Undergraduate Research Symposium May 17, 2013 Mary Gates Hall

Online Proceedings

POSTER SESSION 1

Commons East, Easel 74

11:00 AM to 12:30 PM

Small Heat Shock Proteins: Investigating Client Binding and Oligomer Diversity

Emily Duncan, Senior, Biochemistry
Ashwin Nitin (Ashwin) Karnik, Senior, Biochemistry, Anthropology: Medical Anth & Global Hlth, Neurobiology
Mentor: Rachel Klevit, Biochemistry
Mentor: Scott Patrick Delbecq

Proteins perform a vast array of functions within all living organisms. These functions are heavily dependent on the protein's 3-D structure. The loss of protein structure can lead to a wide variety of problems, one being the formation of insoluble protein aggregates, which can result from cellular stress. Aggregates can inhibit proper protein function, disrupt cellular homeostasis, and are implicated in many diseases. In order to combat aggregate formation, a family of proteins exists that interact with misfolded and aggregate prone proteins (clients). This family, known as the small heat shock proteins (sHSPs), delays the formation of insoluble aggregates in the cell. Their expression and activity as molecular chaperones have been seen to increase under stress conditions. However, how sHSPs delay aggregation is not well understood. We seek to better understand binding between sHSPs and their clients. Interactions between the sHSP αB crystallin and the model client Δ131Δ (a mutant of staphylococcal nuclease) have been characterized by Nuclear Magnetic Resonance (NMR). We hope to test the observations made from this simplified system in more functionally applicable assays. sHSPs not only interact with clients, but also amongst themselves. There are ten known human sHSPs, some of which have been shown to interact with each other. While this interaction is not well understood, we do know that sHSP monomers associate non-covalently to form dimers, which in turn form higher ordered oligomers. To begin understanding these interactions, we seek to investigate whether sHSPs can exchange their monomer subunits to form heterodimers. The ability to heterodimerize would suggest an even greater diversity of oligomer structure and function. We are interested in characterizing the properties of this proposed heterodimerization. Through site directed mutagenesis, experimental based assays, and gel electrophoresis, we seek to gain a detailed description of these proteins that play such a critical role in cellular health.

POSTER SESSION 1

Commons West, Easel 32

11:00 AM to 12:30 PM

Developing an Instrument to Characterize Active Learning in Large Classes

Mercedes Simone (Mercedes) Converse, Senior, Germanics
Mentor: Sarah Eddy, Biology
Mentor: Mary Pat Wenderoth, BIOLOGY
Mentor: Scott Freeman, Biology

Active learning generally increases student achievement, but not all instructors experience the same magnitude of gains. This variation in student achievement is likely due to differences in how active learning is implemented in the classroom as well as differences in total classroom time devoted to active learning. Although multiple tools exist for characterizing active learning in the classroom, none have been used to explain variation in student achievement. We are developing a new type of Classroom Observation Tool (COT) that characterizes how closely an instructor's use of active learning matches the best practices suggested in education literature and can be correlated with observed variation in student exam achievement. Currently, we are using the COT to analyze 3 randomly selected classroom sessions from 27 different introductory biology instructors using archived footage. We will create a linear model that combines instructor's COT scores with controls for variability in student ability and exam challenge between instructors to predict student exam performance. This model will allow us to identify which elements measured by the COT are most strongly correlated with variation in student performance. With this baseline data, we will be able to recommend the use of the COT to help Faculty assess the effectiveness of their instruction, thereby enhancing teaching and student learning not only within Biology education at UW, but also across all postsecondary education.

POSTER SESSION 1

Commons East, Easel 62

11:00 AM to 12:30 PM

Characterizing HIF-1 Downstream Targets That Affect Lifespan

Alison Claire (Alison) Leonard, Junior, Pre-Sciences
Hillary Ann (Hillary) Miller, Senior, Biology (Molecular, Cellular & Developmental)
Mentor: Matt Kaeberlein, Pathology
Mentor: Scott Leiser, Pathology

