Undergraduate Research Symposium May 18, 2018 Mary Gates Hall

Online Proceedings

POSTER SESSION 1

Commons West, Easel 25

11:00 AM to 1:00 PM

Ventures of Veterans

Shamus Martin Nolan, Senior, Education, Communities and Organizations
Mentor: Jondou Chen, College of Education

Post 9/11 Veterans are more equipped to be successful than any other veteran generation. After three years of honorable enlistment, service members can use the G.I. bill to receive 36 months of tuition and living expenses for education at state and private institutions. Despite increased access to education, there is a decrease in veteran entrepreneurs compared to post WWII veterans. The present demographics in the military consist of individuals from a wide range of cultures and backgrounds with more female and non-white ethnicities represented. Additionally, the current military service is largely non-combatant and voluntary, which contrasts to the conflicts in the last century such as a draft in the Vietnam Era and WWII. The diversity and skill sets of the current veteran population align more with the growing diverse general population. Yet, Bunker Labs has found primarily a specific demographic of the veteran population, white male officers, pursue entrepreneurship disproportionately. Bunker Labs and other similarly focused organizations look to continue positive leadership experiences that the military establishes, that are hard to find after service. This research looks to compare the barriers and assets veterans specific to Bunker Labs and the local veteran populace face as entrepreneurs, and how the not for profits such as Bunker Labs and institutions such as the University of Washington, business, and local governments can work to create a successful startup ecosystem. This paper reflects the differences between different types of backgrounds, rankings, and specializations that veterans bring into business to understand the kind of needs that our nation's heroes require to make their dreams come true.

POSTER SESSION 1

MGH 206, Easel 166

11:00 AM to 1:00 PM

Identification of a Causal Gene for a Novel Form of Spinocerebellar Ataxia

Olga Sarby Cherepakhin, Senior, Biology (Molecular, Cellular & Developmental), Anthropology: Medical Anth & Global Hlth
Mary Gates Scholar
Mentor: Dong-Hui Chen, Neurology

Spinocerebellar Ataxia (SCA) is a group of inherited autosomal dominant disorders characterized by the loss of coordination in the limbs and atrophy of the cerebellum. SCA progresses gradually and has a diverse presentation of symptoms from debilitating to mild amongst its different forms. There are many genetic causes for SCA, however, they remain unknown in many cases. Although there is no treatment, recent scientific advances have illuminated mechanisms of pathogenesis and potential gene therapies to help patients with SCA. My project in the Raskind Lab contributes to this research by attempting to identify the causal gene for a family with a novel form of autosomal dominant SCA. Whole exome sequencing is currently being conducted on the DNA of three affected members of the family. From the exome sequencing, we will receive all the genetic differences in the protein-coding region from a reference sequence in any of these three subjects; we will first search for variants with genes known for SCA. I will then begin the process of choosing candidate variants for further analysis. I am choosing them by first filtering for variants that are heterozygous in all three exomes and have a prevalence of less than 0.01% in genetic databases and then prioritizing the remaining variants based on the type of mutation, model-predicted effect of the variant, and relevance of the gene function to SCA. For each chosen candidate variant, I will amplify and sequence the DNA from each family member to determine whether it co-segregates by being present in all those who are affected and absent from those who are not. Once a co-segregating variant is identified, other studies will be conducted to support its causality. My research will contribute to our understanding of SCA and neurodegenerative disorders.

POSTER SESSION 2

MGH 241, Easel 133

1:00 PM to 2:30 PM

Cas9/CRISPR Activating System in Zebrafish
Marilyn Erin Moelhman, Senior, Biology (Physiology), Germanics
Mentor: Eleanor Chen, Pathology
Mentor: Michael Phelps

Cas9 has long been used as an effective genome-editing tool for its ability to knock out genes with high efficiency; only in recent years has it been used to activate genes as well. Our current research aims to develop Cas9 as a gene activating tool in zebrafish, and to use that tool to target genes associated with rhabdomyosarcoma, a devastating pediatric cancer, in order to better understand the genetic factors and interactions leading to tumor growth and progression. When a dead form of Cas9 is used (dCas9), it will bind to the specified site without cutting/knocking out the gene. We have developed a gene-activating system using dead Cas9 fused with a transcriptional activator (dCas9-VPR), and are currently optimizing its use with Csy4 in order to activate multiple genes in a pathway or genetic network. We have seen low efficiency success so far by injecting zebrafish with DNA coding for Csy4, dCas9-VPR, and guide RNAs downstream of the ubiquitin promoter. Once the system is optimized, we hope to use it to test interactions between multiple genes simultaneously, which would allow us to determine how interactions between genes impact cell behavior. This will allow us to gain a more wholistic understanding of how a genetic pathway works.

