Online Proceedings

POSTER SESSION 2

Balcony, Easel 110

1:00 PM to 2:30 PM

Genetically Manipulating U2OS Bone Cells to Target Inhibitor Drugs to the Kinetochore during Mitosis

Irvin Garcia, Senior, Biology (Molecular, Cellular & Developmental)

Louis Stokes Alliance for Minority Participation

Mentor: John Scott, Pharmacology

Mentor: Paula Bucko, Pharmacology

Mitosis is an essential cellular process in which a cell divides to produce two genetically identical daughter cells. When this process becomes dysregulated cells divide uncontrollably leading to diseases such as cancer. Polo-like kinase 1 (Plk1) is a key enzyme that is necessary for coordinating numerous events during mitosis. When Plk1 becomes dysregulated or mislocalized, mitotic spindle assembly, protein organization, and mitotic timing impairments may occur. One of the many subcellular locations where Plk1 carries out essential mitotic functions is the kinetochore. The kinetochore is the interface between the chromosomes and the mitotic spindle and is critical for ensuring proper DNA to microtubule attachments early on in mitosis. Historically, the small-molecule inhibitor drug BI2536 has been used to inhibit the activity of Plk1 in order to study its role in regulating various mitotic processes. However, traditional inhibitor drugs turn off entire protein kinase populations, inhibiting the activity of Plk1 all throughout the cell, not just at the kinetochore. This can lead to unwanted side effects and limits our understanding of Plk1's role at specific subcellular locations. To improve the specificity of BI2536 drug delivery, we utilized SNAP-tag, a tool in which a self-labeling enzyme can irreversibly react with substrates linked to a chloropyrimidine (CLP) functional group. By genetically manipulating human bone cancer (U2OS) cells, we expressed a kinetochore localizing SNAP. We also generated a BI2536 conjugated to a CLP group. By treating our genetically modified cells with CLP-BI2536, we can target Plk1 inhibiting drug to the kinetochore to study Plk1's role at this specific location. Using super-resolution structured illumination microscopy (SIM), we demonstrate that we can effectively target fluorescently labeled CLP substrates to kinetochores in our cell line. In future work, we will target our CLP-BI2536 drugs to the kinetochore and investigate how local Plk1 inhibition affects mitotic timing.

POSTER SESSION 2

MGH 241, Easel 145

1:00 PM to 2:30 PM

Developing and Validating a Method to Blind Immunoassays Results from End Users

Charlie Denton Glaser, Junior, Bioengineering

Mentor: Kamal G. Shah

Mentor: Paul Yager, Bioengineering

Many illnesses such as influenza and the common cold present similar symptoms, which renders them difficult to diagnose without a formal molecular diagnostic test. Designing a diagnostic test that could be run in patients' homes would address limitations of existing assays, but with the risk of patients attempting to self-treat without consulting healthcare professionals. As a result, this project has developed a lateral flow assay (LFA), the same type of assay as an at-home pregnancy test, that is adapted to detect an infectious disease while blinding the end user from the result. Traditional LFAs indicate the presence or absence of a biomarker by capturing the biomarker with antibodies and labeling the capture event with colored nanoparticles; two lines indicate the presence of the biomarker and one line indicates its absence. We've proposed two methods of blinding the end user from the results. One is a system where two lines always appear in an LFA even in the absence of the biomarker, preventing the end user from interpreting the result. The color intensity of the two lines will be proportional to the amount of biomarker present; this relies on humans' inability to reliably detect absolute color intensities to blind the assay results. Preliminary testing of an influenza LFA suggests that the proposed scheme successfully blinds immunoassays to the end user, but the limit of detection (LOD) is 20 times worse than traditional LFAs. The second method uses a randomized array of antibodies spotted on an LFA as a way to obfuscate the result but through imaging can later be interpreted. We've optimized the proposed schemes to improve the LOD, demonstrate that the assay can be quantified with a cell-phone, and enable quantitative detection of infectious disease biomarkers in the home with a blinded immunoassay.

