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Molecular Mechanisms of Somatosensory System Development

The somatosensory system is the part of the body that is responsible for detecting mechanical, chemical and thermal stimuli from the environment. Abnormalities in the somatosensory system can lead to severe problems such as chronic pain disorders, migraines, and headaches. The cause of such problems can be the result of improper neuron firing, often caused by improper neuron development. The trigeminal nerve is the part of the somatosensory system that is responsible for detecting these stimuli in the face and the head. The trigeminal ganglion contains subtypes of sensory neurons, which have unique morphologies and functions. While the functions of several trigeminal neuron subtypes are known, the way in which they acquire these functions during development is not yet understood (Pan, Y.A. et al 2012). We are interested in understanding the developmental mechanisms underlying how these sensory neurons acquire their unique functions.

Previously, my advisor Dr. Ian Woods identified several genes that are enriched in sensory neurons in zebrafish. These genes code for proteins that are important in the development of neurons such as signaling, cytoskeletal, and adhesion proteins. Using a method called *in situ* hybridization, we visualized where each of our candidate genes are expressed within the zebrafish nervous system. Visualizing where each gene is expressed helps us to determine if their expression is solely in the trigeminal ganglion or more globally expressed throughout the brain. Genes that are expressed primarily in the trigeminal ganglion may be vitally important in the development of these specific sensory neurons. In addition, we can utilize known trigeminal neuron subtype markers with a technique called *double in situ* hybridization. For each candidate gene we can observe its expression compared to the expression of the subtype marker. If our candidate gene is found in a specific subtype we can hypothesize that the gene has a role in the development or function of that neuron subtype.

We have also identified possible morphological differences among neurons expressing different genes, which suggests their importance in sensory neuron development. To better understand if our candidate genes are necessary for the proper development of neurons, we are generating CRISPR gene knockout fish. In these fish, we removed our candidate gene and can thus determine if normal gene function is required for normal development and activity of these neurons. Using these knockout fish, we can do further analyses of behavior by testing the fish with various stimuli. The movement of the fish in response to the specific stimuli is tracked using a computer program. The responses of the knockout fish would be different when compared to wild type fish.

Currently we have observed expression of candidate genes primarily in the trigeminal ganglion. This suggests that these genes are important for the development of sensory neurons

specifically. We have injected CRISPR to generate knockout fish for five of our top candidate genes and have confirmed the success of one. At this time we are working on confirming the success of the other four injected CRISPR fish. Using the CRISPR fish, we hope to find differences in behavior when tested with various stimuli such as chemical or thermal. We also hope to find differences in neuron morphology in these knockout fish. Identifying these changes among fish without the candidate gene present will allow us to make further hypotheses about how these genes are affecting neuron development. All of our data together will allow us to define the functional role each of our candidate genes has in the development of sensory neurons.

Our goal for this project is to understand the mechanisms underlying sensory neuron development. By carefully documenting the expression of each gene, and determining the functional consequences of overexpressing and under expressing these genes, we will gain a more thorough understanding of the development of trigeminal neurons. In defining the mechanism of the development of sensory neurons we can better understand diseases that are caused by improper neuron development. Understanding mechanisms behind many of the diseases and disorders of the somatosensory system can allow researchers in the future to better design treatments to help patients with these conditions.

Citations:

Pan, Y.A., Choy, M., Prober, D.A., Schier, A.F. 2012. Robo2 determines subtype-specific axonal projections of trigeminal sensory neurons. Development. 139: 591-600.