UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 19, 2017 Mary Gates Hall

Online Proceedings

SESSION 1O

CANCER BIOLOGY

Session Moderator: Hannele Ruohola-Baker, Biochemistry
MGH 389
12:30 PM to 2:15 PM

* Note: Titles in order of presentation.

Investigating the Role of Proline-Rich Tyrosine Kinase 2 (Pyk2) in Epithelial-Mesenchymal Transition and Tumor Metastasis
Jiye (Stella) Shin, Senior, Biochemistry
Mentor: Taran Gujral, Human Biology, Fred Hutchinson Cancer Center

The epithelial-mesenchymal transition (EMT) is a reversible process in which epithelial cells adopt mesenchymal properties by altering their morphology, adhesion, and migratory capacity. During tumor progression, the EMT underlies a process that allows benign tumor cells to infiltrate surrounding tissue and metastasize to distant sites. Our lab has identified a non-canonical Wnt signaling that involves ligands (Wnt 5a/b) and Frizzled2 receptor (Fzd2) in regulating EMT as well as tumor metastasis. Inhibition of Fzd2 signaling suppresses EMT and the progression of metastatic cancer cells both in vitro and in vivo. Recently, we have discovered a non-receptor proline-rich tyrosine kinase 2 (Pyk2) that plays a critical role in Fzd2-mediated cell migration. However, details of Fzd2-mediated activation of Pyk2 and mechanistic understanding of Pyk2 interactions in the pathway still need to be elucidated. We hypothesized that phosphorylation of Fzd2 induces activation of Pyk2, a possible contributor in Fzd2-mediated EMT pathway and tumor metastasis and aimed to uncover 1) the role Pyk2 in Fzd2-mediated EMT induction and cancer metastasis 2) the new mechanistic understanding of how Pyk2 interacts with proteins in the Fzd2 complex. Our preliminary data showed that inhibiting kinase activity of Pyk2 downregulated mesenchymal markers such as vimentin and upregulated epithelial markers such as E-cadherin. Then, the study focused on perturbing Pyk2 expression by RNAi and assessing EMT markers, and cell motility as well as gaining a mechanistic understanding of how Pyk2 interacts with other proteins in the complex. A better understanding of Fzd2-Pyk2 signaling would not only help in connecting critical nodes in Wnt pathway but may open up potential treatment options for metastatic cancers.

POSTER SESSION 2

MGH 241, Easel 162
1:00 PM to 2:30 PM

Analysis of Hippocampal-Dependent Cognition in Alzheimer's Disease
Briana Eugene Lee, Senior, Biochemistry
Mentor: Tara Madhyastha, Radiology

Alzheimer's disease (AD) is the most prominent cause of dementia worldwide, affecting up to 5.3 million elderly Americans. AD pathology includes decreased neuronal count and synaptic connections, intracellular pathology and increased affinity for neurofibrillary tangles resulting in cognitive deterioration. The hippocampus is known to be particularly vulnerable and is an early structural biomarker of AD. Our aim is to investigate the longitudinal relationships between hippocampal volume and memory performance using neuroimaging data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. The ADNI database contains biomarker, neuroimaging, cognitive, and behavioral data from hundreds of elderly individuals, divided into groups including normal/normal aging (CN), Alzheimer's Disease (AD), Early Mild Cognitive Impairment (EMCI), and Late Mild Cognitive Impairment (LMCI). Cerebrospinal fluid biomarkers are a "gold standard" for detecting the presence of amyloid and tau pathology. Neuroimaging methods include amyloid PET tracers (i.e. F-18 florbetapir), which detects amyloid beta plaques and FDG-PET imaging which measures metabolic activity within the brain. Both techniques reflect neurodegeneration and synaptic dysfunction. Structural MRI imaging is used to assess neuroanatomy as a measure of brain atrophy and changes in neuronal density. Cognitive assessment data quantifies the extent of memory loss and general cognitive decline. Using the R programming language, we will conduct longitudinal analyses of neuroimaging analyses to examine the relationship between cognitive, structural and metabolic neuroimaging variables across different diagnostic groups over time. This initial investigation is preparation for learning longitudinal methods that will later be applied to physiological measures within the entire brain. Our hypothesis is that a decrease in hippocampal volume will be less correlated to decline in memory in CN than in other groups. If our hypothesis is correct, it suggests that compensatory mech-

anisms preserve cognition in early stages of AD, which we can explore using subsequent extended analyses of functional connectivity.