POSTER SESSION 2

Balcony, Easel 115

1:00 PM to 2:30 PM

Efficacy of Immunotherapy in Merkel Cell Carcinoma Patients with Concurrent Chronic Lymphocytic Leukemia

Lauren Zawacki, Senior, Public Health-Global Health
UW Honors Program
Mentor: Paul Nghiem, Dermatology
Mentor: Kristina Lachance, Medicine, Dermatology

Merkel cell carcinoma (MCC) is a rare and aggressive cutaneous malignancy with a high propensity for recurrence and distant metastasis. Individuals with chronic immunosuppression have both a higher predilection towards developing MCC and tend to have a more aggressive disease course. Chronic lymphocytic leukemia (CLL) is among the most common types of immunosuppression associated with MCC. Immune-checkpoint inhibitors (such as anti-PD1 or anti PD-L1 therapies recently approved for cancer treatment) are associated with improved disease-specific survival and are often used to treat patients with progressive, metastatic MCC. However, the effectiveness and side-effect profile associated with treating metastatic MCC in CLL patients with immunotherapy is not well categorized. This study seeks to understand the risk-benefit profile of immunotherapy in this setting, and a possible combined role for radiation in the treatment of CLL patients. Data was abstracted from a Seattle-based prospective registry of 1,439 MCC patients in which 9 patients were identified to have had CLL and been treated with immunotherapy. Patients were assessed for side effects of immunotherapy, progression of disease and survival status. Six patients had side effects from immunotherapy with 5 of the patients having side effects that resulted in termination of treatment. The average number of doses of immunotherapy received before termination was 3. Eight patients had progressive disease after the initiation of immunotherapy, 4 of whom have died of progressive MCC. No patients have had a complete and ongoing response to immunotherapy. These findings suggest that despite the efficacy of immunotherapy in immune-competent MCC patients, this approach may be less effective in CLL patients than immunocompetent patients. In additional, the side effect profile seemed to be more frequent in CLL-MCC patients. Neutron radiation and combination therapy are discussed as potential treatment options. Further investigation into treatment options for MCC patients with immunosuppression, such as CLL, is needed.

POSTER SESSION 2

Balcony, Easel 114

1:00 PM to 2:30 PM

Antibody Titers in Merkel Cell Carcinoma Patients Undergoing Immunotherapy Reflects Disease Burden

Kelsey Cahill, Senior, Biology (Molecular, Cellular & Developmental)
Mentor: Paul Nghiem, Dermatology

Merkel cell carcinoma (MCC) is a rare and aggressive skin cancer with a recurrence rate of ˜40%. The Merkel cell polyomavirus (MCPyV) is causally linked to 80% of MCC cases, while the remaining 20% are caused by UV-induced mutations. A blood test has been developed to detect antibodies to the MCPyV oncoprotein, as these antibody levels have been shown to correlate with disease burden. This test is a useful tool for tracking disease recurrence in patients who produce antibodies and is recognized by the 2018 National Comprehensive Cancer Network (NCCN) Guidelines for this purpose. However, as systemic immunotherapies are increasingly integrated into the standard of care for patients who develop metastatic disease, it is critical to understand the impact of immuno-stimulatory drugs on oncoprotein antibody levels. Using a Seattle-based MCC repository of 1,444 patients, I identified 64 patients who produced antibodies to the MCPyV oncoprotein and received immuno-therapeutic treatment. Eighteen of these patients had serial antibody tests during treatment, providing sufficient data for analysis. To establish a comparison for measuring disease status, I identified imaging studies from patient medical charts, such as PET/CT and MRI, or clinical evaluations administered within 45 days of the antibody test. The imaging studies were used as comparison due to their efficacy and reliability in disease detection. Among all 18 patients, those with increasing tumor burden, had increased antibody titers, while those with decreasing tumor burden had falling or low antibody titers. These results suggest that this antibody test is also an effective indicator of recurrence in MCC patients who are receiving immunotherapy.

