

Undergraduate Research Symposium May 19, 2017 Mary Gates Hall

Online Proceedings

POSTER SESSION 1

MGH 241, Easel 147

11:00 AM to 1:00 PM

Fighting the Stereotype: Insights to the Enigmatic Ubiquitin Conjugating Enzyme, Ube2W

Donovan Y Phua, Senior, Biochemistry

Mary Gates Scholar, UW Honors Program

Mentor: Rachel Klevit, Biochemistry

Mentor: Tobias Ritterhoff, Department of Biochemistry

Posttranslational modification with the small protein ubiquitin (Ub) is an universal and essential process in various regulatory pathways of eukaryotes (from yeast to humans), ranging from protein degradation to DNA repair. Misregulation of ubiquitination is associated with diseases such as cancer and neurodegenerative disorders. Ubiquitination is accomplished by an enzymatic cascade that involves a family of ~40 E2 conjugating enzymes, which form high-energy thioester (R-S-CO-R) intermediates with Ub, called E2conjugates. For the majority of ubiquitination reactions, it is the E2 that covalently attaches Ub to substrate proteins. While the overwhelming majority of E2s ubiquitinate the ϵ -amino group of substrates' lysine residues, important exceptions have recently been discovered. For example, Ube2W has been identified as the only human E2 that attaches Ub exclusively to the α -amino group of substrates' unstructured N-termini. Knockout of Ube2W in mice has led to severe developmental abnormalities, suggesting it is important for early postnatal survival. Little is known about the molecular mechanism of Ube2W's unusual specificity and structural insights to the catalytically-relevant species, the Ube2Wconjugate, are lacking. Through mutational analysis and biochemical assays, I seek to understand the following question: What role does Ube2W's capability to dimerize and its unusually high number of cysteine residues play in its catalytic mechanism? In addition, I am using a combination of chemical biology and nuclear magnetic resonance (NMR) to study the Ube2Wconjugate to track structural changes at the E2's active site during catalysis. This investigation will provide insight into biochemically fascinating and biologically highly relevant enzyme.

POSTER SESSION 1

Commons East, Easel 83

11:00 AM to 1:00 PM

Before Our Eyes and Under Our Noses: Sex Trafficking in the U.S.

Eleanore (Cendri) Johnson, Sophomore, Linguistics, International Studies, Shoreline Community College

Mentor: Rachel David, Gender Studies, Shoreline Community College

Sex trafficking, the practice of transporting and coercing persons into commercial sexual exploitation, is a global problem that's supported by our actions (or lack thereof) here in the U.S. The question this report seeks to answer is how international sex trafficking continues to be supported in the U.S. and in Washington State in particular. Sex trafficking is a difficult topic to research, as most data lies in illegal activities among hidden populations. If, however, people are able to inform themselves about the impact of sex trafficking on the sex industry in the U.S., they may demand reform on both a societal and governmental level to combat sex slavery. My prediction is that a large factor contributing to sex trafficking's success is simply the public's lack of knowledge on the subject. Additionally, it's likely that laws and societal norms as well as lack of resources/funding for anti-trafficking efforts are also contributing factors. To answer my research question I've read through various encyclopedias, scholarly journals, organization websites, and even a report on human trafficking in Washington State. I've also conducted an interview with a survivor of sex trafficking who now volunteers with helping victims of trafficking. My research focuses on development of sex trafficking, who supports it, why it thrives in Seattle, and what needs to be done to stop it. Research shows that sex trafficking is prominent in Washington State due to location, proximity to the border, and client supply. Changes in societal attitudes in conjunction with revised laws that better protect victims and punish the traffickers and greater support/funding for organizations against sex trafficking will all serve to combat this problem. If the world decided to stop human sex trafficking, then millions of people could be spared from a very tragic fate.

