Undergraduate Research Symposium May 19, 2017 Mary Gates Hall

Online Proceedings

Poster Session 2

MGH 241, Easel 144

1:00 PM to 2:30 PM

Pharmacological Intervention Treatment for Severe Muscular Dystrophy in Zebrafish

Emily Frances Jackson, Senior, Neurobiology
UW Honors Program
Mentor: Lisa Maves, Pediatrics

Muscular dystrophy affects millions of people across the globe; the disease leads to the progressive degeneration of skeletal and cardiac muscle tissues. The goal of this project is to identify a pharmacological treatment for muscular dystrophy in zebrafish. The disorder results from a mutation in the DMD gene, which encodes the instructions for producing the dystrophin protein. Dystrophin both protects and strengthens muscle fibers. Because of their genetic similarity to humans and the relative ease of introducing genetic mutations, we used zebrafish as a model. The lab utilizes a method that renders the dystrophin-encoding gene non-functional, eliminating the dystrophin protein in zebrafish larvae and producing a DMD zebrafish mutant strain. Without the protective effects of dystrophin, these zebrafish develop a severe form of muscular dystrophy. Previous results indicated that Trichostatin A (TSA), a selective inhibitor of some histone deactylase enzymes, is an effective treatment for salvaging deteriorating muscle fibers in mutant larvae. TSA disrupts the removal of acetyl groups and thus alters gene expression. We hypothesized that we could use the mutant DMD zebrafish to identify additional new pharmacological interventions. Upon testing new drugs, we looked for fish exhibiting less muscle deterioration than mutant DMD zebrafish with no drug treatment. After zebrafish larvae from fish carrying the DMD mutation were treated with novel drugs or control media, we performed genotyping on the larvae to identify the DMD homozygous mutants. Once animals were genotyped, we scored the animals for muscle defects using microscopy. We predicted that effective drug treatments for zebrafish DMD would show improved muscle in the larvae when compared to the untreated control DMD larvae. This research may provide a foundation for drug therapy and treatment possibilities in humans with muscular dystrophy.

Session 2L

Water, Waste, and Monkeys

Session Moderator: Stevan Harrell, Anthropology

MGH 284

3:30 PM to 5:15 PM

* Note: Titles in order of presentation.

When Monkeys Push your Buttons: Mapping Human-Macaque Conflict in Singapore

Dana Joy Needelman, Senior, Anthropology: Human Evolutionary Biology, Anthropology: Medical Anth & Global Hlth
UW Honors Program
Mentor: Lisa Jones-Engel, Anthropology
Mentor: Amy Klegarth, Anthropology, Center for Studies in Demography and Ecology

Global urbanization and deforestation are erasing spatial buffers between the two most widespread primates, humans and macaques. This dynamic interspecies interface can cause competition over space and resources and may precipitate general conflict, which may include property damage, physical harm, or disease transmission. In the highly urban island city-state of Singapore, multiple organizations are tasked with responding to nuisance reports and may cull, translocate, sterilize, or export macaques to manage these conflicts. This research employs a multi-disciplinary approach to assess which variables drive this interspecies conflict. From 2010-2015, 1,109 complaints were registered with National Parks, Singapore. These complaints spanned 41 subzones of Singapore where nearly 2,000 macaques in 64 troops were distributed. The complaint data were spatially plotted using ArcGIS in order to analyze where complaints occurred. These complaint data were then compared to macaque demographic data such as habituation score and group size, as well as land usage, in order to analyze factors that contribute to a high frequency of complaints in some areas. These findings have the potential to inform stakeholders, including community, government and non-governmental organizations, of more effective and sustainable management options.

SESSION 2O

USING MODERN GENETIC APPROACHES TO INVESTIGATE DEVELOPMENT AND DISEASE

Session Moderator: Celeste Berg, Genome Sciences
MGH 389
3:30 PM to 5:15 PM
* Note: Titles in order of presentation.

Engineering Zebrafish to Model Human Genes Related to Congenital Heart Defects
Kimia Imani, Senior, Biochemistry
Mary Gates Scholar, NASA Space Grant Scholar
Mentor: Lisa Maves, Pediatrics