POSTER SESSION 2

Commons West, Easel 21

1:00 PM to 2:30 PM

Effect of Levodopa on Fentanyl Oral Self-Administration in Rats

Janet Suhjung Lee, Senior, Neurobiology
UW Honors Program
Mentor: Paul Phillips, Psychiatry & Behavioral Sciences
Mentor: Ryan Farero, Psychiatry and Behavioral Sciences

Drug addiction is a neuropsychiatric disease characterized by compulsive and uncontrolled drug use. Rodent self-administration models can represent certain aspects of substance abuse in humans. Studies have shown drug use and drug-associated cues increase dopamine transmission. Data from the Paul Phillip's Lab demonstrated rats that escalated in their cocaine intake had a decrement in dopamine release to cues in the nucleus accumbens. Administration of Levodopa (L-DOPA), the molecular precursor to dopamine, decreased cocaine consumption to pre-escalated levels. However, we have not yet confirmed whether the impact of drug-associated stimuli and its dopamine-mediated aspects can be generalized

to opioid use. Thus, the current study investigates if increased dopaminergic signaling via L-DOPA decreases consumption of fentanyl, a highly potent synthetic opioid. We tested L-DOPA's effect in two separate behavioral assays. The first assay is a two-bottle choice paradigm in which the animal is given 3-hour access to liquid fentanyl (50μg/mL) and water. Additionally, animals were trained to self-administer fentanyl, in which rats were required to nose poke for liquid drug delivery. Preliminary data shows intraperitoneal injection of L-DOPA significantly decreases overall fentanyl consumption in both two-bottle choice ($p<0.05$) and in the instrumental task ($p<0.05$). These data imply that dopamine release is regulating opioid consumption. A second aim of the current work is to characterize drug-taking patterns in animals self-administering fentanyl orally. Permitting animals to extended access to drugs of abuse is known to induce escalation of drug intake. Utilizing this paradigm we provide six hours of liquid fentanyl access and examine intake patterns of individual animals across sessions. Future studies will utilize electrochemical detection techniques to examine subsecond changes in dopaminergic signaling during oral self-administration. Overall, this work provides evidence that dopaminergic signaling regulates fentanyl consumption and treatment with L-DOPA can stabilize and reduce drug intake.

POSTER SESSION 2

Commons West, Easel 6

1:00 PM to 2:30 PM

Method Development for Measurement of Diesel Exhaust Particulate Matter in Household Dust

Mae Belle Coker, Senior, Public Health-Global Health
Mentor: Christopher Simpson, Environmental & Occupational Health Sciences
Mentor: Michael Paulsen, Environmental and Occupational Health Sciences

Short-term exposure to diesel exhaust particulate matter can cause headaches, dizziness, and irritation of the nose, throat, and eyes. Prolonged exposure has been shown to increase the risk of developing cardiovascular disease, respiratory disease and lung cancer. Because heavy machinery is often fueled by diesel, occupations such as coal miners, truck drivers, railroad workers, and construction workers are at high risk of exposure. Non-occupational exposures are also of concern, especially in locations impacted by high volumes of vehicle traffic. A potential way to determine diesel exhaust exposure is by measuring the amount of nitrated polycyclic aromatic hydrocarbons (NPAHs) in household dust. There is no current method for measuring NPAHs in dust. We conducted a literature review of methods for measuring related chemicals in household dust and measuring NPAHs in other matrices. We tested three different methods before establishing the optimized sample preparation and cleanup process using silica gel solid phase extraction followed by analysis using high performance liquid chromatohraphy with tandem mass spectrometry detection (HPLC/MS/MS). To evaluate method performance we analyzed replicates of spiked and unspiked household dust and silica gel. The method was used to analyze 42 household dust samples collected in two communities – one with expected high and one with expected low traffic-related air pollution. Future research should include comparisons between dust NPAH measurements and other measures of diesel exhaust exposure, including NP (nitropyrene) metabolites in urine, air filter NP, or *a priori* predicted exposure based on home location.