POSTER SESSION 1

MGH 241, Easel 146

11:00 AM to 1:00 PM

Insights from Worms? Developing a *Caenorhabditis elegans* Model for BRCA1 Breast Cancer Variants

Natali M. Shumlak, Senior, Biochemistry

Mary Gates Scholar

Mentor: Rachel Klevit, Biochemistry

Mentor: Mikaela Stewart, Biochemistry

Even though *Breast Cancer type 1 gene (BRCA1)* was the first gene to be definitively linked to hereditary breast and ovarian cancer, much is still unknown about how *BRCA1* influences cancer risk. What is known is that certain *BRCA1* variants confer an increased risk of early onset breast, ovarian, prostate and peritoneal cancer, but there are also many patients with variants of unknown significance that have yet to be characterized. Current methods for variant characterization require arduous genetic manipulations of mammalian cell lines, which could be simplified if a homologous model organism was used. A *BRCA1* homolog has been identified in the nematode, *Caenorhabditis elegans*, indicating that the nematode could be a useful *BRCA1* model system. My preliminary results indicate that activity of *BRCA1*, the gene product of *BRCA1*, is conserved in the worm homolog as both proteins expressed functionally homologous ubiquitin-ligase activity when studied using purified components. In order to investigate the conserved residues in the *C. elegans* homolog that lead to the conserved activity, I am comparing the interactions of both *BRCA1* homologs with the E2 enzyme (required for ubiquitin-ligase activity). Using site-directed mutagenesis, I am producing mutations at the hypothesized E2 binding site on the worm homolog that I predict will inhibit ubiquitin-ligase activity by preventing E2 binding. The impact of these mutations are being studied through biochemical ubiquitin-ligase assays using purified components. A nematode-based *BRCA1* model would allow for hypotheses developed through in vitro or in cellulo studies to be tested in a whole organism, significantly expediting variant characterization. Understanding the importance of the conserved residues between the homologs will identify key regions of *BRCA1* where patient variations may be more likely to pose a risk.

SESSION 2F

POLITICS AND CULTURE

Session Moderator: John Wilkerson, Political Science

MGH 242

3:30 PM to 5:15 PM

* Note: Titles in order of presentation.

The Longitudinal Effect of Defined Contribution Pension Plans on Employees in Public Sectors

Judy Zhuang, Senior, Economics, Mathematics

UW Honors Program

Mentor: Christopher Anderson, Aquatic and Fishery Sciences

Mentor: Rachel Heath, Economics

Many scholars have constantly claimed that a shift from defined benefit plans to defined contribution plans has been the wrong course of action in policy and it has brought direr effect to the economy. Economists have argued that defined contribution plans are generating inefficiency pension income for employees in the private sectors, creating further cost burden for taxpayers and discouraging employees to stay at a job. While most observers are accepting the current situation by sticking to the traditional defined benefit plans, there are significant indicators in which the shift to defined contribution plans is inevitable. Economic shocks such as financial crisis, new health policy like Affordable Care Act and Congress abolishment of the Aid to Families with Dependent Children federal assistance program have changed the tides. They have brought a great deal of attention on how defined contribution pension plans can shape agents' behavior in the labor market. Using datasets from the Survey of Income and Program Participation (SIPP) Synthetic Beta file and the National Quarterly Workforce Indicators, this paper examines the proposition that defined contribution plans motivate newly hired workers to stay at a job for a much longer period and gain higher weeks at pay without federal assistance programs taken place. This occurs particularly for male employees in public sectors. Regression analysis (OLS and logistic) demonstrates that workers enrolled in defined contribution pension plans have increasing personal level annual earnings taxed under FICA, higher probability in having employer-based health insurance and a larger family size in their individual households. Furthermore, this paper attempts to explain whether defined contribution plans have transitory or permeant effect on workers' wellbeing during economic shocks using unit root test to determine whether there exists a stochastic trend. Keywords: defined contribution pension plans, labor market, individual households, workers

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Big Brother's Democratic Debate: National Security versus the Right to Privacy

Eleanor Oralee (Eleanor) Mount, Senior, Law, Societies, & Justice, Political Science

UW Honors Program

Mentor: Rachel Cichowski, Department of Political Science

This project examines the relationship between government use of technology through mass surveillance and the individual's right to privacy. In what some have called the "Big Brother" age of democracy, states often use mass surveillance technologies such as drones, wiretapping phones, intercepting internet communications, and other forms of secret surveillance. States argue technology aids efforts to combat security threats to the state, keep the public safe, and prevent crime. Individuals and NGOs argue that these practices can violate their rights to privacy. In a global age marked by global terrorism threats and a broadening use of mass surveillance technologies, the right to privacy is often portrayed as the loser. International courts are beginning to change this dynamic. This project analyzes the emerging field of mass surveillance case law of the European Court of Human Rights (ECtHR) to understand the role of individuals, states and courts in shaping this area of law. Cases were selected directly from the ECtHR Factsheet titled "Mass Surveillance" and a specific emphasis is placed on cases with a significant domestic impact. The findings bring into question dominant understandings of state power, and reveal the court does not hesitate to uphold individual and group privacy rights in the face of state opposition. Yet the findings also warn that rights to privacy are not absolute in the global "war on terror" and in the new "Big Brother" era of mass surveillance. In a field that will only continue to grow with a surge of technology, this project has important implications for future relationships between privacy and state security.