The hypoxia-inducible factor (HIF-1) is an oxygen-dependent transcription factor that plays a crucial role in an animal's response to changing oxygen availability. When oxygen is plentiful, HIF-1 is ubiquitinated and targeted for degradation by the von Hippel Lindau protein (VHL-1), which inactivates HIF-1. Recent studies have shown that HIF-1 stabilization through mutation of vhl-1 increases longevity in the model organism Caenorhabditis elegans. This is contrary to humans, where VHL-1 mutations cause a disease characterized by angiomas, renal carcinomas and various other tumors as a direct result of aberrant HIF-1 activation. Since nematodes are post-mitotic organisms in adulthood, constitutive activation of HIF-1 does not cause tumor formation and is able to increase lifespan. In order to better understand how HIF-1 increases longevity and to relate these findings to mammals, our project aims to find the specific genes and tissues downstream of HIF-1 that benefit worm longevity without the consequences of VHL disease. To identify these genes, we conducted an RNAi screen for genes that are necessary for HIF-1-mediated longevity. Using the results of this screen, we are creating transgenic worms that overexpress these genes under specific nematode promoters. To test for the tissue specificity of HIF-1-mediated longevity, we are stabilizing HIF-1 in different tissues using tissue specific promoters. Our initial data are promising; we have found two genes downstream of HIF-1 that when overexpressed increase nematode longevity. At least one of these genes, flavin-monooxygenase-2, is a well-conserved protein known to be involved in xenobiotic metabolism. Additionally, we have found that expressing stabilized HIF-1 in neurons is sufficient to increase nematode lifespan. Our continuing studies will identify additional target genes and tissues important for HIF-1 mediated longevity and will attempt to elucidate the mechanism by which they increase lifespan.

SESSION 1U

GENOTYPIC AND PHENOTYPIC CONSEQUENCES OF NUTRIENT AVAILABILITY

Session Moderator: Celia Payen, Genome Sciences
175 JHN
1:15 PM to 2:45 PM

* Note: Titles in order of presentation.

Age Related Vulval Integrity Defects: A Mechanism for Nematode Aging at Low Temperatures

Melissa Jane (Melissa) Primitivo, Senior, Biochemistry, Biology (General)
Mary Gates Scholar
Mentor: Matt Kaeberlein, Pathology
Mentor: Scott Leiser, Pathology

Organisms have evolved specific mechanisms to respond to molecular and environmental stress. These stress-response pathways are evolutionarily conserved and can modify lifespan in model organisms, making them popular targets of aging research. Using the nematode *Caenorhabditis elegans* (*C. elegans*), we have found the loss of important genes in stress-response pathways can cause a phenomenon called age-related vulval integrity defects (Avid). Worms with Avid show a small protrusion near their vulva that can eventually lead to expulsion of the intestine and premature death. While many labs have noted this phenotype, it is unknown if Avid is a natural part of C. elegans aging or if genetic and environmental factors induce this phenotype. Because of this, there is confusion as to whether worms with Avid should be censored in aging experiments. The goal of our project is to determine the mechanism of Avid and whether it is part of normal worm aging. Our initial work has identified several conditions and genetic pathways important for Avid, including temperature, food availability, the hypoxic response pathway, the oxidative stress response pathway, and the protein assembly pathway. We have also identified that the reproductive period of the C. elegans lifecycle is influential on Avid frequency, despite the phenotype occurring post-reproductively. We are currently testing the hypothesis that Avid is caused by secretions from the bacteria worms eat that influence nematode physiology and lead to Avid. We hypothesize that the pathways that influence Avid frequency do so by altering the digestion of bacteria in the intestine or by modifying the worm's immune response. To test our hypothesis we measured the quantity of bacteria ingested and digested by various worm strains at different temperatures and tested whether bacterial metabolites can cause Avid. We intend to combine our results and develop a more complete model of Avid.

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Hillary Ann (Hillary) Miller, Senior, Biology (Molecular, Cellular & Developmental)
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The hypoxia-inducible factor (HIF-1) is an oxygen-dependent transcription factor that plays a crucial role in an animal's response to changing oxygen availability. When oxygen is plentiful, HIF-1 is ubiquitinated and targeted for degradation by the von Hippel Lindau protein (VHL-1). Recent studies have shown that HIF-1 stabilization through mutation of vhl-1 increases longevity in the model organism Caenorhabditis elegans. This is contrary to humans, where VHL-1 mutations cause a disease characterized by angiomas, renal carcinomas and various other tumors as a direct result of aberrant HIF-1 activation. Since nematodes are post-mitotic organisms in adulthood, constitutive activation of HIF-1 does not cause tumor formation and is able to increase lifespan. In order to better understand the how HIF-1 increases longevity and to relate these findings to mammals, our project aims to find the specific genes and tissues downstream of HIF-1 necessary for its effect on worm longevity. Our goal is to find genes downstream of HIF-1 that benefit longevity without the consequences of VHL disease. To identify these genes, we conducted an RNAi screen for genes that are necessary for HIF-1-mediated longevity. Using the results of this screen, we are creating transgenic worms that overexpress these genes under specific nematode promoters. To test for the tissue specificity of HIF-1-mediated longevity, we are stabilizing HIF-1 in different tissues using tissue specific promoters. Our initial data are promising; we have found two genes downstream of HIF-1 that when overexpressed, increase nematode longevity. At least one of these genes, flavin-monooxygenase-2, is a well-conserved protein known to be involved in xenobiotic metabolism. Additionally, we have found that expressing stabilized HIF-1 in neurons is sufficient to increase nematode lifespan. Our continuing studies will identify additional target genes and tissues important for HIF-1 mediated longevity and will attempt to elucidate the mechanism for their action.