POSTER SESSION 2

MGH 258, Easel 183

1:00 PM to 2:30 PM

Characterizing a Repeat Expansion in Amyotrophic Lateral Sclerosis

Kosuke Winston, Senior, Bioengineering
Mary Gates Scholar
Mentor: Paul Valdmanis, Medicine (Medical Genetics)
Mentor: Kathryn Gudsnuk, Medicine, Medical Genetics
Mentor: Meredith Course

Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disease that results in progressive degeneration of upper and lower motor neurons, leading to muscle weakness, paralysis and death. Currently, ALS affects 15,000 Americans in the U.S., who have an average life expectancy of three to five years at the time of diagnosis. There are only two FDA-approved medications for ALS treatment, which minimally slow but do not reverse the progression of the disease. Understanding the genetic causes of ALS can help us to identify more effective treatments, therefore we seek to identify pathogenic variants and investigate how they contribute to the death of motor neurons. We previously showed that a tandem repeat in an intron of the gene WD-repeat-containing protein 7 (WDR7) may be involved in ALS. To better characterize this repeat, we PCR-amplified the repeat region and quantified repeat size in 500 ALS samples, including those from sporadic cases and those with known pathogenic variants. These repeat sizes were compared to approximately 500 Parkinson disease samples, 100 Primary Lateral Sclerosis samples, and 500 control samples from the Coriell Cell Repository, to verify whether expansion of this repeat was specific to ALS. Furthermore, to determine if repeat blocks were enhanced in certain subsets of patients, the lengths of the intronic repeats in genomes of ALS patients were profiled and compared with de-identified phenotypic information. To resolve the exact sequence of repeat in ALS samples, a subset of patient DNA samples and controls were sequenced using single molecule real-time (SMRT) sequencing. Together, these findings help us gain insight into the disease and guide

us to develop a better treatment.

SESSION 2E

ANIMAL RESPONSES TO THEIR ENVIRONMENT

Session Moderator: Jay Parrish, Biology
MGH 238
3:30 PM to 5:15 PM
* Note: Titles in order of presentation.

The Effects of Chronic L-DOPA on Operant Responding for Alcohol in Rats
Kayla Wang, Senior, Psychology
Mentor: Nathan Holtz, Psychiatry and Behavioral Sciences
Mentor: Paul Phillips, Psychiatry & Behavioral Sciences

Dysregulation of the dopamine system is a central mechanism driving substance use disorders. Our laboratory has shown that chronic cocaine consumption decreases dopamine release in the nucleus accumbens of the rat, which is a brain area that is important in reinforcement learning. This study also found that restoring dopamine transmission through the administration of the dopaminergic drug, L-DOPA, decreased their cocaine consumption. Recently, we have also shown that acute administration of L-DOPA decreases ethanol (EtOH) intake. Thus, the present study sought to examine the effects of chronic L-DOPA on operant responding for EtOH in adult male rats. Rats were presented with a 2-bottle choice between an EtOH (20%) solution or water, daily for 21 days. Next, animals made nose poke responses (FR1) for 0.2 mLs of an EtOH (20%) solution over 1-h daily sessions for 35 days. On Days 26-35, rats consecutively received either vehicle or L-DOPA (30 mg/kg) for 5 days, counterbalanced across days, and L-DOPA decreased operant responding for EtOH compared to VEH. We are presently examining the effects of L-DOPA on dopamine release during operant responding for EtOH. Together, these data may suggest the efficacy of L-DOPA as a treatment for patients with alcoholism.

POSTER SESSION 3

Commons West, Easel 30
2:30 PM to 4:00 PM

Characterizing the "Stress-Reward" Pathway: The Effect of α-CRF Injection on Decision-Making Behavior in Male and Female Mice
Kevin H. Li, Senior, Economics, Biochemistry
Mentor: Paul Phillips, Psychiatry & Behavioral Sciences
Mentor: Rapheal Williams, Psychiatry and Behavioral Sciences, University of Washington Neuroscience Graduate Program

