMYAIPWQTSVGCQVAGFLGVLSCELSVYTL
TR27789|c0_g1_i VTNLAFADFFMGLYLGFLAVVDASTLGEFRMYAIPWQTSVGCQVAGFLGVLSCELSVYTL
                ************************************************************

Bursicon        TVITMERNYAITHAMHLNKRLSLRHAAYIMVLGWLFACTMALLPLIGVSDYRKFAVCLPI
TR27789|c0_g1_i TVITMERNYAITHAMHLNKRLSLRHAAYIMVLGWLFACTMALLPLIGVSDYRKFAVCLPI
                ************************************************************
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```
Bursicon        ETKGAGLGYVVFLMFINGVAFLILMGCYLKIYCAIRGSQAWNSNDSRIAKRMALLVFTDF
TR27789|c0_g1_i ETKGAGLGYVVFLMFINGVAFLILMGCYLKIYCAIRGSQAWNSNDSRIAKRMALLVFTDF
                ************************************************************

Bursicon        ICWAPIAFFSLTAAFGLQLISLKEAKVFTVFILPFNSCCNPFLYALLTKQFKKDCVMLCK
TR27789|c0_g1_i ICWAPIAFFSLTAAFGLQLISLKEAKVFTVFILPFNSCCNPFLYALLTKQFKKDCVMLCK
                ************************************************************

Bursicon        TIEESRVTRGIGRCRHSSNFSNRQTPANTNSALENSSRQDNQLCRCQNKTQESQKLHHRL
TR27789|c0_g1_i TIEESRVTRGIGRCRHSSNFSNRQTPA--------------------------------
                ***************************

Bursicon        RISALKYLFCHKDTEGLNSTSDFSYQPTKSAVKSKRHTSVSSETYSSSWSDTWRRGHAAM
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        SLRILDRRHHNSWYLSRKPSQESNLSSSRNDSSATTASTSTWRISRSSVSSDISSSGSRG
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        VGKSDVAPTLRLGSLRERRGECHIQIPTRQITHHHQALLVRQQSGASGQRSAPITSAVRI
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        KPRLQRQSAIERETYIPNKAAGGQNEITCPLHQRSDNLSCVYEQESYEEEDHEASKDYLN
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        PRCPMAGLTVTFIPRKLSTISSHSVSVVRDAEGDEPAVGPCVDVHSSSDPFPMSNCDFSR
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        GGKCVSLTLLPQSSSQTSPSRFPSDGHLPRSPRCTELLYFTNLAAPALIVPSTEQNAESP
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        PKDLDATPKNHYGQAILIHSQPRSPQSLEHDECMESTALMDDDCYGDDEVFEEENKSRER
TR27789|c0_g1_i ------------------------------------------------------------


Bursicon        PLETHFPLDDPPGETRPLI
TR27789|c0_g1_i --------------------
```

DH31

Receptor 2

TR48162|c0_g1_i2

```
DH31            MEGNETDSVMDDWAWEEMSATKQDNSSSTEAGSSKGWEGTFKQKQEIARRQAECEALHAT
TR48162|c0_g1_i MEGNETDSVMDDWAWEEMSATKQDNSSSTEAGSSKGWEGTFKQKQEIARRQAECEALHAT
                ************************************************************

DH31            MPIPEPSFGPYCPRTFDGWSCWNDTPAGTRAHVQCPSFIHGFDPQRSGHKDCDENGTWFT
TR48162|c0_g1_i MPIPEPSFGPYCPRTFDGWSCWNDTPAGTRAHVQCPSFIHGFDPQRSGHKDCDENGTWFT
                ************************************************************

DH31            HPDTNNFWSNYTTCIDVSNLELHQGVNTIYIAGYSMSLVALCISLFIFFFFKSLKCTRVT
TR48162|c0_g1_i HPDTNNFWSNYTTCIDVSNLELHQGVNTIYIAGYSMSLVALCISLFIFFFFKSLKCTRVT
                ************************************************************

DH31            IHKNLFVSFIINNAMWLVWFECVVGRVDVVFSNTVGCQVLHVFLHYFLVSNYFWMFCEGL
TR48162|c0_g1_i IHKNLFVSFIINNAMWLVWFECVVGRVDVVFSNTVGCQVLHVFLHYFLVSNYFWMFCEGL
                ************************************************************

