UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 18, 2012 Mary Gates Hall

Online Proceedings

Poster Session 2

Balcony, Easel 121

2:00 PM to 3:30 PM

Sexual Behavior of the Male *Macaca fascicularis* as a Function of Dominance

Shiva Nath (Shiva) Das, Senior, Psychology
Mentor: Randall Kyes, Psychology

An animal's particular level of dominance within the group that they live with has been observed by various studies on its impact in regards to obtaining food, finding sexual partners, and how conflict is dealt with. *Macaca fascicularis* is a species of primate found all over Southeast Asia in countries such as Malaysia, Indonesia, India, Vietnam, and Thailand. They are most commonly known as long-tailed macaques. Studies show that they are matrilineal the males leave tend to leave their groups upon sexual maturity, preserving an abundant of female to male ratio. Studies show that the more dominant males within groups containing multiple males are given higher priority for the access of essential elements such as food and mate selection, sustaining the fitness of the individual. The males who are dominant to the other males should displaying aggressive behavior such as biting, kicking, directed vocalization, lunging, chasing, and threatening gestures suggesting imminent attack whilst the submissive male must in turn perform a submissive behavior. These include lip smacking, fleeing, avoiding, vocalization, or grimacing. We found, through open field observance, that between the only two adult male long-tailed macaques that lived in the observed group, that there was a significant difference in perceived dominance based on agonistic and submissive interactions. Also, the dominant male spent significantly more time engaging in sexual behavior than the submissive male, which aids the supporting the hypothesis that there is a link between dominance and frequency of sexual behavior in groups of long-tailed macaques. The observations that made helped discern how aggressiveness impacts the lives of male animals and their ability to survive and reproduce and provided data on group dynamics, which is important to the overall management of the island population. Supported in part by the UW Center for Global Field Study; PSSP-IPB, Indonesia.

Session 2E

Models, Maps and the Making of Global Health

Session Moderator: Matthew Sparke, Geography

Mary Gates Hall 242

3:30 PM to 5:00 PM

* Note: Titles in order of presentation.

Mathematical Modeling of Home-Based Counseling and Testing for HIV in KwaZulu-Natal, South Africa

Roger Ying, Senior, Bioengineering
Mary Gates Scholar
Mentor: Ruanne Barnabas, Global Health

South Africa's KwaZulu-Natal province currently has the highest HIV prevalence in the world at approximately 30%. The University of Washington's International Clinical Research Center is currently conducting a pilot program for a new HIV testing method, Home-Based Counseling and Testing for HIV (HBCT), to address the HIV epidemic. A mathematical model of heterosexual HIV transmission in KwaZulu-Natal was created to evaluate the long-term consequences of HBCT on HIV prevalence. This model simulates a population of susceptible and infected individuals with varying sexual activity levels and therefore, risk. The model also divides the population among twelve age cohorts and the infected individuals are further divided into three HIV stages and a final AIDS stage, as defined by the World Health Organization. The model was created in MATLAB and validated with HIV prevalence data for KwaZulu-Natal from the Joint United Nations Programme on HIV/AIDS. Preliminary results from the model indicate that HBCT will diagnose more cases of HIV than other testing methods and, with successful linkage to care, will decrease HIV prevalence in the future. While the possibility of HIV elimination by HBCT is yet to be determined, preliminary results indicate that HBCT is effective at linking infected individuals with care, including antiretroviral therapy. This work has the potential to guide health policy in South Africa, and given the newfound effectiveness of pre-exposure prophylaxis and treatment as prevention, HBCT provides a promising future for controlling the HIV epidemic.

SESSION 2Q

ORGANISMS IN THE OCEAN

Session Moderator: Rick Keil, Oceanography
Johnson Hall 022
3:30 PM to 5:00 PM

* Note: Titles in order of presentation.