POSTER SESSION 2

MGH 241, Easel 134
1:00 PM to 2:30 PM

Identification of Potential Cancer Stem Cell Markers in Rhabdomyosarcoma
Phuong Van, Senior, Biology (Molecular, Cellular & Developmental)
Mary Gates Scholar
Mentor: Eleanor Chen, Pathology
Mentor: Thao Pham, Pathology

Rhabdomyosarcoma (RMS) is a rare and devastating pediatric soft tissue sarcoma, predominantly diagnosed in children and adolescents. Metastases and disease relapse rates continue to remain poor with a 5-year survival rate of less than 30%. Current therapeutic methods continue to remain inefficient in causing complete remission. Cancer stem cells (CSCs), a subpopulation of cells within tumors, are able to resist standard therapeutic treatments leading to disease relapse and metastases. Studies using human cells and a zebrafish model of RMS has shown that a population of CSCs exists within RMS. Thus, I am interested in characterizing potential genes that serve as a marker for CSCs in RMS. I am currently pursuing two candidate genes called PAX7 and CD82. Both PAX7 and CD82 have been demonstrated to play an essential role in regulating the function of skeletal muscle stems cells. The molecular signature of the CSCs in RMS is similar to that of skeletal muscle stem cells. Our preliminary data in the Chen lab also demonstrated increased expression of CD82 in a sphere assay, a surrogate in vitro assay to assess stem-like features in tumor cells. Based on these findings, my central hypothesis is that PAX7 and CD82 can potentially serve as specific markers of the CSCs in RMS. To test the hypothesis, I tagged PAX7 and CD82 with the aid of the CRISPR/Cas9 genome editing technology in order to isolate populations of RMS cells that either express PAX7 or CD82. I will perform cell-based assays in order to assess whether the stem-like qualities are enriched in isolated PAX7 and CD82-labeled RMS cell population. The identification of the CSCs in RMS will provide insight for a novel solution in overcoming drug-resistant RMS, tumor recurrence, and metastasis, through CSC-targeted drug therapy.

POSTER SESSION 2

MGH 241, Easel 132
1:00 PM to 2:30 PM

Developing Tissue-Specific Gene Editing Model in Zebrafish Muscle
Jessica Erin Gianopulos, Senior, Biology (Molecular, Cellular & Developmental)
Mary Gates Scholar, UW Honors Program
Mentor: Eleanor Chen, Pathology

Rhabdomyosarcoma (RMS) is a rare pediatric cancer characterized by abnormal muscle development. In order to provide insight into muscle development and the pathogenesis of rhabdomyosarcoma, I developed a muscle cell lineage-specific CRISPR/Cas9 gene targeting system in zebrafish that will enable the study of gene function specifically in muscle cells. To create the zebrafish muscle tissue-specific CRISPR/Cas9 gene-editing model without disrupting endogenous gene function, I inserted the *Cas9* gene at the end of the zebrafish *myf5* gene locus. *Myf5* is a gene expressed in developing skeletal muscle tissue and muscle stem cells. By inserting *Cas9* downstream of the *myf5* gene, *Cas9* expression will be induced by the *myf5* promoter resulting in gene targeting specifically in muscle tissue. I accomplished this by microinjecting zebrafish embryos with DNA containing the *Cas9* gene flanked by short myf5 sequences matching the genome. *Cas9* will be inserted at the *myf5* locus through a homology independent CRISPR/Cas9-mediated gene knock-in approach which uses a cut and paste mechanism to insert genes into specific locations in the genome. All injected zebrafish embryos were screened for correct integration using polymerase chain reaction (PCR). Founder zebrafish (those with correct integration) were bred to create a stable line of *myf5-Cas9* zebrafish. The *myf5-Cas9* expressing zebrafish line will be used to target genes specifically in muscle cells

and in our zebrafish model of rhabdomyosarcoma (RMS) to identify genes essential for growth of RMS cancer cells. Identification of genes essential for RMS growth will enable the development of new targeted therapies to improve survival of cancer patients.