DH31            YLHTLLVVAFVAEDRIMKWFYMLGWGAPAVFTIIYGACRGTDDEQSVYCWMEDGNYNYIL
TR48162|c0_g1_i YLHTLLVVAFVAEDRIMKWFYMLGWGAPAVFTIIYGACRGTDDEQSVYCWMEDGNYNYIL
                ************************************************************

DH31            NVPVVLSMLLNLFFLVNIVRVLVTKLRAVNTAPDTHSTRKAVRATLILIPLLGLHYILIP
TR48162|c0_g1_i NVPVVLSMLLNLFFLVNIVRVLVTKLRAVNTAPDTHSTRKAVRATLILIPLLGLHYILI-
                ************************************************************

DH31            FRPPKGSPAEGFYLVVSAIAASLQGLGVSLLFCFFNGEXXXXXXXXHEIEYG
TR48162|c0_g1_i ------------------------------------------------------
```

TR48162|c0_g1_i1

```
DH31            MEGNETDSVMDDWAWEEMSATKQDNSSSTEAGSSKGWEGTFKQKQEIARRQAECEALHAT
TR48162|c0_g1_i MEGNETDSVMDDWAWEEMSATKQDNSSSTEAGSSKGWEGTFKQKQEIARRQAECEALHAT
                ************************************************************

DH31            MPIPEPSFGPYCPRTFDGWSCWNDTPAGTRAHVQCPSFIHGFDPQRSGHKDCDENGTWFT
TR48162|c0_g1_i MPIPEPSFGPYCPRTFDGWSCWNDTPAGTRAHVQCPSFIHGFDPQLS-------------
                ******************************************** *

DH31            HPDTNNFWSNYTTCIDVSNLELHQGVNTIYIAGYSMSLVALCISLFIFFFFKSLKCTRVT
TR48162|c0_g1_i ------------------------------------------------------------


DH31            IHKNLFVSFIINNAMWLVWFECVVGRVDVVFSNTVGCQVLHVFLHYFLVSNYFWMFCEGL
TR48162|c0_g1_i ----------------------LSAR-----------------------------------
                                      : .*

DH31            YLHTLLVVAFVAEDRIMKWFYMLGWGAPAVFTIIYGACRGTDDEQSVYCWMEDGNYNYIL
TR48162|c0_g1_i ------------------------------------------------------------


DH31            NVPVVLSMLLNLFFLVNIVRVLVTKLRAVNTAPDTHSTRKAVRATLILIPLLGLHYILIP
TR48162|c0_g1_i ------TIVLDLFCL----------LTAVDQAP-----RRSER----------IHR----
                      :::*:** *          * **: **     *:: *          :*

DH31            FRPPKGSPAEGFYLVVSAIAASLQGLGVSLLFCFFNGEXXXXXXXXHEIEYG
TR48162|c0_g1_i -------------------ERSAQDLAMSV----------------------
                                  * *.*.:*:
```

DH44

Receptor 1

TR32466|c0_g1_i1

```
DH44            MPSITAPTEFPSYSLSDPAETEEEDSDEIYITLWRKFMEQSALINATNGDHKMLQCFNMY
TR32466|c0_g1_i ------------------------------------------------------------


DH44            LNTTMDPESDPGACPVKFDGVSCWPETPPDTTRAIPCFNDFNGVHYEPSDYNATLYCYPN
TR32466|c0_g1_i ------------------------------------------------------------


DH44            GTWSKKSFYNFCLNAVTNNSEVQGSTVNTISTIFYIGNSVSLVAVTLALWIFISFKDLRC
TR32466|c0_g1_i ------------------------------------------------------------


DH44            LRNTIHTNLLFTYLLHNLFWIVYASVQTLVNVSVGCSFFVALNYFTLTNFMWMFVEGFYL
TR32466|c0_g1_i -----------------------------------------------------MWMFVEGFYL
                                                                     **********

DH44            YMLVVKTFSVENIKLRVYTLIGWGVPVPIIISWVILKSQLATTHPAGMEGHELEGLVRNC
TR32466|c0_g1_i YMLVVKTFSVENIKLRVYTLIGWGVPVPIIISWVILKSQLATTHPAGMEGHELEGLVRNC
                ************************************************************

