UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 18, 2018 Mary Gates Hall

Online Proceedings

Poster Session 1

MGH 206, Easel 170

11:00 AM to 1:00 PM

Versican Regulation in Response to Lung Infection

Sarah Marie Wells, Junior, Pre-Social Sciences
Mentor: Charles W Frevert, Comparative Medicine
Mentor: Mary Chang, Comparative Medicine

The importance of understanding the inflammatory response in the lungs is underscored by the fact that pneumonia and influenza illnesses led to an estimated 12,000 deaths in the 2015-16 U.S. flu season. Our research investigates the expression and regulation of versican in response to lung infections, both viral and bacterial. Versican is a chondroitin sulfate proteoglycan present in the extracellular matrix; it is expressed in lungs during embryonic development, mostly absent during healthy adulthood, and re-expressed in instances of inflammatory lung injury or infection. We are interested in understanding the pathways that result in versican upregulation, as preliminary data suggest that versican can be either pro- or anti-inflammatory, depending on the type of cell it arises from. My research project investigates this differential regulation phenomenon - recently, I have incorporated chromatin immunoprecipitation (ChIP) of versican transcription in both viral-stimulated macrophages and lung fibroblasts to explore the epigenetic factors that control expression. ChIP allows us to establish and quantify interactions between proteins and DNA; in our case, we are interested in transcription factors that follow interferon beta signaling (IFNb), which has been shown by our lab to be a key mediator of versican expression. IFNb itself is a known anti-viral cytokine, suggesting that versican may also follow this response to viral infection. If we can determine which transcription factors, if any, lead to an increased response of versican, we will have identified a signaling pathway by which to manipulate versican expression. The ultimate goal of this work is to develop a lung inflammation therapy by driving production of versican in an anti-inflammatory state. Utilizing versican's power as an immunomodulatory molecule could be a new tool for fighting severe inflammation associated with respiratory illnesses.

Poster Session 2

Commons East, Easel 50

1:00 PM to 2:30 PM

Inhibiting B-Cell Lymphoma by Targeting *Raptor*

Janella Sorin Kang, Senior, Biochemistry
Mentor: Brian Iritani, Comparative Medicine

Mechanistic Target of Rapamycin (mTOR) is a highly conserved serine/threonine kinase originally discovered in yeast as a central regulator of cellular growth and proliferation in response to adequate nutrients and energy levels. mTOR is activated in a complex with an essential co-activator called *Raptor*. Our lab recently discovered that mTOR holds an essential role in early murine B-cell development; B-cell specific disruption of *Raptor* inhibited mTOR activity and resulted in a complete block in B cell development at the precursor-B (pre-B) cell stage. We hypothesize that B-cell specific disruption of *Raptor* will inhibit B-cell transformation induced by the Myc oncogene, and/or will inhibit the survival of B-cell lymphoma cells, by inhibiting cell growth induced by mTOR. We conditionally disrupted Raptor using gene targeting strategies in a mouse model of Burkitts Lymphoma whereby the c-Myc oncogene is expressed under control of the immunoglobulin heavy chain enhancer. We found that *Raptor* deficient mice took significantly longer to develop B-cell tumors when bred to c-Myc transgenic mice; our Kaplan-Meier Survival curve revealed that disruption of *Raptor* improved survival rates significantly, such that Raptor knockouts rarely showed growth of tumors. To better understand cellular mechanisms by which *Raptor* may inhibit B-cell lymphoma formation, we utilized flow cytometry to measure cell proliferation and survival of B cell lymphoma cells in the presence or absence of *Raptor*. Our results revealed a distinct reduction in both cellular proliferation and survival in the absence of Raptor, which suggests Myc driven B-cell proliferation and survival is highly dependent on *Raptor* and mTOR activity. In the next part of our studies, we will inducibly disrupt *Raptor* in already established primary Myc-induced B-cell lymphomas to determine whether *Raptor* and mTOR activity are essential for lymphoma cell survival. Through these results we will be able to determine whether inhibition of *Raptor* could be utilized as a strategy to inhibit cancer cell proliferation and/or survival.

POSTER SESSION 3

MGH 241, Easel 145

2:30 PM to 4:00 PM

2E01 Computationally Designed Protein and Differentiation in Stem Cells

Andrew Patrick Mc Alister, Senior, Biochemistry
Mentor: Julie Mathieu, Comparative Medicine
Mentor: Hannele Ruohola-Baker, Biochemistry

Understanding how extracellular environments facilitate the differentiation of stem cells holds much promise for the field of regenerative medicine. Non-muscle myosin II (NMII) plays an important role in cell morphology and also generates forces that alfter biochemical signalling. It has been shown that the activity of NMII controls mechanoreceptors and integrins facilitating stem cell fate. More specifically, mechanotransduction of transcriptional coactivators YAP/TAZ facilitate differentiation of mesenchymal stem cells (MSCs). YAP and TAZ are responsible for upregulating genes associated with stem cell differentiation. Under external stresses mesenchymal stem cells differentiate into osteocytes whereas softer extracellular conditions favor the differentiation into adipocytes through mechanotransduction of YAP and TAZ.To further explore the role of physical forces determining the fate of stem cells, we used a computationally designed self-assembling homo-polymer called 2E01, generated by the Institute for Protein Design (IPD). Mechanical stress and the physical activity of NMII can be mimicked by controlled expression of the length of the E01 protein fiber. We introduced the 2E01 gene under a doxycycline-inducible promoter into the AAVS1 ”safe harbor” locus of the induced pluripotent stem cells (iPSC). Expression of the E01 fiber in iPSCs lead to changes in colony morphology and subsequent differentiation of those cells, suggesting that changing the morphology of cells can change their fate. I want to see if I can use the 2E01 fiber as a tool to accelerate differentiation from IPSCs to neuronal cells and cardiomyocytes. In addition, we expressed 2E01 in mesenchymal stem cells, a cell type currently used in lab, and observed the activity of YAP and TAZ as an indicator of differentiation. Utilization of the 2E01 fiber could be benefical to the field of regenerative medicine as a directed agent of physical manipulation towards desired stem cell fate.