UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 17, 2019 Mary Gates Hall

Online Proceedings

Poster Session 1

Commons West, Easel 43

11:00 AM to 1:00 PM

Reliability of Goniometer Measurements to Determine Ankle Dorsiflexion: Implications for Assessment of Gastrocnemius Equinus

Cristina Gildee, Senior, Anthropology: Medical Anth & Global Hlth, Anthropology: Human Evolutionary Biology, Anthropology: Archaeological Sciences
Mentor: Patricia Kramer, Anthropology
Mentor: Elen Feuerriegel, Anthropology

Ankle range of motion (ROM) is frequently measured in clinical settings for the purpose of diagnosing and treating foot and ankle pathologies. Gastrocnemius equinus (GE), a condition in which isolated gastrocnemius contracture inhibits ankle ROM, contributing to foot pain in otherwise neurologically healthy individuals. Controversy surrounds the definition of GE, however, and the reliability of goniometer-based measurements of dorsiflexion—and consequently identification of gastrocnemius contracture—is untested. This study examines the reliability of using a goniometer to measure ankle dorsiflexion. Two observers (KR and CG) measured ankle dorsiflexion in 14 neurologically healthy individuals (6M/8F; ages 20-56 years; 6 participants measured by both observers) with the knee in fully-extended and flexed positions. Three measurements were taken for each position with the goniometer fulcrum on the lateral malleolus; stationary and moving arms aligned with the fibular head and fifth metatarsal, respectively. Inter- and intra-observer reliability was assessed using Cronbach's alpha. Intra-observer Cronbach's alpha was 0.230 (CG) and 0.533 (KR) for dorsiflexion with the knee extended, and 0.805 (CG) and -0.350 (KR) for dorsiflexion with the knee flexed. Inter-observer Cronbach's alpha was 0.656 for extension and -0.245 for flexion. Little correlation exists within or between observers for goniometer-based ankle dorsiflexion measurements in either a flexed-knee or extended-knee position. The clinically-accepted practice of using a goniometer to determine ankle ROM, and consequently to diagnose and treat GE, may be unreliable and needs further evaluation.

Session 1P

McNair Session - Biological Manipulations to Develop Medical and Environmental Interventions

Session Moderator: Barbara Juarez, Pharmacology

MGH 295

12:30 PM to 2:15 PM

* Note: Titles in order of presentation.

Structure Elucidation of Marine Bacterial Compounds that Induce Biofilm Production in Mycobacteria

Thuy Tran, Junior, Biochemistry, Calif St University San Marcos
McNair Scholar
Mentor: Jackie Trischman, Department of Chemistry and Biochemistry, California State University San Marcos

Tuberculosis (TB) kills more than one million people annually. Bacteria of the Mycobacterium genus, including M. tuberculosis, build a complex cell wall containing mycolic acids. This cell wall is difficult to penetrate, so specialized antibiotics are needed. Even with newly developed drugs, bacteria adapt quickly and exhibit resistance at an alarmingly rapid pace. One adaptation that allows the community to survive is production of biofilms. Formation of biofilm is one of many quorum sensing behaviors known in pathogenic mycobacteria. This additional layer surrounds a microenvironment where bacteria can thrive with a very low concentration of antibiotic. Thus, one alternative method to treat TB is to control biofilm formation. In this research, a set of marine bacterial strains, including several bacteria that exhibited swarming behaviors and several from the same environmental samples that did not, were cultured, extracted, and analyzed by 1H NMR and LC-MS as well as in newly-developed biofilm and growth inhibition assays. Initial results showed one group of bacteria produced an organic compound that induced biofilm production in mycobacteria. This was an unexpected result. One representative strain producing a strong biofilm inducer was grown on large scale (10L) then extracted using progressively less polar eluents on a reversed-phase SPE column. The biofilm-inducing fraction was then separated using flask column chromatography. One major compo-

nent was analyzed spectroscopically using 1D and 2D NMR techniques along with Mass Spectrometry. This compound could result in a strategy to interfere with biofilm formation in mycobacteria, thus making antibiotics more effective.