POSTER SESSION 2

Commons West, Easel 28

12:45 PM to 2:15 PM

Want to Be Ethical? Just Don't Think About It: The Effect of Thought Suppression on Ethical Decision-Making

Katharine Mary (Katie) Jung, Junior, Accounting
Colin Chang, Senior, Business Administration (Entrepreneurship)
Mentor: Kai Chi Yam, Management and Organization
Mentor: Scott Reynolds, Management and Organization

In today's world of globalization and expanding corporations, it is crucial that leaders act ethically to avoid the scandals, fraud, and financial collapses whose vibrations resonate internationally. Our research is guided by a desire to discover more successful strategies to teach ethics to business professionals and students. Unethical behavior spans an extensive range, all of which is financially costly for a company. Drawing from Ironic Thought Processing Theory, we hypothesize people will commit counterintentional errors when under a mental load, such as stress, fear, and distraction. In application to ethics, we hypothesize that participants directed not to think about ethics will consequently engage in less unethical behavior. Our hypothesis was tested with a sample of undergraduate business students, who were randomly assigned to one of three conditions. In the first two conditions, participants read passages about ethical principles, but one was instructed to reflect upon the ethics they read, whereas the other group was instructed not to consider ethical principles they read. Our third condition served as a control group, who read a similar length, yet irrelevant news article. Participants then attempted to complete 10 unsolvable math problems, requiring them to add impossible sets of numbers to 15, and report if they could successfully solve problems for extra cash payment. Results show that students who read about ethics, but are instructed not to think about it, engage in less unethical behavior when compared to the other conditions. Our study has broad implications. First, it is an application of the Ironic Thought Processing Theory in a new domain, widening its theoretical application. Second, our research will provide preliminary evidence to aid administrators to better structure business ethics curriculum.

POSTER SESSION 2

Commons East, Easel 49

12:45 PM to 2:15 PM

Quantification of Ribonucleotide Reductase in Human Embryonic Stem Cell-Derived Cardiomyocyte Cell Therapy

Sean Austin (Sean) Murphy, Junior, Bioengineering
Mary Gates Scholar
Mentor: Scott Lundy, Bioengineering
Mentor: Michael Laflamme, Pathology

Cardiovascular disease is the leading cause of death worldwide, and current treatments for heart failure are limited to slowing the disease progression or transplanting a donor heart. One potential approach to restore heart function is to transplant human embryonic stem cell-derived cardiomyocytes (hESC-CMs). An independent and similarly promising approach is to overexpress the enzyme ribonucleotide reductase (RR), the enzyme responsible for the production of the small molecule deoxy-ATP, which has been previously shown to improve contractility and diffuse between car-

diomyocytes via gap junctions. We hypothesize that by overexpressing RR in hESC-CMs and then transplanting the latter into infarcted hearts, we will improve global cardiac function by increasing dATP content throughout the myocardium. To begin testing this hypothesis, I will test the efficacy of an RR adenovirus in hESC-CMs *in vitro* using quantitative PCR and immunostaining, and I will then correlate the subsequent improvement in fractional shortening following *in vivo* transplantation to the amount of successfully engrafted cells. To date, I have successfully developed an immunofluorescence staining protocol for RR. I am currently working on designing an immunohistochemistry protocol to identify graft tissue and stain for RR and GFP and localize RR in relation to the infarct. After confirming the protocol, I plan to apply it to the fixed rat heart slices to assist in the proof of concept of the transplantation of hESC-CMs overexpressing RR as a novel therapeutic method.