DH44            PLMPDSTVDWIQKIPVLFLLSTNLIFLTRIMWVLITKLRSANTVETQRYRKATKALLVLI
TR32466|c0_g1_i PLMPDSTVDWIQKIPVLFLLSTNLIFLTRIMWVLITKL----------------------
                ************************************

DH44            PLLGLTYMLLIALPQELEHVRAILLSTQGFWVALFYCFLNSEVQNSIRHHIERWKTARGL
TR32466|c0_g1_i ------------------------------------------------------------


DH44            ADPRHASVRHGRDGSPRPKTDCSSYSRRLFGGKRESLCSEVTTMTTYVANGYNPVSTQTG
TR32466|c0_g1_i ------------------------------------------------------------


DH44            GPPQQQQSLLQPAPQQPPTATGQHLTYRNSNAGIAPNSGGDPDVKSTVKDSLL
TR32466|c0_g1_i ------------------------------------------------------
```

Myosuppressin

Receptor 4 Variant 1

TR17352|c0_g1_i1

```
Myosuppressin   MMTAGSGEMVHHLEELEAYIPREELASILPNLTKDQASYLLQLLPVLNNDTRFSVELPSP
TR17352|c0_g1_i ------------------------------------------------------------


Myosuppressin   SAIPTDHAFCDVGFRDGYKEVHGYLALMICLVGAFTNVLNMIILTRREMINSTNTILTGL
TR17352|c0_g1_i ------------------------------------------------------------


Myosuppressin   AVADFLLLMEYSFYATSYIKGQESMFDSYFHSVFILFHAHYTQVTHTIAICLTITLAVWR
TR17352|c0_g1_i ------------------------------------------------------------


Myosuppressin   YIAICKPHLNLFLCTLPRARLAVCIAYVVSPILSVPNYLMYSIHQRTDKHTNTSLYHVDF
TR17352|c0_g1_i ------------------------------------------------------------


Myosuppressin   SDRARASNGLLQSVHFWFYSVLIKILPCLLLTFFIYHIIRAMYTAKRRKENLIKMGTPSM
TR17352|c0_g1_i ----------------------------------------MYTAKRRKENLIKMGTPSM
                                                        ******************

Myosuppressin   ETERKLPRMEKMTEKTTRMLLTVLLLFLATELPQGILAFLSGVYGHSFFRQCYLHWGEVM
TR17352|c0_g1_i ETERKLPRMEKMTEKTTRMLLTVLLLFLATELPQGILAFLSGVYGHSFFRQCYLHWGEVM
                ************************************************************

Myosuppressin   DLLALINGAVNFLLYYIMSHQFRVTFRFLLSPPQPVNLSPRLPGETVSTQL
TR17352|c0_g1_i DLLALINGAVNFLLYYIMSHQFR----------------------------
                ***********************
```

Receptor 4 Variant 2

TR17352|c0_g1_i1

```
Myosuppressin   MMTAGSGEMVHHLEELEAYIPREELASILPNLTKDQASYLLQLLPVLNNDTRFSVELPSP
TR17352|c0_g1_i ------------------------------------------------------------


Myosuppressin   SAIPTDHAFCDVGFRDGYKEVHGYLALMICLVGAFTNVLNMIILTRREMINSTNTILTGL
TR17352|c0_g1_i ------------------------------------------------------------


Myosuppressin   AVADFLLLMEYSFYATSYIKGQESMFDSYFHSVFILFHAHYTQVTHTIAICLTITLAVWR
TR17352|c0_g1_i ------------------------------------------------------------


Myosuppressin   YIAICKPHLNLFLCTLPRARLAVCIAYVVSPILSVPNYLMYSIHQRTDKHTNTSLYHVDF
TR17352|c0_g1_i ------------------------------------------------------------


Myosuppressin   SDRARASNGLLQSVHFWFYSVLIKILPCLLLTFFIYHIIRAMYTAKRRKENLIKMGTPSM
TR17352|c0_g1_i ----------------------------------------MYTAKRRKENLIKMGTPSM
                                                        ******************

