2013 FoM SUMMER STUDENT RESEARCH PROGRAM
PROJECT SUMMARY REPORT FORM

FACULTY OF MEDICINE

Background

To maintain cognitive ability with age, the structural integrity of the axons of the neurons that allow for the relaying and processing of information must be preserved. Numerous neurodegenerative diseases, such as Alzheimer's and Parkinson's disease, are attributed to the loss of neuronal connections and integrity in the higher processing centers of the brain that allow us to perform everyday activities. Although the importance of this upkeep is well accepted, how and what is involved in the regulation of the morphological stability of axons in the nervous system of an average person's life span has yet to be defined.

What hypothesis or question(s) does your project aim to address?

Long-term stability of the structures and integrity of the nervous system is essential. Our nervous system is composed of a highly complex network of neurons and its extensions that allow us to react to stimulus. In our lab, it has been shown that the structural stability of an axon, an extension of a neuron that reacts to a stimulus, is an active process that relies on a constant suppression of axonal branching. We hypothesize that by manipulating the factors involved in suppression, we can generate new branches from stable axons in the intact nervous system that do not normally branch out or lengthen past a particular length.

Project Overview

In order to test the hypothesis, we first looked at the previous results of a graduate student who had helped generate the preliminary data that allowed us to come up with our current hypothesis. Expanding on the fruit fly genetic work that she had already performed that allowed us to see the promising physical manifestations in the nervous system of the fly when certain factors were allowed to be present at levels over the usual amount, I set out to build flies that not only had this factor hyperactively present but also that had the suppressive factors themselves suppressed in the fly's nervous system. In doing so, we hoped to see an additive, if not synergistic, effect on the amount of branching and lengthening on a particular set of neurons that normally lack branching in its axons and were not usually longer than a certain length.

In order to build these particular flies that possessed these attributes in their genetics, I first devised a series of genetic crosses that would tell me what types of fruit flies to mate with each other in order to end up with fruit fly larva that possessed the genes that would allow for the correct factors to either be suppressed or up-regulated. Once the actual crosses were done and I was able to identify the fly larva that possessed the correct genes, the larva were dissected, preserved and stained with reagents that would allow me to see the physical manifestations of my genetic manipulation of the fly nervous system under a fluorescent microscope. Once visualized on the fluorescent microscope, I was able to capture images of the unique physical manifestations that I saw when my particular factors of interest were suppressed or up-regulated and analyze them against my normal fly larva that were not genetically manipulated.

What are the results of your project and what (potential) impact(s) will they have?

Based on what I observed in my fluorescent images of the fly larva that were genetically altered to possess the factors of interest either increased in activity or suppressed, I was able to conclude that there is indeed an additive effect when the factor that is normally suppressed in activity in my particular neuron of interest, was increased in the nervous system and when the suppressive factor is suppressed in its activity. When only the suppressed factor is allowed to be present in the nervous system at higher than normal levels, my neurons of interest were found to increase drastically in length. When the activities of the suppressive factors were

suppressed, we observed the normally unbranched neurons branching out. When both cases were present together in one system, an additive effect was seen where both branching and lengthening of the axons of the neuron of interest was observed. Thus, we can tentatively conclude that our factors of interest are important in the structural maintenance and integrity of the nervous system. These results will allow us to determine whether our particular factors are good targets, whether it be for drug development or therapeutics, for patients that suffer from neurodegenerative diseases where the main symptom is a drastic loss of neurons and the structural integrity of their nervous system, like Alzheimer's and Parkinson's disease. The identification of key factors involved in the health of our nervous system will allow us to improve the livelihood of patients suffering from these types of diseases and perhaps one day, even find a cure.