SESSION 2S

MODULATION OF CELL BEHAVIOR AND ITS COMPONENTS

Session Moderator: Valerie Daggett, Bioengineering

JHN 175

3:30 PM to 5:15 PM

* Note: Titles in order of presentation.

Characterizing the Effect of Zinc Binding on the Structure and Chaperone Activity of a Small Heat Shock Protein

Bobby Shih, Senior, Chemistry, Biochemistry

UW Honors Program

Mentor: Rachel Klevit, Biochemistry

Mentor: Amanda Clouser, Biochemistry

Proteins serve very specific and powerful functions in the cell by maintaining a specific shape through chemical interactions in the protein sequence. Under stress conditions however, these chemical interactions holding the protein together may break apart, leading to the protein's loss of function and exposure of hydrophobic patches that can interact with other proteins to form toxic aggregates. Heat shock proteins (sHSPs) act as safeguards under conditions of stress and protein misfolding as molecular chaperones that interact with exposed hydrophobic patches to stabilize unfolded proteins. The importance of sHSPs in the cell is exemplified through various disease associated mutations of sHSPs. sHSPs are a large and diverse family of proteins distinctive in their ability to form multimers of various sizes, which correlates with varying ability to prevent aggregation. However, little is known about how different structural elements of sHSPs influence function. The Klevit lab aims to better understand the molecular interactions of human sHSPs with themselves, how these sHSPs are activated in cellular conditions, and how they recognize and bind unfolded protein. My work focuses on the characterization of the structure and function of the human sHSP, HSPB8. Specifically, I am studying the effects of HSPB8 binding to zinc, the cellular levels of which vary in response to stress and regulate the function of many other proteins. By comparing zinc bound and non-zinc bound protein samples using various biophysical techniques such as NMR, circular dichroism and fluorescence, I aim to elucidate the effects of zinc binding on structural and functional elements of HSPB8.

POSTER SESSION 3

Balcony, Easel 116

2:30 PM to 4:00 PM

Protocol Optimization of Oral Swab Analysis, a Novel Tuberculosis Detection Method

Alaina M Olson, Senior, Biology (General)

Mentor: Gerard Cangelosi, Environmental and Occupational Health Sciences

Mentor: Rachel Wood, Department of Environmental & Occupational Health Sciences

Mycobacterium tuberculosis complex (MTBC) infects one third of the global population, with 5-10% developing active tuberculosis. As a contemporary global health concern, highly effective tuberculosis detection methods are crucial for diagnosis and control. The gold standard approach involves hazardous, difficult collection of sputum samples, followed by pathogen detection either by molecular methods (PCR) or bacterial culture. Oral Swab Analysis (OSA) uniquely uses oral swabs to collect epithelial and bacterial cells from the interior of the mouth. The swabs are then analyzed using an in-house extraction and quantitative polymerase chain reaction (qPCR) protocol. In a previous study, OSA accurately

detected MTBC in 90% of TB patients. OSA provides a non-invasive, simpler, and faster detection method for MTBC. The current project aimed to optimize the sample preparation and qPCR detection methodologies. Of particular interest is a modified DNA re-suspension step that originally took 60 minutes and was performed using 5ul of a storage buffer. We hypothesized that a reduction in incubation time in conjunction with increasing the re-suspension solution to 15ul would have a negligible effect on the final DNA yield. Using spiked samples at known dilutions, re-suspension incubations were tested at fifteen and sixty minutes. The modified protocol produced DNA yields that outperformed the original protocol. The average changes in qPCR signal strength for the three dilutions were by 3.9, 4.9 and 5.1 units. Based on this performance, the modified re-suspension has been adopted into the official protocol. The modified protocol conserves valuable lab time enabling continued expansion of OSA benefits. Generating a faster turnaround time is not only relevant for high priority samples of this project, but for future TB detection application on a global scale.