Attenuation of the Fish Pathogen *Francisella noatunensis* by Mutation of the Pathogenicity Island Gene pdpA
Karina Gretta (Karina) Ray, Senior, Microbiology
Mary Gates Scholar
Mentor: John Hansen, Pathobiology

Different species within the bacterial genus *Francisella* are pathogenic in mammals. Recently, an emerging pathogen in fish, *F. noatunensis*, has been causing significant mortalities in tilapia and Atlantic cod. The Francisella Pathogenicity Island (FPI) is a gene dense region on the *Francisella* chromosome that encodes essential virulence factors for the mammalian pathogens *F. tularensis* and *novicida*. To determine if the functionality of virulence factors has been conserved for the genus, a gene knockout for the pathogenicity determinant protein A (pdpA) gene in the *F. noatunensis* FPI was generated as a potential vaccine candidate. PdpA has been shown to be essential for the ability of *Francisella* to cause disease for the human pathogen. The *F. noatunensis* knockout was generated via homologous recombination using a suicide vector containing an antibiotic cassette flanked by portions of pdpA. Since polarity can be an issue for knockouts in gene dense regions, two different pdpA mutants were generated in opposing polarity. It has recently been shown that *F. noatunensis* infection in zebrafish closely mimics *Francisella* infection in mammals implying conserved virulence strategies for the genus. Therefore, zebrafish were used to assess the level of attenuation for the *F. noatunensis* pdpA knockouts generated in our laboratory. In addition, iglC is another gene found in the FPI that results in attenuation after it has been inactivated in the human pathogen. Our laboratory has acquired an iglC mutant for *F. noatunensis* from a collaborator that has reduced virulence in tilapia and will serve as a reference for our pdpA knockout infections in zebrafish. The results from this study will show the physiological similarities within the genus relative to their phylogenetic relationships.

POSTER SESSION 3

MGH 241, Easel 160
4:00 PM to 5:30 PM

Lipid Analysis of the HCC Mouse Model
Antonious Ziad Hazim, Junior, Biology (Molecular, Cellular & Developmental)
Mary Gates Scholar
Mentor: Laura Beretta, Public Health Sciences - Molecular Diagnostics, Fred Hutchinson Cancer Research Center
Mentor: Kyle Muir, Public Health Sciences, Fred Hutchinson Cancer Research Center

Fatty acids are vital for proper cell function, serving as a source of energy, a structural component of the plasma membrane, and a signaling molecule. Imbalance of these fatty acids can change the homeostasis of the cell and can lead to major consequences, including cancer. We propose that lipid levels could be analyzed and serve as a diagnostic and preventative measure for human hepatocellular carcinoma (HCC). In our study, we use a hepatic-specific PTEN knockout mouse which recapitulates the progression of HCC. Phosphatase-and-tensin homologue (PTEN) is a tumor suppressor gene involved in cell cycle regulation and mutations have been observed in many types of cancers, including HCC. We collected plasma and liver tissue from 12 month old PTEN KO mice and proper controls to undergo quantitative lipid analysis. Human serum samples from cirrhotic patients with and without HCC underwent similar lipid analysis. This analysis was done for 4 lipid fractions (FFA (free fatty acids), PL (Phospholipids), TG (Triglycerides) and CE (Cholesterol esters) and determined the relative abundance of nearly 30 lipids. In addition, we quantified the abundance of several genes important in lipid metabolism using q-RT PCR. We found several lipids that showed strong correlation to tumor development. Further, the abundance of the genes involved in metabolism of these specific lipids was altered in the PTEN KO mice and showed significant correlation to both lipid levels and tumor development. Similar results were found through analysis of human samples of HCC compared to the cirrhotic controls. This infers that analyzing lipid levels and related gene expression may serve as a potential method for diagnosis and, eventually, prevention of human HCC.

