UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 18, 2012 Mary Gates Hall

Online Proceedings

Poster Session 1

Balcony, Easel 105

12:00 PM to 1:30 PM

Mechanisms of Glycemic Improvement after Gastrointestinal Surgery (RYGB Mechanisms)

Adam Ching (Adam) Tanaka, Junior, Biology (Physiology)
Mentor: Andrew Wright
Mentor: Caro Slingluff, Surgery

Diabetes is an escalating health issue that can lead to a multitude of health problems, including heart disease, blindness and death. In 2011, the Center for Disease Control reported that diabetes afflicts 25.8 million Americans, is the seventh leading cause of death, and that it incurs an annual cost of $174 billion. Type II Diabetes Mellitus (T2DM) accounts for 90-95% of adult diabetes, for which there is no definitive cure. Studies show that 84% of patients undergoing Roux-en-Y Gastric Bypass (RYGB) experience near immediate, weight-independent remission of T2DM, and virtually all achieve improved glycemic control. The exact mechanism of remission is a quandary, however the hypothesis is that RYGB improves glucose homeostasis and insulin sensitivity through differential expression of gastrointestinal peptides. To explore the molecular mechanisms of this, 44 Ossabaw pigs are obtained and raised on a high fat diet that promotes weight gain and insulin resistance. Pigs are randomized to undergo one of 5 operations: RYGB (n=8), RYGB with Vagotomy (n=8), Gastrojejunostomy (n=8), Gastrojejunostomy with Duodenal Exclusion (n=8), or sham (n=4). Intravenous glucose tolerance tests (IVGTT) and meal tolerance tests (MTT) are performed once before the surgery, then again at 30 and 60 days after the surgery. Gastrointestinal tissue samples are collected during surgery and at necropsy on day 60. Samples are taken from the following sites: the stomach, proximal and distal duodenum, proximal and distal jejunum, proximal and distal ileum, and the pancreas. IVGTT and MTT blood samples will be used to determine the physiologic response by analyzing glucose, insulin, GLP-1, PYY, GIP, and ghrelin levels. GI and pancreatic tissue samples will undergo histopathological and mRNA analysis to provide insight into the differential expression of peptides at various locations. The conclusions of this study will help determine the mechanism of glycemic improvement and the cause of T2DM remission.

Poster Session 3

Balcony, Easel 118

4:00 PM to 5:30 PM

The Impact of Mammalian Target of Rapamycin Complex 1 on Primary Liver Cancers

Rebecca Lynn (Rebecca) Mc Intyre, Senior, Biology (Molecular, Cellular & Developmental)
Mentor: Raymond Yeung, surgery
Mentor: Heidi Kenerson, Surgery

Hepatocellular Carcinoma (HCC) and Cholangiocarcinoma (CC) are the two prominent forms of liver cancer in humans. Current treatments show limited success. To further study the molecular mechanism of these diseases, I have made use of a genetically modified mouse model in which two tumor suppressor genes, Tsc1 and Pten, have been knocked out in the liver. I treated these mice with rapamycin, an inhibitor of mammalian target of rapamycin complex 1 (mTORC1) to determine its contribution in tumor development. mTOR is an important pathway involved in the regulation of cell growth, cell proliferation, and protein synthesis, and is implicated in tumor development. The livers of these mice phenotypically display an early onset of HCC and CC by twelve weeks of age. I hypothesized that treatment of these mice with rapamycin would result in decreased mTORC1 activity, which would negatively impact the growth of one or both types of tumors. Additionally, I predicted that mTORC1 activity would have an impact on hepatic steatosis (fatty liver disease). Following a two week treatment with rapamycin, liver tissue was harvested and analyzed for protein expression and activity using western blotting techniques and immunohistochemistry staining. Preliminary results suggest that rapamycin was effective in downregulating mTORC1 activity and in reducing cell and tumor size. Additionally, I witnessed a greater reduction in HCC lesions compared to CC in the treated livers, as well as an increase in steatosis. If future studies confirm these observations, the results suggest that 1) mTORC1 plays a functional role in the development of primary liver tumors, 2) HCC and CC respond to mTORC1 inhibition separately, and 3) rapamycin promotes steatosis. These findings may have implications in the treatment of liver cancers.