POSTER SESSION 2

MGH 258, Easel 186

1:00 PM to 2:30 PM

Column Calibration for Boron Isotope Geochemistry

Esten Jacob King, Senior, Earth and Space Sciences: Geology
UW Honors Program
Mentor: Fangzhen Teng, Earth and Space Sciences
Mentor: Xinyang Chen, Earth and Space Sciences

The main control of ocean acidity is the concentration of dissolved CO_2, which depends on the concentration of CO_2 in the atmosphere. CO_2 is a greenhouse gas that plays a vital role in climate change. Boron isotopes in marine carbonates can be used as a paleo-pH proxy for the oceans, and therefore can shed new light in paleo-climate reconstruction. A method that accurately and precisely analyzes boron isotopic compositions must be developed before analyzing any natural samples. This study aims to establish an optimized boron extraction procedure that is done by column chemistry using boron specific resin (Amberlite IRA-743). This resin has a high affinity to boron at pH $>$ 5 and will be bound to the resin. Lowering the pH will decrease the resin's affinity for boron and release it from the resin. In this calibration we tested three mirco-columns (made in house) of our standard (NIST- SRM951a) in a slightly basic solution (pH ˜8) and then elute them with H_2O and HNO_3 through the columns. Each column is eluted with 100μl of 1N HNO_3 10 times and collected. Inductively-Coupled Plasma Mass Spectrometry (ICP-MS) is then used to determine the total recovery rate and how many times the column must be eluted to get 100% yield. This column calibration procedure is an important step towards quantitative analysis on boron in natural carbonate samples.

POSTER SESSION 3

Balcony, Easel 86

2:30 PM to 4:00 PM

UW Solar Power Monitor

Kamil Jiwa, Senior, Electrical Engineering
Yuxuan Chen, Senior, Electrical Engineering
Nathan Hills, Junior, Electrical Engineering
Jerome Paliakkara, Freshman, Pre Engineering
Mentor: Daniel Kirschen, Electrical Engineering

UW's electricity bill is around $1MM per month, making it Seattle City Light's second-largest customer. Solar power represents one way that UW can reduce load on the city's power grid. In 2017, UW Housing and Food Services completed installation of four solar panel arrays to its buildings on campus. How have those panels performed, and has UW benefited from their presence? To gain insights into the effect of these installations, we developed the UW Solar Power Monitor to collect and present data about solar power usage within these buildings. The data was analyzed, interpreted, and integrated into the dashboard. Our hope is that the tools we have developed will enable UW administrators to make informed decisions about power infrastructure on campus, educate the public and promote awareness about solar projects on campus, facilitate the study and analysis of solar power, and encourage increased investment in solar infrastructure at the University of Washington.

POSTER SESSION 3

MGH 241, Easel 147

2:30 PM to 4:00 PM

Age Associated Activation of Msn2 Drives a Pathological Glucose Starvation Response

Yen Chi (Travis) Feng, Senior, Biochemistry
Mary Gates Scholar
Mentor: Matt Kaeberlein, Pathology
Mentor: Kenneth Chen, Genome Sciences

As the average population lifespan increases in many countries, study into age-associated diseases and the basic biology of aging has become even more important. Studying age-associated changes and lifespan-altering genes in the budding yeast has revealed fundamental insights into the aging process. To measure replicative lifespan of budding yeast cells, we image hundreds of isolated yeast cells trapped in a microfluidic device over the aging process. Using fluorescently labeled strains allows the measurement of protein expression and localization during aging.We observe that Msn2, a general stress-response transcription factor, becomes increasingly activated with age in the budding yeast. Paradoxically, knockout of Msn2 and its homolog Msn4 results in increased lifespan, indicating that the Msn2-driven transcriptional stress response is detrimental to longevity. This effect is mediated by the inappropriate upregulation of a cohort of genes associated with the glucose starvation response despite replete glucose conditions. Deletion of these genes—glucokinase (Glk1), phosphoglucomutase (Pgm2), and glycogen synthase (Gsy1)—also results in increased lifespan. These genes are associated with the accumulation of glycogen during glucose starvation, and by staining old cells trapped in our microfluidic device, we find that glycogen content increases with age. We see that overexpression of the glycogen catabolism gene glycogen phospho-

rylase (Gph1) increases lifespan, indicating that the mechanisms underlying the detrimental effects of the Msn2-driven age-associated transcriptional program may be driven, at least in part, by the build-up of glycogen in aged cells. Accumulated glycogen is seen in the aged cells of a number of evolutionarily distant species including bacteria and human brain tissue and is implicated in multiple human diseases. Thus, our work may elucidate the details of a fundamental frailty of the metabolic network during aging.