POSTER SESSION 2

MGH 206, Easel 171

1:00 PM to 2:30 PM

The Role of Kinesins in Asymmetric Cell Division

Varun Sridhar, Junior, Pre-Health Sciences
Mentor: Clemens Cabernard, Biology
Mentor: Tri Pham, Biology

Asymmetric cell division (ACD), a process that generates daughter cells with different cell fates and sizes, is a fundamental mechanism for generating cellular diversity during development. We use *Drosophila* melanogaster neural stem cells, or neuroblasts, to study ACD. Neuroblasts provide an ideal model for ACD since they are intrinsically polarized and divide with physical as well as molecular asymmetry, resulting in a self-renewed stem cell and a smaller ganglion mother cell (GMC). Kinesins, plus-end-directed motor proteins, have previously been implicated in asymmetric cell division and spindle dynamics. However, the specific kinesins that influence ACD and the mechanism by which they do so remains unknown. Elucidating the function of kinesins in cell division will help establish a more holistic view of cell development. To learn the role that kinesins play in asymmetric cell division, we performed an RNAi knockdown-based live-cell imaging screen of most kinesins in *Drosophila*. We found that knocking down the *Drosophila* kinesin genes Klp3A, Klp10A, Klp59C, Klp67A, Klp68D, CG14535, cos, or ncd causes the mitotic spindle to bend during metaphase and anaphase. We hypothesize that this phenotype is due to the spindle being so large that it buckles under the pressure of the cell as it divides. We are currently investigating this hypothesis by imaging knockout mutants to confirm this phenotype and tagging each kinesin with GFP to study how these proteins are localized during typical ACD.

POSTER SESSION 2

Balcony, Easel 108

1:00 PM to 2:30 PM

Characterizing Stem Cell Specific-Kinases as Regulators of Self-Renewal in Rhabdomyosarcoma

Shelly Lin, Senior, Biology (General)
Mentor: Eleanor Chen, Pathology
Mentor: Thao Pham, Pathology

Rhabdomyosarcoma (RMS) is the most common pediatric soft tissue sarcoma. The survival outcomes are poor for patients with relapsed and metastatic disease. Embryonal RMS (ERMS), a major subtype of RMS, is driven by genetic mutations in the RAS pathway. Cancer stem cells (CSCs) drive the process of self-renewal to recapitulate the heterogeneity of the cancer and are thought to be responsible for cancer relapse due to their resistance to conventional chemotherapy. In ERMS cells, a population of CSCs has been identified and is believed to play a critical role in tumor relapse and metastasis. A previous screen of all known human kinases identified candidates that played a role in regulating self-renewal of ERMS CSCs. I have prioritized two most promising candidates, ERN1 and MAPK10, for further characterization. I hypothesize that these kinases regulate the self-renewal capacity of CSCs but do not affect growth of non-CSC tumor cells. Using the gene-editing tool, CRISPR (Clustered Regulatory Interspaced Short Palindromic Repeats)/Cas9, I knocked out ERN1 and MAPK10 in ERMS cells and assessed their role in regulating ERMS CSC cell growth and self-renewal. To assess whether the effects of gene disruption are specific to the changes in the CSC population in vitro and in vivo, I used an ERMS CSC reporter cell line that specifically expresses Green Fluorescent Protein (GFP) in CSCs. The ERMS CSC reporter cell lines harboring ERN1 or MAPK10 gene disruption are subjected to self-renewal assays in cultured ERMS cells in vitro and ERMS xenograft model in vivo. My findings will provide new insights into the biological mechanism underlying as well as new potential targets against relapse and metastasis of ERMS.

POSTER SESSION 2

MGH 206, Easel 170

1:00 PM to 2:30 PM

Impact of Na+/H+ Antiporter on Asymmetric Cell Division in *Drosophila* Neural Stem Cells

Mackenzie Elizabeth Coston, Senior, Biology (Molecular, Cellular & Developmental)
Mentor: Clemens Cabernard, Biology
Mentor: Tri Pham, Biology