Myosuppressin   ETERKLPRMEKMTEKTTRMLLTVLLLFLATELPQGILAFLSGVYGHSFFRQCYLHWGEVM
TR17352|c0_g1_i ETERKLPRMEKMTEKTTRMLLTVLLLFLATELPQGILAFLSGVYGHSFFRQCYLHWGEVM
                ************************************************************

Myosuppressin   DLLALINGAVNFLLYYIMSHQFRVTFRFLLQTVSTQL
TR17352|c0_g1_i DLLALINGAVNFLLYYIMSHQFR--------------
                ***********************
```

Amines

Octopamine β

Receptor 2

TR42209|c0_g1_i1

```
Octopamine      MQGETAIMGESGELSTNGTWVGDMWVTANTSVDGTVDSVSGPEWKDLTVGIVKGVCMAVI
TR42209|c0_g1_i ------------------------------------------------------------


Octopamine      IVCAVLGNLLVVVSVVRHRRLRIITNYFVVSLAIADILVALMAMPFNASVELTGRWLFSY
TR42209|c0_g1_i ------------------------------------------------------------


Octopamine      RMCDLWNSFDVFASTVSILHLCSISIDRYYAIVRPLEYPRLMTKGRAVIMLCHVWLAPLV
TR42209|c0_g1_i -MCDLWNSFDVFASTVSILHLCSISIDRYYAIVRPLEYPRLMTKGRAVIMLCHVWLAPLV
                 ************************************************************

Octopamine      ISFLPIFMGWYTTEEHLAERAANPSRCIFEVNTTYAVVSSSISFWMPCSVMVYMYYRIYL
TR42209|c0_g1_i ISFLPIFMGWYTTEEHLAERAANPSRCIFEVNTTYAVVSSSISFWMPCSVMVYMYYRIYL
                ************************************************************

Octopamine      EAARQERIMHRNTRLSSASQAAVVVSNNSTNTTITTASAGTNGVGSDNAGSLGLGSGGSG
TR42209|c0_g1_i EAARQERIMHRNTRLSSASQAAVVVSNNSTNTTITTASAGTNGVGSDNAGSLGLGSGGSG
                ************************************************************

Octopamine      RRLMAHRPSSDTQEATPTKNNLIKLKRERKAARTLGIIMGAFIVCWLPFFTWYVTITLCG
TR42209|c0_g1_i RRLMAHRPSSDTQEATPTKNNLIKLKRERKAARTLGIIM----------------------
                ************************************

Octopamine      EACPCPEIIVSILFWIGYFNSMLNPAIYAYFNRDFREAFRRTLQCVFRCGRPVDPWRGQL
TR42209|c0_g1_i ------------------------------------------------------------


Octopamine      GPPYDSDLCLQHNGHSTIVKAKARRYSTECGV
TR42209|c0_g1_i --------------------------------
```

TR34866|c0_g1_i1

```
Octopamine      MQGETAIMGESGELSTNGTWVGDMWVTANTSVDGTVDSVSGPEWKDLTVGIVKGVCMAVI
TR34866|c0_g1_i ------------------------------------------------------------


Octopamine      IVCAVLGNLLVVVSVVRHRRLRIITNYFVVSLAIADILVALMAMPFNASVELTGRWLFSY
TR34866|c0_g1_i ------------------------------------------------------------


Octopamine      RMCDLWNSFDVFASTVSILHLCSISIDRYYAIVRPLEYPRLMTKGRAVIMLCHVWLAPLV
TR34866|c0_g1_i ------------------------------------------------------------


Octopamine      ISFLPIFMGWYTTEEHLAERAANPSRCIFEVNTTYAVVSSSISFWMPCSVMVYMYYRIYL
TR34866|c0_g1_i ------------------------------------------------------------


Octopamine      EAARQERIMHRNTRLSSASQAAVVVSNNSTNTTITTASAGTNGVGSDNAGSLGLGSGGSG
TR34866|c0_g1_i ------------------------------------------------------------


Octopamine      RRLMAHRPSSDTQEATPTKNNLIKLKRERKAARTLGIIMGAFIVCWLPFFTWYVTITLCG
TR34866|c0_g1_i -----------------------------------MGAFIVCWLPFFTWYVTITLCG
                                                   **********************