POSTER SESSION 2

MGH 241, Easel 163

1:00 PM to 2:30 PM

Evaluation of a Novel Method for Diffusion Tensor Imaging and Analysis

Sabreena Shanthoshi (Sabreena Rajan) Rajan, Senior, Biochemistry
Jonathan Wolf, Junior, Computer Science
Mentor: Tara Madhyastha, Radiology

The axons in the nervous system are collectively referred to as white matter. White matter forms intricate fiber connections among the brain's grey matter (neurons). These connections change with development, learning, and disease, and therefore are of interest to several medical researchers. Tract-Based Spatial Statistics (TBSS) is an analysis technique which is used to analyze white matter integrity. Currently, this is the best existing method to align and analyze white matter. However, we are creating and evaluating an improved method to more accurately measure changes to integrity. Diffusion Tensor Imaging (DTI) Voxel Based Morphometry (DTIVBM) is a technique that we are developing which allows us to compare white matter statistics by using nonlinear registration to align the DTI image to a structural image and then a standard template. We are comparing several variations of DTIVBM with the established method of TBSS. We are using four different datasets, three of which contain adult brains ranging from ages 18-35, and one containing preteen/teen brains ranging from ages 11-15. One of the datasets also contains a mixture of normal brains and brains affected by neurodegenerative disease. Each subject has two separate brain images taken within a month's gap. By running both the DTIVBM scripts and TBSS scripts on these brain images, we will be able to determine which method is more reliable, as measured using an Intra-Class Correlation (ICC) statistic. We are currently in the process of gathering the results, but we expect to see that DTIVBM will have higher reliability on most datasets than TBSS over a wider range of white matter. If this is true, we would have demonstrated a potentially better method to analyze white matter changes through aging and development, which will require fewer people and allow us to see changes in more of the brain.

POSTER SESSION 2

MGH 241, Easel 161

1:00 PM to 2:30 PM

Using the Generalized Additive Model Regression Algorithm to Predict Depression Levels in Individuals with Alzheimer's and Mild Cognitive Impairment

Johnathan Hill, Senior, Psychology
Mary Gates Scholar
Mentor: Tara Madhyastha, Radiology

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by decline predominantly in episodic memory. Previous research has demonstrated that individuals with AD suffer from depression at higher rates than healthy individuals. Predicting depression levels in individuals with AD may be important for mental health care preparation as the disease progresses. To predict depression levels, I trained a generalized additive model (GAM) regression algorithm to predict scores on the Geriatric Depression Scale (GDS) using diffusion tensor imaging (DTI) data of fraction anisotropy (FA) means in 15 different regions of interest (ROIs). The GAM regression algorithm is a non-parametric expansion of the linear regression model. Data were gathered from the Alzheimer's Disease Neuroimaging Initiative (ADNI). This data set includes 150 subjects with DTI and GDS scores at the 6-month visit for individuals with AD, early mild cognitive impairment (EMCI), late mild cognitive impairment (LMCI) and healthy controls. A k-fold cross-validation method was used to split data into testing and training data. After training and testing the data on a GAM regression algorithm, we attempted to predict depression scores from contemporaneous FA data. The accuracy of this algorithm was assessed by calculating the mean-squared error (MSE) of the testing data. The MSE measured how well the GAM regression model formed from the training data fits the testing data. We evaluated sensitivity, specificity and area under the receiver operator curve for depression prediction as a binary outcome. The purpose of this project was largely to gain experience with machine learning. Fitting a predictive model could inform our understanding of how white matter microstructure might relate to depression in AD.