Congenital Heart Disease (CHD) is the most common inborn defect in babies and is responsible for 1/3 of all major congenital anomalies. With its continuous prevalence in the human population, the genetic causes remain poorly understood. Previous findings have shown that *Pbx* transcription factors control gene expression during development. Studies in zebrafish shows that *pbx4* has significant requirements for heart muscle differentiation. Our hypothesis states that mutations in human *Pbx* genes can lead to heart defects. The purpose of this study is to acquire further insight about the role of *Pbx* genes in the context of CHD and analyze cardiac dysmorphic patterns in *pbx* gene mutants. By using the genomic editing system CRISPR/Cas9 (Clustered regulatory interspaced short palindromic repeats), we have been able to make exact genetic changes in *Pbx* genes in zebrafish (*Danio rerio*) animal models. In particular, we have engineered a *Pbx* gene mutation found in humans with heart defects, known as *Pbx4* SNP (single nucleotide polymorphism). For our experiments, samples of zebrafish DNA are obtained and genotyped with various assays for mutations. We use microscopy and transgenic markers to analyze heart defects in mutant embryos. *Pbx4* mutant zebrafish display distinct phenotypessuch as precardial edema and bulged ventricles, but it is not clear at what stages these morphogenesis defects occur. To further investigate the dysmorphic phenotypes, our next step is to conduct cardiomyocyte counting analysis in *Pbx4* SNP and *Pbx2/Pbx4* double mutant fish and gather data at 24 and 48 hours of development. This experiment will assist in better understanding the heart defects previously seen in the single *Pbx4* mutant samples. Understanding the mechanisms and discovering the genes of CHD, as well as cardiac morphogenesis patterns, will contribute to finding therapies and improving genetic screenings for patients with lifelong heart defects.

POSTER SESSION 3

Balcony, Easel 104
2:30 PM to 4:00 PM

A Multi-Technique Approach for Studying the Effect of Protein G B1 Orientation on Antibody Binding
Nhu T. Nguyen, Senior, Chemical Engineering
Mentor: David Castner, Bioengineering
Mentor: Elisa Harrison, Chemical engineering

Development of antibody-based diagnostics, biomolecular sensors, and biomaterial with reactive surface requires the ability to control the adsorption of bioactive protein at a surface. All medical devices exposed in an in vivo biological environment are immediately coated with a layer of adsorbed protein that plays an important role in the body's behaviors towards the devices and the effectiveness of the devices themselves. In this study, we use a multi-technique approach to characterize the effect of protein G B1 (6 kDa) orientation on multi-layer antibody binding. By conjugating a cysteine group at different positions along the protein's surface, we can immobilize five variants of the protein (V21C, D35C, E42C, T11C, and WT) onto maleimide and bare gold surfaces. We have confirmed through X-ray photoelectron spectroscopy and time-of-flight secondary ion mass spectrometry experiments that the proteins adsorb onto these surfaces. In addition, we introduced primary IgG and secondary F(ab')2 antibodies to investigate if the protein's orientation will affect the binding of the antibodies. The adsorbed mass are measured using quartz crystal microbalance with dissipation monitoring. We have demonstrated that the cysteine mutants orient better on maleimide surfaces and encourage more IgG binding. We will also study the effect of temperature on adsorption mass and extend the experiments to amine and carboxyl functionalized surfaces. Fully developed techniques to accurately characterize the orientation and quantify the amount of protein and secondary adsorption will significantly contribute to understanding the interactions of biomaterials with the biological environment.

POSTER SESSION 3

Balcony, Easel 91
2:30 PM to 4:00 PM

Chemical Control of Burrowing Shrimp on Shellfish Beds in Washington: Is Emamectin Benzoate a Viable Alternative to Imidacloprid?
Shannon Heather (Shannon) Obrien, Junior, Environmental Science & Resource Management
Mentor: Christian Grue, Aquatic & Fishery Sciences
Mentor: Lisa Crosson

Imidacloprid (IMI), a neonicotinoid, is being sought as an

alternative to the carbamate pesticide, carbaryl, to control burrowing shrimp (ghost shrimp, *Neotropea californiensis*) in Willapa Bay and Grays Harbor. The shrimp destabilize sediments resulting in poor survival and low yields of the commercially harvested Pacific oyster. Previous laboratory tests indicate ghost shrimp are overtly affected (immobilized) when exposed to IMI at concentrations up to 1 million ppb in artificial seawater (SW), but not killed and subsequently recover. Our objective was to determine if emamectin benzoate (EB) is a better alternative to IMI. EB, the active ingredient (a.i.) in Slice(R), is currently registered for use in marine waters for the control of sea lice on farmed salmon. We simulated a 6-hour tidal exposure of adult non-gravid female ghost shrimp to concentrations of EB (as the insecticide Proclaim(R)) ranging from 0.01 to 100 ppb a.i. within artificial seawater alone or sediment + seawater. No treatment-related mortality was observed within the 96-hour test, but overt effects were observed, particularly at 100 ppb in both seawater (abnormal body position) and sediment (lethargy, inability to burrow). Results suggest that the 6-hour exposure was not sufficient to cause mortality. In a subsequent 96-hour test, we will expose the shrimp to EB mixed directly into the sediment simulated tidal cycle. As the shrimp re-establish their burrows, we anticipate increased exposure to the chemical and mortality. EB is more effective as a pesticide when ingested and, in comparison to IMI, targets the primary neurophysiology of crustaceans including sea lice and burrowing shrimp.