Asymmetric cell division (ACD) is an integral process that multicellular organisms use to create cellular diversity. For instance, stem cells use ACD to form differentiating sibling cells while recreating the stem cell in order to maintain the stem cell pool. Defects in ACD can result in a variety of diseases ranging from neurodevelopmental disorders to cancer. Using *Drosophila melanogaster* neural stem cells (neuroblasts) as a model to study cellular asymmetries, we recently found that hydrostatic pressure is an important factor contributing to ACD. However, the mechanisms and proteins that regulate hydrostatic pressure are unknown. Based on our previous results, I hypothesized that Na+/H+ antiporters are involved in establishing hydrostatic pressure. To examine this hypothesis, I tested the function of four Na+/H+ channels in

Drosophila using RNAi knock-down experiments and subsequent live cell imaging. This imaging allowed visualization of fluorescently tagged myosin and microtubules–two critical components of the cell division process. I found that knocking down each of the four antiporters results in a bent mitotic spindle, delayed division times, and centrosome abnormalities. I conclude that the four antiporters play a role during ACD in fly neural stem cells. To validate these results, I will use CRISPR/Cas9 gene editing to develop deletion mutants and EGFP-tagged versions of the four antiporters—two crucial steps in studying the regulation of Na+/H+ channels. Further in the future, I will use CRISPR/Cas9 to create optogenetically controllable Na+/H+ antiporters, such that I can use light to control hydrostatic pressure in *Drosophila* neuroblasts. I also plan on measuring the intracellular pH using genetically edited *Drosophila*, as disruptions in pH could cause the described phenotypes. These studies will provide mechanistic and functional insight into how hydrostatic pressure contributes to successful ACD.

POSTER SESSION 2

MGH 241, Easel 139

1:00 PM to 2:30 PM

Understanding Methylmercury Accumulation in Rice: Experimental Control of Oxygenation and Root Carbon Levels in the Rhizosphere of *Oryza sativa*

Sarah Katherine Larson, Senior, Biology (Plant)
Mary Gates Scholar, NASA Space Grant Scholar
Mentor: Rachel Strickman, Civil and Environmental Engineering
Mentor: Rebecca Neumann, Civil and Environmental Engineering

Methylmercury (MeHg) is a bioaccumulative neurotoxin, dangerous to human health even at trace levels. In inundated soils, MeHg is formed from inorganic mercury by mercury-methylating microorganisms; a process termed methylation. Demethylation, by contrast, converts MeHg into less-dangerous inorganic mercury, and also occurs via microbial activity throughout the aquatic soil profile. Rice grains can be contaminated with MeHg when grown in soils where methylation rates are high; human exposure to MeHg is thus a serious public health concern in places where rice cultivation, high rates of consumption, and soil mercury (Hg) contamination overlap. Our research aims to better understand the soil conditions that favor demethylation over methylation – this information can then be used to reduce rice grain contamination through agricultural practices or rice breeding programs. Specifically, our research focuses on the role of oxygenation and carbon root exudates on the net MeHg accumulation throughout the soil profile. Rice plants grow in flooded, oxygen-free (anoxic) soils, but their roots can leak oxygen (making the rice rhizosphere oxygenated in varying degrees), as well as carbon root exudates. Our project simulated both fully oxic and transiently-oxic (transition) zones, with two different levels of root exudates; we use isotopic tracers to assess respective methylation and demethylation rates in all four treatments in both the vegetated (rhizosphere) and non-vegetated (bulk) soil. Carbon root exudates have been collected from hydroponically-grown rice variety *M-206,* and can be applied to different soil zones via tubules. Oxygenation of the soil can be measured with mm-scale optode imagery, which allows delicate testing of various oxygen-introduction designs. My role in this interdisciplinary project has been to develop, scale-up, automate, and verify the accuracy and dependability of root-oxygenation and root-exudate introduction systems to be used in upcoming experiments.