POSTER SESSION 3

MGH 241, Easel 133
4:00 PM to 5:30 PM

Identification and Classification of Malaria Mosquito Species on Tinjil Island, Indonesia
Anna L. Schier, Non-Matriculated,
Mentor: Randall Kyes, Psychology

Malaria is a complex disease that poses an immense global public health burden with an annual death rate estimated between 1.5 and 2.5 million. An inclusive understanding of transmission dynamics is essential for the continuing development, improvement, and implementation of vector control strategies. Success will depend on extensive taxonomic re-

search and advanced knowledge of malaria vectors, malaria parasites, and their developing resistance to insecticides and drugs. Examinations into host-parasite relationships among nonhuman primate malarias are needed to identify other likely species of *Plasmodium* malaria parasites capable of causing zoonoses. The vectors of malaria belong to the mosquito genus *Anopheles* and there are more than a dozen species of *Anopheles* malaria vectors affecting Indonesia. In July, I will travel to Tinjil Island, located off the coast of West Java. There is no current record of mosquito fauna for Tinjil and consequently no data regarding which malaria parasites affect it. My investigations into these matters will be essential to the operation of local fisherman camps and the natural habitat breeding colony of *Macaca fascicularis*, the long-tailed macaque. I will collect samples of larvae, pupae and adult forms of mosquitoes on mainland Java for confirmation of the *Anopheles* genus before heading to Tinjil. On Tinjil I will collect samples of larvae, pupae and adult forms for genus and species identification by utilizing an onsite stereomicroscope. I expect to follow up this initial entomological survey with molecular detection methods to identify possible members of a species complex, morphologically indistinguishable *Anopheles* taxa, which may display differing abilities to transmit malaria. By identifying these species of mosquito, the implementation of integrated vector management policies needed to improve the current vector control strategies for West Java and surrounding areas will be possible.

POSTER SESSION 3

MGH 241, Easel 159

4:00 PM to 5:30 PM

MicroRNA Regulation upon Liver Stem Cell Differentiation

Michael Wyatt (Michael) Crawford, Senior, Biochemistry
Mentor: Laura Beretta, Public Health Sciences - Molecular Diagnostics, Fred Hutchinson Cancer Research Center

Research studies suggest that up to 40% of hepatocellular carcinomas may be caused by liver stem cell carcinogenesis, in which stem cells, due to their high proliferative abilities, become neoplastic and maintain cancer growth and metastasis. MicroRNA are post-transcriptional gene regulators that have been found to be involved in many cellular processes such as differentiation of stem cells. This project focused on the role microRNA play specifically in liver stem cell differentiation. Finding which microRNA are important in liver cell differentiation could provide new methods for diagnosis and treatment of liver cancer originating from stem cells. I used a stem-cell-like liver progenitor cell line capable of differentiating into mature liver tissue from a proliferative state, providing an ideal *in vitro* model for liver stem cell differentiation. Relative quantification of microRNA by real-time PCR and microarray was performed on samples taken from various time points during differentiation leading to the characterization of two microRNAs strongly upregulated in differentiation. In order to validate the importance of these microRNAs, I will use a viral vector to induce their overexpression and monitor any subsequent changes in the differentiation process. In the end, this project may provide additional insights into neoplastic liver stem cells.

POSTER SESSION 3

Balcony, Easel 111

4:00 PM to 5:30 PM

Gonococcal Antimicrobial Resistance Surveillance in Seattle, Washington

Cassandra Lee (Cassandra) Czarnetzke, Senior, Biology (General)
Mentor: Olusegun Soge, Global Health
Mentor: King Holmes, Global Health

In 1986, the United States' Centers for Disease Control and Prevention (CDC) established the Gonococcal Isolate Surveillance Project (GISP) to monitor the trends of increasing antimicrobial resistance of urethral *Neisseria gonorrhoeae* isolates from men who have sex with men (MSM). Since then, such strains of *N. gonorrhoeae*, the bacterium that causes gonorrhea, have been observed to repeatedly develop resistance to antimicrobials including sulfonamides, penicillin, tetracyclines, and most recently, fluoroquinolones. The effectiveness of the cephalosporins, the last remaining option for empirical first-line treatment of gonorrhea, is threatened by declining gonococcal susceptibility to cephalosporins in the US and worldwide. In correlation with the University of Washington Neisseria Reference Laboratory, *N. gonorrhoeae* isolates recovered from non-urethral sites were screened for antimicrobial resistance, in an attempt to identify these previously unmonitored trends. Prior to this, there was no data concerning antimicrobial resistance trends of extra-genital *N. gonorrhoeae* isolates. The experimental approach employed was disk diffusion of cefpodoxime (cephalosporin) and azithromycin (macrolide). Diameters of zones of inhibited growth, which can be seen directly on agar plates, were measured. Analysis of results was visual, and it was often clear whether or not an isolate was resistant to an antimicrobial agent. By observing non-urethral isolates, information is gained regarding the management and treatment of gonorrhea based on other anatomical sites. Experimental analysis spanning two years of isolates (2008-2009) suggests similar susceptibility trends when compared to prior GISP data. While more exact trends will be determined based on a longer span of time, totaling ten years, completion of this work will inform treatment guidelines that consider a larger variety of *N. gonorrhoeae* isolates.