POSTER SESSION 4

Commons West, Easel 43

4:00 PM to 6:00 PM

Method Development: Collecting and Measuring Cortisol in Afro-Textured Hair

Tayla Simone Bolden, Senior, Psychology
Mentor: Steven Goodreau, Anthropology
Mentor: Julius Doyle, Anthropology
Mentor: Eleanor Brindle, CSDE

Cortisol, a biomarker of stress, is deposited into blood, skin, saliva, as well as into growing strands of hair. A previously established method for extracting and analyzing cortisol from hair showed that it can serve as a longitudinal measure of psychophysiological stress activity as the hormone is incorporated into the hair strand. While working under a Doctoral Candidate's research on measuring hair cortisol in Black men in the Seattle area, we determined that the prevailing methodology for collecting hair is inefficient in its applications to this group. The current collection method is likely to repel potential Black research participants for many reasons including stylistic concerns as well as their inability to provide adequate volume, resulting in their non-participance. We have developed and standardized an Afro-textured friendly method for hair sample collection, and applied Meyer and Novak's cortisol extraction technique. Where the inefficient method suggests sampling from only the back of the head, our newly developed method collects hair from the entire head and relies upon a homogeneous mixture of the hair to represent an average cortisol output from a single individual. Using traditional statistical computation, we test the validity of this new method by comparing a calculated average of hair from independently measured sections of the head from each participant against homogeneous mixtures from the same participants. We hypothesize that there will be no significant difference between our calculated average of independents and the homogeneous mixture. Detecting no significant difference between these groups will serve to validate this collection method.

POSTER SESSION 4

MGH 241, Easel 138

4:00 PM to 6:00 PM

Effects of Amino Acid Availability on Yeast Replicative Aging

Dexter Euwen Chen, Senior, Biochemistry
Mentor: Kenneth Chen, Genome Sciences

The budding yeast is a popular model organism for aging research. Amino acids are a fundamental building block of biology with crucial roles in metabolism and intracellular signaling, but effects of amino acid levels and ratios in the growth media on yeast aging has never before been tested. We measured the effects of supplementation of different amino acids on yeast replicative lifespan by imaging hundreds of trapped mother cells in a microfluidic device during the course of replicative aging. We find that increased absolute levels of threonine can increase yeast lifespan through reduction of toxic biosynthetic intermediates. Conversely higher relative levels of cysteine depress lifespan. These effects are regulated by the status of the vacuole, which becomes less acidic with age. Thus, we find that longevity promoting optimal amino acid composition can optimized in an age-specific manner.

POSTER SESSION 4

MGH 241, Easel 137

4:00 PM to 6:00 PM

Budget Microfluidic Microscopy to Study Effects of Probiotic Metabolites on Yeast Aging

Toby Nathan Ven, Senior, Bioengineering
Mentor: Kenneth Chen, Genome Sciences

The pathologies of yeast replicative aging are extensively studied as a simple model organism for human aging. The golden standard in measuring yeast lifespan has been microdissection, a time- and labor- intensive process. We have developed a novel microfluidic microscopy system to facilitate more efficient and inexpensive collection of lifespan data. By counting replication through time-lapse imaging of trapped mother cells using consumer-grade microscopes coupled with an in-house auto-focusing system, we can research yeast pathways with significant time- and cost-savings over traditional microdissection and microscopy methods. I applied this system to study the effects of probiotic metabolites on replicative lifespan and have discovered lifespan-extending metabolite treatments.

POSTER SESSION 4

Balcony, Easel 109

4:00 PM to 6:00 PM

Targeting the *NRAS* Oncogene in Rhabdomyosarcoma using CRISPR/Cas9

Shivani Patel, Senior, Biology (Molecular, Cellular & Developmental)
Mary Gates Scholar
Mentor: Michael Phelps
Mentor: Eleanor Chen, Pathology

Rhabdomyosarcoma (RMS) is a devastating pediatric soft tissue sarcoma. The major RMS subtype, embryonal RMS (ERMS), is often driven by abnormal *RAS* activity. Activating mutations in the *NRAS* oncogene, for example, drive cell growth in many types of cancer, including RMS. Unfortunately, there are currently no drugs that can block *NRAS* activity. Recently developed CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)/Cas9 gene editing technology has become a powerful tool to disrupt gene function in a wide range of organisms and cell types. My research investigates the therapeutic potential of using CRISPR/Cas9 gene editing in RMS to target a cancer-causing mutation in the *NRAS* oncogene. To target the mutation in *NRAS*, I used a Gibson molecular cloning strategy to create a DNA construct expressing the SaCas9 coding sequence DNA and two CRISPR gRNAs. One of the gRNAs precisely matches the activating A183T *NRAS* mutation found in some ERMS tumors. Lentiviruses were produced from these constructs to deliver the gene editing *NRAS* A183T therapy to ERMS cancer cells. The efficiency for targeted disruption of the *NRAS* mutation by the CRISPR/Cas9 technology has been confirmed as comparable to general targeting of *NRAS*, and the mutations produced by this therapy have been profiled through next-generation sequencing to analyze targeting specificity in normal cells. If this therapy is effective in inhibiting RMS tumor growth, this mutation-specific CRISPR/Cas9 targeting strategy can be further developed into a treatment for cancer caused by this mutation. In contrast to conventional chemotherapy treatment, which kills both normal and cancer cells, this CRISPR/Cas9 gene editing therapy could be introduced with the aid of a suitable delivery system into the cancer cells of a patient carrying the *NRAS* A183T mutation. The treatment would then target and selectively kill NRAS mutant cancer cells, thereby achieving therapeutic results without causing significant side effects.