POSTER SESSION 2

Balcony, Easel 104

1:00 PM to 2:30 PM

Detection of 8-Oxoguanine Lesions in Plastid DNA of Maize Plants

Ardizon Cajuguiran Valdez, Senior, Biology (Molecular, Cellular & Developmental)
Mentor: Diwaker Tripathi, Biology

The level of plastid DNA (ptDNA) declines as plastids develop from colorless proplastids to green chloroplasts. The decline in ptDNA is associated with an increase in DNA damage resulting from oxidative stress and ultraviolet (UV) radiation. 8-oxoguanine (8-oxoG) is a lesion in ptDNA that results from the oxidation of guanine. Our lab previously found a reduced amount of ptDNA in light-grown plants compared to dark-grown plants, likely due to increased oxidative stress that increases ptDNA damage. Here, our objective is to quantify ptDNA damage by assessing 8-oxoG lesions during the greening of maize leaves. We hypothesize that as plastids mature, 8-oxoG lesions increase. Our experimental outline involves the quantification of 8-oxoG by the enzyme-linked immunosorbent assay (ELISA), as well as immunofluorescence microscopy using antibodies that target 8-oxoG. We are examining plastids isolated from light-grown and dark-grown stalk and leaf tissues. As 8-oxoG lesions are one of the markers of oxidative DNA damage, our results will be used to assess DNA damage during development of maize plants. This research will provide a better understanding of role of oxidative stress in plant development

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SESSION 2H

MEDICAL IMAGING AND DEVICES

Session Moderator: Eric Seibel, Mechanical Engineering

MGH 251

3:30 PM to 5:15 PM

* Note: Titles in order of presentation.

Optimizing Diffusion Weighted MRI for Non-Contrast Enhanced Breast Cancer Detection
Michaela Del Priore, Senior, Bioengineering
Mentor: Savannah Partridge, Radiology
Mentor: Debosmita Biswas, Radiology

Dynamic-contrast enhanced (DCE) MRI has a very high sensitivity for breast cancer detection. However, the high costs, long scan-times and safety issues associated with injecting gadolinium-based contrast agents prompt the need to explore non-invasive, non-contrast-based diffusion-weighted imaging (DWI) as a possible alternative. DWI reflects the microscopic cellular environment and at high sensitizations (b-values), DWI can highlight malignant breast tissues without the aid of gadolinium. Acquiring images at high b-values increases image distortions and lengthens scan times. By simulating these high b-value images, lesion conspicuity can be increased while minimizing scan time and maintaining image quality. The purpose of this study was to compare lesion conspicuity across b-values and between acquired (aDWI) and computed (cDWI) DWI. Twenty women with invasive breast cancer were enrolled to undergo a research DWI scan. aDWI was acquired at multiple b-values of b=0/100/800/1500/2500 s/mm^2. Apparent diffusion coefficient (ADC) maps were generated and cDWI images were then computed for b-values ranging from b=200-2500s/mm^2 using: S_b = $S_1$00 e$^-$$\Delta$b*ADC.$Lesioncontrast-to-noiseratio(CNR)wascalculatedforbothaDWIandcDWIatexplo-value.CNRmeasuresacrossb-valuesfromcDWIandaDWIwerecomparedbyWilcoxonsigned-ranktest.Lesionconspicuity,asmeasuredbyCNR,increasedwithincreasingb-value,withnosignificantdifferencebetweenaDWIandcDWI.Ourfindingsshowthemaxiumlesionconspicuityon DWI is achieve 1100 - 1500s/mm^2$, which is higher than typical diagnostic breast DWI protocols. However, lesion conspicuity likely varies with breast density and other patient and tumor characteristics. Potential advantages of cDWI include shorter scan times and flexibility to retrospectively generate images at any b-value for optimal interpretation, warranting further exploration of the value of this technique for breast imaging.

SESSION 2J

MEASURING CELL GROWTH AND EVOLUTION

Session Moderator: Kristin Anderson, Immunology
MGH 271
3:30 PM to 5:15 PM

* Note: Titles in order of presentation.

Reversing Rate-Adaptation with Water-In-Oil Emulsions
Jordana K. Sevigny, Sophomore, Pre-Health Sciences
Mary Gates Scholar
Mentor: Benjamin Kerr, Biology
Mentor: Katrina van Raay, Biology

