UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 20, 2016 Mary Gates Hall

Online Proceedings

Poster Session 1

Balcony, Easel 88

11:00 AM to 1:00 PM

Mechanisms and Factors of Loss of Heterozygosity in Cancer

Kevin John Khoo, Senior, Biochemistry
Mentor: Nancy Maizels, Immunology and Biochemistry
Mentor: Luther Davis, Immunology
Mentor: Henry Olson, Biology, South Seattle College
Mentor: Kostantin Kiianitsa

Loss of heterozygosity (LOH) frequently occurs in tumor cells and is associated with the expression of deleterious recessive phenotypes. However, relatively little is known of its mechanisms or the various functional/regulatory factors involved. The goal of our research is to characterize the mechanisms of LOH and identify the factors involved. One cause of LOH is homology-directed repair (HDR), which uses the homologous chromosome as a donor to repair DNA damage like DNA nicks or double stranded breaks (DSBs). In HDR, the homologous chromosome functions as a template for repairing the damaged DNA strand. In order to study the mechanisms and factors involved in LOH, we developed a novel flow-based reporter model that utilizes an endogenous gene. This model was developed by making genetic modifications in a human cancer cell line (HT1080) in such a way that would allow the detection of a LOH event. Using our flow-based reporter, we will target DNA nicks and DSBs using CRISPR/Cas9 and quantify the resulting LOH events using our flow-based reporter. We will also use siRNA knockdowns to assay other candidate factors potentially involved in the mechanisms and regulation of LOH. To simulate mutations seen in tumors, we will downregulate the expression of common tumor suppressors (BRCA1, BRCA2 and PTEN) with siRNA and determine how these factors affect LOH. When common tumor suppressors are downregulated in our model, mutations that take place are expected to follow a similar mechanism to mutations seen in tumors. Using our model in this way, we will verify which common tumor suppressors are involved in the mechanisms of LOH often seen in tumors. With a better understanding of the factors involved in LOH, prophylactic therapies can be developed to minimize occurrence of LOH and tumorigenesis.

Poster Session 3

MGH 241, Easel 150

2:30 PM to 4:00 PM

Identifying the Role of Caspase-10 in Programmed Cell Death

Everet Wang, Senior, Materials Science & Engineering
Mentor: Andrew Oberst, Immunology
Mentor: Kimberley Gutierrez, Immunology

There are different types of programmed cell death: the well-understood apoptosis, and the inflammatory process of necroptosis. The enzyme Caspase-8 has been defined as a key initiator of apoptosis and inhibitor of necroptosis from studies using knockout mouse models. While Caspase-8 is found in both humans and rodents, a close homolog of the enzyme called Caspase-10, is not found in rodents. To add on, the role of Caspase-10 pertaining to the necroptosis pathway is still undefined. The goal of this project is to understand how Caspase-10 functions in human cells, and how the apoptotic and necroptotic roles of Caspase-8 described in rodents may be divided between Caspase-8 and Caspase-10 in humans. To investigate this idea, we silenced Caspase-8 and/or Caspase-10 expression in human cells, induced Necroptosis using chemical signals and inhibitory drugs, and investigated expression levels of proteins Caspase-10 may interact with. Our results will be critical in uncovering the role of Caspase-10 pertaining to necroptosis, as well as why Caspase-10 is present in humans but not mice.

Poster Session 4

MGH 241, Easel 135

4:00 PM to 6:00 PM

Genetically Engineered *Lactococcus lactis* Producing Type III Interferon to Cure Viral Infection of the Gut

Jennifer W. (Jennifer) Look, Senior, Biology (General), Comparative History of Ideas
CoMotion Mary Gates Innovation Scholar, Mary Gates Scholar
Mentor: Ram Savan, Immunology

Norovirus is one of the leading causes of gastroenteritis in the world. Although the virus affects multiple populations, from passengers on cruise ships to communities lacking efficient

water sanitation systems, a safe and effective vaccine is still under development. However, progress has been made in our understanding of how the body clears norovirus infection. We now understand that interferon lambda (IFNL) is associated with viral clearance in murine models by activating the JAK-STAT signal transduction pathway and inducing transcription of anti-viral genes. With this information, our current project seeks to implement a novel treatment method by using bacteria which secrete IFNL3 to cure the viral infection. We plan to use *Lactococcus lactis,* a probiotic, as a delivery vehicle for secreting IFNL3. We designed a plasmid construct containing a *L. lactis* specific promoter that secretes a codon-optimized IFNL3. Currently, cloning and transformation processes to introduce the IFNL3 gene into *L. lactis* are being optimized. We will then test the functional activity of IFNL3 secreted by *L. lactis* by incubating these bacteria on macrophage and gut epithelial cell lines infected with norovirus. These initial studies will lead to experiments in murine norovirus models. This treatment method will demonstrate the potential of innovative therapies against infectious diseases and is expected to be beneficial for its low-cost and easy administration.