POSTER SESSION 4

Balcony, Easel 110

4:00 PM to 6:00 PM

Characterizing SWI/SNF Complex Components through CRISPR/Cas9 Multiplex Library in Rhabdomyosarcoma

Texia Loh, Senior, Biochemistry, Biology (Molecular, Cellular & Developmental)
Mentor: Michael Phelps
Mentor: Eleanor Chen, Pathology

Rhabdomyosarcoma (RMS) is an aggressive malignant pediatric cancer characterized by pathological skeletal muscle development. Due to a small accumulation of genetic mutations, RMS tumor progression is believed to be driven by epigenetic regulators, which modify chromatin structures to control gene expression. Through gene expression and knockout experiments, our lab identified components of the Switch/Sucrose non-fermentable (SWI/SNF) complex as being potentially involved in RMS growth. SWI/SNF is a family of chromatin remodeling complexes that may function in histone binding and chromatin organization to regulate gene expression. To identify any possible interactions and understand the role SWI/SNF genes in RMS, we developed a large-scale multiplex CRISPR/Cas9 genetic screening system that targets 50 epigenetic regulators, including all the SWI/SNF components. These genes are targeted individually and in every possible two-gene combination. CRISPR, a gene editing technology which uses guide RNA (gRNA) sequences to direct double-stranded cuts in DNA, allows us to knock out genes in cells to gain insight into their function. I have made the CRISPR targeting DNA constructs for the SWI/SNF genes to be included in the library of epigenetic regulators for the genetic screen. We are currently introducing the CRISPR library into human RMS cells to assess the effects of all possible combinations of single-gene and dual gene-knockouts on tumor cell growth. Using this large-scale multiplex genetic interaction screen, we hope to identify genes and gene combinations that are essential to the growth of RMS cells. If two genes have cooperative or redundant function in promoting RMS tumor growth, a dual-gene knockout is expected to result in a more significant reduction in cell growth compared to targeted disruption of either gene alone. The study will provide valuable insight into genetic interactions among key epigenetic regulators in RMS and potentially identify novel therapeutic targets for the treatment of RMS.

POSTER SESSION 4

Balcony, Easel 93

4:00 PM to 6:00 PM

The Development of our Longitudinal Data Visualization Tool

Adam Samir Alayli, Sophomore, Pre Engineering
Mentor: Elizabeth Krakow, Clinical Research Division/Medical Oncology, Fred Hutch
Mentor: Michael Zager, Director's Office
Mentor: Gretchen Krenn

Researchers often deal with massive longitudinal data sets. Currently-available tools visualize large amounts of longitudinal data but are very rigid or require strict formatting of the data to process it and translate it into visuals. We created an online longitudinal data visualization tool that can be

customized by its user in nearly every way. We aimed to visualize trends in sequentially-applied anti-cancer therapies in a cohort of patients from the Fred Hutchinson Cancer Research Center who received cell transplantation for leukemia, but later relapsed. The researchers wanted to visualize multiple disease statuses in parallel to the treatment-and-response trajectories. My objective was to make this tool as customizable as possible, so that it could be used by other researchers with different longitudinal data. I first created a prototype using JavaFX that allowed the user to construct customizable swimmer plots. My design allowed the user to customize visuals such as the colors, shapes, and scale of events in the swimmer plot. To further improve the dynamic features and efficiency of this tool, I approached the developers of Oncoscape, an open source JavaScript software that allows for data visualization and exploratory data analysis, to refine and incorporate my tool into the Oncoscape suite. The current iteration of our tool provides unparalleled flexibility to accommodate any longitudinal data set. It allows researchers to select subsets of subjects based on multiple shared characteristics, allow simultaneous visualization of two or more sequences per subject, and allow researchers to zoom in to a granular level of detail for each subject. This tool will provide doctors a means to quickly study which treatments were administered in which order to similar, historical patients, and their associated outcomes. Thus, by disseminating this tool, we will help doctors make better therapeutic decisions during key moments in an individual patient's treatment course.