Octopamine      EACPCPEIIVSILFWIGYFNSMLNPAIYAYFNRDFREAFRRTLQCVFRCGRPVDPWRGQL
TR34866|c0_g1_i EACPCPEIIVSILFWIGYFNSMLNPAIYAYFNRDFREAFRRTLQCVFRCGRPVDPWRGQL
                ************************************************************

Octopamine      GPPYDSDLCLQHNGHSTIVKAKARRYSTECGV
TR34866|c0_g1_i GPPYDSDLCLQHNGHSTIVKAKARRYSTECGV
                *********************************
```

Serotonin

Receptor Type 7

TR54400|c0_g1_i1

```
Serotonin       MLASAGVASPTPSLHPLFNISHAAKLILQPSEAAHTPAEGAQGPMVGTDSALVTVDPVNY
TR54400|c0_g1_i ------------------------------------------------------------


Serotonin       TVLGDGGVETGGSALYMLFTTVLVVLVLLMIIVGTVVGNLLVCVAVCLVRKLRRPYNYLL
TR54400|c0_g1_i ------------------------------------------------------------


Serotonin       VSLAVSDLCVALLVMPMALLHELLGEWQFGQLACDVWVSFDVLSCTASILNLCMISVDRY
TR54400|c0_g1_i --------------MPMALLHELLGEWQFGQLACDVWVSFDVLSCTASILNLCMISVDRY
                             *********************************************

Serotonin       LAITRPLEYGVKRTPRRMVAYIAFVWLGAAFISVPPILILGNEHGDGSICEVCQNFWYQI
TR54400|c0_g1_i LAITRPLEYGVKRTPRRMVAYIAFVWLGAAFISVPPILILGNEHGDGSICEVCQNFWYQI
                ************************************************************

Serotonin       YATFGSFYIPLTVMVIVYYKIFCAAKRIVDEERKAQAHLRLVEEAEADARASTAVLGSYT
TR54400|c0_g1_i YATFGSFYIPLTVMVIVYYKIFCAAKRIVDEERKAQAHLRLVEEAEADARASTAVLGSYT
                ************************************************************

Serotonin       QLKPVSRYSVVEVNNGGVETRLAPEAPPLSSKDETGSLLGPDSPHHLEVPPRLVVCSSSV
TR54400|c0_g1_i QLKPVSRYSVVEVNNGGVETRLAPEAPPLSSKDETGSLLGPDSPHPLEVTPRLVVCSSSV
                ********************************************* ***.**********

Serotonin       SSAASADSTTGSRWSLCETNGKAHPPNANAGARTPTQPQHGHNCYNACQSTNGSGTNGSP
TR54400|c0_g1_i SSAASAH-------------------------------------------------------
                ******.

Serotonin       RKRSHPPKIKLKFALAKERKASTTLGIIMSAFVVCWLPFFVLALVRPFKKPSAIPAWISS
TR54400|c0_g1_i ------------------------------------------------------------


Serotonin       LFLWLGYANSLLNPIIYATLNKDFRKPFQEILCLRCASLNLLMREEFYHSQYGGPDTPTL
TR54400|c0_g1_i ------------------------------------------------------------


Serotonin       SAVRTHTHTNPRNSSEIHLAIADPREASISEEAHESKI
TR54400|c0_g1_i -------------------------------------
```

TR40843|c0_g1_i1

```
Serotonin       MLASAGVASPTPSLHPLFNISHAAKLILQPSEAAHTPAEGAQGPMVGTDSALVTVDPVNY
TR40843|c0_g1_i M-------------------------------------------------------------
                *

Serotonin       TVLGDGGVETGGSALYMLFTTVLVVLVLLMIIVGTVVGNLLVCVAVCLVRKLRRPYNYLL
TR40843|c0_g1_i ---------------------------------------------------------------


Serotonin       VSLAVSDLCVALLVMPMALLHELLGEWQFGQLACDVWVSFDVLSCTASILNLCMISVDRY
TR40843|c0_g1_i ---------------------------------------------------------------


Serotonin       LAITRPLEYGVKRTPRRMVAYIAFVWLGAAFISVPPILILGNEHGDGSICEVCQNFWYQI
TR40843|c0_g1_i ---------------------------------------------------------------