POSTER SESSION 3

Balcony, Easel 100

4:00 PM to 5:30 PM

Improving Maternal and Neonatal Care in the Context of Political Instability in Côte d'Ivoire

Rachel Kelly (Rachel) Beck, Junior, International Studies
Mentor: Matthew Sparke, Geography, UCSC

Since political violence first broke out in 1999, Côte d'Ivoire has experienced a drastic loss of medical equipment, drugs, and skilled health personnel. Two civil wars in the past decade have posed significant challenges to outside intervention from international NGOs, and the weakening economy has provided little support for a state-funded health system. Currently, Côte d'Ivoire suffers from some of the highest maternal and neonatal mortality rates in the world, resulting from problems ranging from infection and hemorrhages to the compound effects of malaria, malnutrition, and HIV/AIDS. My research responds to these challenges by exploring what would be needed in a grant proposal to The Global Fund, a global funding agency that supports the fight against HIV/AIDS, malaria, and tuberculosis in developing countries. Of the thirteen Global Fund grants approved for Côte d'Ivoire in the past, none specifically address the problems of maternal and neonatal mortality. This project aims to understand why this gap in maternal and neonatal care persists and how it can be diminished in the context of political instability. To assess the efficacy of attempts to address health care gaps in Côte d'Ivoire, I analyzed the interventions currently in place to see if they were meeting their established goals and if not, why. Building upon this data and development theory, I created a proposal for improving maternal and neonatal mortality through a self-sufficient system that can remain in place should political violence persist. Preliminary research suggests that weak medical assistance is a leading cause of birth complications. Increased health monitoring during and immediately following pregnancy, as well as greater education for mothers on the crucial steps during this time period are vital to reducing mortality. Establishing self-sustaining health systems that are resilient in the face of violence and political uncertainty is invaluable across the developing world.

POSTER SESSION 3

Balcony, Easel 102

4:00 PM to 5:30 PM

Generating Recombinant *Staphylococcal aureus* Cap5O to Detect Activity in the Tyrosine-kinase CapB2

Fabiola (Faby) Arroyo, Sophomore, Business Administration
NASA Space Grant Scholar
Mentor: Corrie Ortega, Global Health
Mentor: Christoph Grundner, Tuberculosis group, Seattle BioMed

Drug resistant strains of *Staphylococcus aureus* are now possibly responsible for more deaths than any other infectious disease in the United States. Phosphosignaling enzymes are thought to constitute a major class of drug targets in humans, but their potential as drug targets in bacteria are yet to be known to their full extent. In this study, we sought to develop an assay to test activity of an *S. aureus* signaling molecule, the tyrosine kinase CapB, which controls capsule biosynthesis. By interfering with capsule biosynthesis, we hope to interfere with virulence of *S. aureus*, allowing better clearance of the infection by the immune system. To assay for kinase activity, we recombinantly expressed the known kinase substrate Cap5O. Cloning of the Cap5O insert into the pQE30 vector created an expression plasmid with a 6XHis-tag on the C-terminus of Cap5O. The plasmid was grown and harvested in Rosetta cells. Purification of the protein was carried out through Metal Affinity Chromatograpy to obtain pure protein for activity assays. The results of this study will provide the starting point for an assay to screen for compounds that interfere with capsule biosynthesis. To date, no screens for the bacterial tyrosine kinases have been developed.