Major Depressive Disorder (MDD) has the largest life time prevalence (17%) of mood and anxiety-related disease. The prevalence of MDD is also 1.7 times greater in women than men. Chronic stress and anhedonia are the primary symptoms of depression, and decisions are affected. Our laboratory has shown that corticotropin releasing factor (CRF), the stress hormone, potentiates dopamine release in the core of the nucleus accumbens (NAc), suggesting a relationship between stress and reward processing. While it is known that an individual's decision making is altered in a depressed state, the precise neurological pathway between stress and reward processing in the brain is unclear. To characterize this "stress-reward" pathway, I used a novel decision-making framework where a cohort of male and female mice performed an operant concurrent-choice task choosing between 0.1M sucrose solution or water. Mice were injected intracranially with α-CRF, a non-selective CRF antagonist, or vehicle in the NAc prior to performing the task. I measured task performance. I hypothesize that mice injected with α-CRF demonstrate less appetitive and reward-seeking behavior compared to the vehicle group, implicating a lower sucrose nosepoke percentage, sucrose choice percentage, and higher sucrose latency during the decision-making task. I also hypothesize that females have a greater reward sensitivity system than males, resulting in an augmented decline in appetitive and reward-seeking behavior compared to males. If these results indicate a significance in further elucidating the "stress-reward pathway" through the decision-making task, this can pave way for potential new treatments targeting this pathway for depression.

POSTER SESSION 3

Commons East, Easel 74
2:30 PM to 4:00 PM

Marine Insects of Puget Sound
Tristan Carette-Meyers, Junior, Entomology, The Evergreen State College
Mentor: Pauline Yu, Evergreen State College

The Puget Sound is an economically and culturally important marine ecosystem, and insects are a little understood part of this ecosystem. Research suggests that insects are an important food source for near shore juvenile salmon which has wider ecological and conservation implications, including at higher trophic levels; while some work has been done in

coastal British Columbia, little work has been done on the insects themselves within the environment of the Puget Sound. To close this biodiversity knowledge gap, field and museum collection surveys were and are being conducted to gain a better understanding of the insects of Puget Sound. Various hand sampling techniques were utilized including net, aspirator and insect vacuum. So far, 15 individual species of 6 families of 2 different orders of insects were confirmed present in Puget Sound in this study. Additionally, 10 species of 2 families of 2 different orders of insects were reported in similar conditions in the literature, but were not observed in this survey or found in museum collections. The most abundant order was Diptera. In all, 14 beaches on the Puget Sound have assessed and some contained unique species. Further studies, in seasonality (and food availability), habitat substrate preference, insect behavior, insect population dynamics and a deeper look at predation of marine insects by juvenile salmon could be investigated based off the work done in this study.

POSTER SESSION 3

Commons East, Easel 69

2:30 PM to 4:00 PM

Characterizing a Broad Sample of Variable Stars from Light Curves and SDSS Spectroscopy

Sierra Alison Dodd, Senior, Astronomy, Physics: Comprehensive Physics
Mary Gates Scholar
Mentor: Paul Green

The Time-Domain Spectroscopic Survey (TDSS) is the largest spectroscopic survey ever carried out specifically targeting variable objects. In this poster we consider the subsample of some 22,000 TDSS variables characterized spectroscopically as stars, and evaluate best methods for retrieval and analysis of light curve data from the Palomar and Catalina surveys. We analyze light curves using Python and the VARTOOLS code of Hartman & Bakos (2016). A combination of the VARTOOLS output, spectroscopic information from Sloan, and classification of periodic variables in Catalina from Drake et al. (2014) is used to guide future classification of the entire TDSS sample, including some discussion of the larger variable sample for which no significant periodicity is found. The particular patterns of each type of variable star we find can be used to learn more about stellar evolution and the physical processes taking place within stars. The discovery of new and unexplained types of variable stars can also act as a driver that leads astronomers to an explanation of the underlying mechanism behind it. The SAO REU program is funded in part by the National Science Foundation REU and Department of Defense ASSURE programs under NSF Grant no. AST-1659473, and by the Smithsonian Institution.