Serotonin       YATFGSFYIPLTVMVIVYYKIFCAAKRIVDEERKAQAHLRLVEEAEADARASTAVLGSYT
TR40843|c0_g1_i ---------------------------------------------------------------


Serotonin       QLKPVSRYSVVEVNNGGVETRLAPEAPPLSSKDETGSLLGPDSPHHLEVPPRLVVCSSSV
TR40843|c0_g1_i -------------------------------------------------VPPRLVVCSSSV
                                                             ************


Serotonin       SSAASADSTTGSRWSLCETNGKAHPPNANAGARTPTQPQHGHNCYNACQSTNGSGTNGSP
TR40843|c0_g1_i SSAASADSTTGSRWSLCETNGKAHPPNANAGARTPTQPQHGHNCYNACQSTNGSGTNGSP
                ************************************************************


Serotonin       RKRSHPPKIKLKFALAKERKASTTLGIIMSAFVVCWLPFFVLALVRPFKKPSAIPAWISS
TR40843|c0_g1_i RKRSHPPKIKLKFALAKERKASTTLGIIMSAFVVCWLPFFVLALVRPFKKPSAIPAWISS
                ************************************************************


Serotonin       LFLWLGYANSLLNPIIYATLNKDFRKPFQEILCLRCASLNLLMREEFYHSQYGGPDTPTL
TR40843|c0_g1_i LFLWLGYANSLLNPIIYATLNKDFRKPFQEILCLRCASLNLLMREEFYHSQYGGPDTPTL
                ************************************************************


Serotonin       SAVRTHTHTNPRNSSEIHLAIADPREASISEEAHESKI
TR40843|c0_g1_i SAVRTHTHTNPRNSSEIHLAIADPREASISEEAHESKI
                ************************************
```

TR14406|c0_g1_i2, TR14406|c0_g1_i1

```
Serotonin       MLASAGVASPTPSLHPLFNISHAAKLILQPSEAAHTPAEGAQGPMVGTDSALVTVDPVNY
TR14406|c0_g1_i MLASAGVASPTPSLHPLFNISHAAKLILQPSEAAHTPAEGAQGPMVGTDSALVTVDPVNY
                ************************************************************

Serotonin       TVLGDGGVETGGSALYMLFTTVLVVLVLLMIIVGTVVGNLLVCVAVCLVRKLRRPYNYLL
TR14406|c0_g1_i TVLGDGGVETGGSALYMLFTTVLVVLVLLMIIVGTVVGNLLVCVAVCLVRKLRRPYNYLL
                ************************************************************

Serotonin       VSLAVSDLCVALLVMPMALLHELLGEWQFGQLACDVWVSFDVLSCTASILNLCMISVDRY
TR14406|c0_g1_i VSLAVSDLCV----------------------------------------------------
                **********

Serotonin       LAITRPLEYGVKRTPRRMVAYIAFVWLGAAFISVPPILILGNEHGDGSICEVCQNFWYQI
TR14406|c0_g1_i ------------------------------------------------------------


Serotonin       YATFGSFYIPLTVMVIVYYKIFCAAKRIVDEERKAQAHLRLVEEAEADARASTAVLGSYT
TR14406|c0_g1_i ------------------------------------------------------------


Serotonin       QLKPVSRYSVVEVNNGGVETRLAPEAPPLSSKDETGSLLGPDSPHHLEVPPRLVVCSSSV
TR14406|c0_g1_i ------------------------------------------------------------


Serotonin       SSAASADSTTGSRWSLCETNGKAHPPNANAGARTPTQPQHGHNCYNACQSTNGSGTNGSP
TR14406|c0_g1_i ------------------------------------------------------------


Serotonin       RKRSHPPKIKLKFALAKERKASTTLGIIMSAFVVCWLPFFVLALVRPFKKPSAIPAWISS
TR14406|c0_g1_i ------------------------------------------------------------


Serotonin       LFLWLGYANSLLNPIIYATLNKDFRKPFQEILCLRCASLNLLMREEFYHSQYGGPDTPTL
TR14406|c0_g1_i ------------------------------------------------------------


Serotonin       SAVRTHTHTNPRNSSEIHLAIADPREASISEEAHESKI
TR14406|c0_g1_i -------------------------------------
```