POSTER SESSION 3

MGH 241, Easel 150

2:30 PM to 4:00 PM

Spatial and Feature-Based Attention Modulate the Pupillary Light Reflex

Omar Abdelbadie, Senior, Neurobiology
Mentor: Scott Murray, Psychology
Mentor: Paola Binda, Psychology

The pupil is an important component of the visual system, changing in size to regulate the amount of light entering the eye and affecting vision quality. Light is the primary determinant of pupil size (the pupil constricts with light increments, a response known as the Pupillary light reflex or PLR), but there are also well known effects of internal states such as cognitive effort and arousal. Recently, our lab discovered an interaction between light and cognitive factors at the level of the pupil: selectively paying attention to brighter areas in the visual field, without looking at them, enhances the PLR. This finding prompts a revision to the neural substrates of the PLR, suggesting that cortical attentional influences modulate the subcortical PLR circuit. To better characterize this Attention-PLR interaction, we tested whether the effect is limited to spatially-directed attention to bright regions, or if it generalizes to cases where attention is directed to bright features from a single localized stimulus. Preliminary data using a psychophysics setup of overlapping dark and bright surfaces shows an effect of feature based attention. Specifically, two overlapping surfaces defined by white and black moving dots were presented at fixation and subjects were cued to attend to either surface. Attending to the bright surface induced a relative pupillary constriction compared to attending to the dark surface. Moreover, ongoing work attempts to quantify the magnitude of the attention effect at different levels of brightness and contrast of the stimuli, and for different spatial extents of the attended regions. In this way we investigate the characteristics, dynamics, and anatomical substrates of the Attentional-PLR effect, while establishing the pupil as a convenient marker of the direction of attention.

POSTER SESSION 3

Commons East, Easel 63

2:30 PM to 4:00 PM

Design of a Multi-Actuator Piezoelectric Stepper System

Cheryl Tan, Sophomore, Pre Engineering
Mentor: Santosh Devasia, Mechanical Engineering
Mentor: Scott Wilcox, Mechanical Engineering

A stepper system is a device that uses multiple small-scale steps to achieve large ranges of motion. There are several fields where stepper systems can be used as positioners such as micro/nano-fabrication, scanning probe microscopy, and alignment of optical components. This stepper design enables a motion stage, whose motion is generated by friction induced with piezoelectric actuators underneath, to move horizontally without vertical displacement. The objective of this research is to investigate a way to support the load of a motion stage while limiting any restriction of motion in the horizontal direction. This restriction of vertical load bearing and horizontal freedom has led to investigating bearings as a component of the support structure. There are many types of bearing designs (i.e. ball, magnetic, and air) that may satisfy the design constraints, so I have performed analysis on various types of bearings and investigated their impact on the design of a new stepper system. For instance, ball bearings support radial loads or thrust loads with forces normal to the ring pathways, but continuous compression, along with expansion, leads to fatigue of the rings, which shortens their lifetime; while magnetic bearings provide support with a distance force that is controlled by the current flow in the circuit, maintaining a more stable and friction-free motion. However, applications may be sensitive to magnetic interference and therefore magnetic bearings may not be suitable for use in some cases. Taking into consideration the benefits and limitations of the different bearing systems, my research has proposed and introduced the design of a stepper support system.

POSTER SESSION 4

Commons East, Easel 71

4:15 PM to 5:45 PM

Mechanical Linkage-Based Leg Mechanism

Kurt Joseph (Kurt) Stalsberg, Senior, Mechanical Engineering: Mechatronics
Mentor: Scott Wilcox, Mechanical Engineering
Mentor: Santosh Devasia, Mechanical Engineering

Multi-Legged terrestrial biological systems demonstrate

complex forms of locomotion by utilizing different gait patterns and leg motions for different environmental conditions. Typically, the footpath of biological systems consists of a smooth flat region when the foot is in contact with the ground where the forward motion of the body occurs. The following research focuses on designing a mechanical linkage-based leg mechanism to effectively mimic the step of a biological system. A simulation of the linkage was performed using MATLAB in order to analyze the dynamics of the foot path and duration of stepping phase that the foot was in contact with the ground. After analyzing the foot motion, the linkage-based leg designs were then constructed using the LEGO Mindstorms NXT robotics kit and tested with various walking patterns. Further analysis of the linkage-based leg motion was done by comparing the resulting motion to biological leg motion; successful linkage-based leg designs should display similar stepping characteristics to the biological motion.