POSTER SESSION 4

MGH 241, Easel 133

4:00 PM to 6:00 PM

Engineering a Wax Valving System for Microfluidic Diagnostic Devices at the Point of Care

Anushri Ramanath, Senior, Pre Engineering
Mentor: Paul Yager, Bioengineering
Mentor: Kamal G. Shah

Infectious diseases contribute to the death of over seventeen million people every year. Early detection of disease allows patients to seek care at earlier stages and improve health outcomes. Nucleic acid amplification tests (NAATs) are one strategy to detect pathogens present in low concentrations in biological samples. Unfortunately, current nucleic acid microfluidic diagnostic tests are expensive, require complex user steps, and take too long to be relevant at the point of care. The Yager Lab uses paper-based microfluidics to make low-cost, simple, and rapid NAATs suitable for the point of care. In order to control the flow rate of fluids, microfluidic devices often utilize chemicals, varied device geometries, and mechanical means as valving mechanisms. My research focuses on engineering a simple valving system for paper-based microfluidic NAATs which automatically delivers a biological sample into fibrous amplification pads after the sample is lysed. The valving system is comprised of a fatty acid wax plug and several layers of hydrophobic and hydrophilic paper-like materials within a laser-cut acrylic cartridge. When heated, the melted wax is absorbed by the hydrophobic layer and the fluid sample is able to flow into downstream pads for amplification of the pathogenic nucleic acids. Optimized through over 30 iterations, I designed a wax plug which could melt over a small heating region. The design had an average fluid release time of 47 seconds (standard deviation 8 seconds) and an average fluid delivery time of 15 seconds. For future designs, valve actuation time and fluid delivery time can be tuned by changing the length, shape, and volume of the wax channel. The development of this valving system will help aid the diagnostic community in the design of simpler and lower cost microfluidic systems, potentially expanding access to point-of-care NAATs and enabling widespread disease detection in low-resource settings.

POSTER SESSION 4

Commons West, Easel 11

4:00 PM to 6:00 PM

Fibroblast Platelet-Derived Growth Factor Receptor Responses in Rheumatoid Arthritis

Kendahl Mariko Sugai, Senior, Biology (Physiology), Psychology
Fanqi Shi, Junior, Biology (Molecular, Cellular & Developmental)
UW Honors Program
Erica Yeesuen Chow, Junior, Biology (Physiology)
Mentor: Erika Noss, Medicine-Rheumatology
Mentor: Paul Panipinto, Rheumatology

Rheumatoid arthritis (RA) is an inflammatory autoimmune disease characterized by elevated inflammatory mediators, bone resorption, and cartilage destruction. These changes are caused in part by fibroblasts, which invade cartilage and amplify inflammation by producing a variety of cytokines and chemokines. Previous research suggests that activation of the receptor tyrosine kinases platelet-derived growth factor receptors (PDGFRs) may play a major role in fibroblast expansion and invasion in RA. These receptors are homo- or heterodimers composed of α or β subunits, and can be stimulated by five different ligands. Although the signaling pathways activated by PDGFR-α and PDGFR-β are very similar, they have been shown to play different roles in disease models. We propose that PDGFR-α and PDGFR-β activation produce independent responses in joint (synovial) fibroblasts, depending on both receptor signaling and ligand availability, contributing to their different roles in disease. We found activation of both receptors stimulated fibroblast proliferation and recycling of Cad-11, a cell-to-cell adhesion molecule that plays an important role in the signaling that produces the inflammatory response. This was found by comparing receptor phosphorylation data from Western Blot, ELISA, and flow cytometry experiments. However, when silencing PDGFRs with a multi-tyrosine kinase inhibitor, only PDGFR-α was found to affect Cad-11, meaning Cad-11 likely works through PDGFR-α to regulate cell proliferation. In contrast, PDGFR-β activation has been shown to induce a more motile morphology change in immunofluorescence experiments with 3D cell cultures. qRT-PCR experiments have also provided evidence that the same cell lines stimulated with different ligands resulted in distinct genotypes. These results support our hypothesis that PDGFR-α and PDGFR-β may have unique functions in synovial fibroblasts that contribute to RA pathology.