Twelve replicate populations of the bacterium *Escherichia coli* have been evolving in Lenski's Long-Term Evolution Experiment (LTEE) for over 67,000 generations in a shared nutrient limited environment. The evolved bacteria grow 70% faster than their ancestor but experience a decrease in number produced during a growth cycle. This is consistent with a trade-off between growth rate and yield (here defined numerically). We explore if populations are constrained by their previous ecolution, and if populations with high growth rate can evolve to have a higher yield (and if so, does this happen at a cost to growth rate?). We do this by adding population structure to growing populations, where selection is relaxed on growth rate and strengthened on yield. Water-in-oil emulsions provide a structured environment where millions of nutrient-filled droplets are isolated by an oil phase. We manipulate population structure by inoculating droplets with either one bacterial cell (low starting density) or more than two bacterial cells (high starting density). We observe that selection acts on faster growing cells in our high density emulsion treatment and higher yield cells in our low density emulsion treatment. We also observe a change in cell size: cells in the high density emulsion treatment get bigger over time, and cells in the low density emulsion treatment get smaller. We explore if there is a relationship between cell size and growth rate/yield trade-off.

SESSION 2K

OUR COMPLEX UNIVERSE: PLANETS, STARS, BLACK HOLES, AND GALAXIES

Session Moderator: Jessica Werk, Astronomy
MGH 284
3:30 PM to 5:15 PM

* Note: Titles in order of presentation.

Observational Astronomy in Tacoma: Analyzing Jupiter's Rotation and the Brightness Profile of Saturn's Rings
Megan Longstaff, Senior, Applied Physics, Pacific Lutheran University
Justin deMattos, Senior, Physics, Pacific Lutheran University
NASA Space Grant Scholar
Mentor: Katrina Hay, Physics, Pacific Lutheran University
Mentor: Sean O'Neill, Physics, Pacific Lutheran University

Jupiter and Saturn are our solar system's largest gas giants

with some of the most popular features of any known planet: Jupiter's Great Red Spot (GRS) and Saturn's rings. Over the summer of 2018, we analyzed these characteristics at Pacific Lutheran University's W. M. Keck Observatory. Closer to the Earth, Jupiter's atmosphere is subject to differential rotation in which the atmosphere of the planet rotate at different speeds. We use feature tracking and 2D to 3D mapping techniques to observationally determine the angular rotation of the GRS and compare it to the expected rotation of 11.5 km/s determined by the magnetosphere. Through our analysis we observe the movement of the GRS over multiple nights and determine the average speed to be around 10.97 km/s, a 4.60% difference from the expected value. Further beyond, Saturn's rings are composed of particles of ice and dust that are thought to be remnants of comets, asteroids, or moons that collided in orbit around the planet. Since these rings are not single structures, their particles feature non-uniform spacing. The light intensity of the rings increase as you approach the B ring from either direction (with the exceptions of the Cassini Division, Encke, and Keeler gaps). Our research focused on determining the spatial variation of these intensities as observed from our land-based observatory and comparing this data to Hubble Space Telescope data quantifying atmospheric scattering in Tacoma.

POSTER SESSION 4

MGH 206, Easel 165

4:00 PM to 6:00 PM

Quantification of Oxidative Damage Caused by Reactive Oxygen Species during Development of Maize Plants

Jerry Chen Bryan, Senior, Biology (General)
Mentor: Diwaker Tripathi, Biology

Reactive oxygen species (ROS) are partially reduced oxygen molecules produced during cellular metabolism in all aerobic organisms including plants. ROS derivatives such as superoxide (O2–) and hydrogen peroxide (H2O2) cause several types of cell damage in plants. Chloroplasts and mitochondria are major sources of ROS because of photosynthesis and aerobic respiration in these organelles, respectively. Previously, our lab showed that light-grown maize plants have more damage in plastid DNA (ptDNA) and mitochondrial DNA (mtDNA) than dark-grown plants and that ptDNA and mtDNA levels decline during leaf development. Here, we hypothesize that increased damage to ptDNA and mtDNA in light-grown leaves is linked to increased ROS generation compared to dark-grown and germline stalk tissues. We used absorbance- and/or fluorescence-based assays to quantify levels of ROS in chloroplasts and mitochondria isolated from leaf and stalk tissues during seedling development. Our data suggest that light-grown leaf has more ROS than light-grown stalk, dark-grown leaf, and dark-grown stalk. Our findings indicate that highly damaged DNA is a consequence of ROS generation in light-grown leaves of maize. Overall, this research will help us further understand the oxidative damage caused by various reactive oxygen species during the development of maize plants.