Online Proceedings

SESSION 1D

MEDICAL THERAPEUTICS AND ENDOCRINOLOGY

Session Moderator: Ian Sweet, Medicine
231 MGH
1:15 PM to 2:45 PM
* Note: Titles in order of presentation.

The In Vivo Effects of BDE-47 in Hepatic Metabolism
Rebecca Lynn (Rebecca) Mc Intyre, Senior, Biology (Molecular, Cellular & Developmental)
Mary Gates Scholar
Mentor: Raymond Yeung, surgery
Mentor: Heidi Kenerson, Surgery

Obesity is a major cause of health-related problems in the developed world and recently studies have demonstrated a link between environmental factors and obesity. 2,2',4,4'-tetrabromodiphenyl ether (BDE-47) is one toxic chemical used as a flame-retardant in consumer products. BDE-47 contaminants are commonly found in dust, air, and soil and their accumulation in the food chain contributes to significant levels found in humans, particularly children. Recent studies have linked BDE-47 to a range of toxic impacts, including disruption of insulin signaling. The objective of this study is to investigate the in vivo effects of BDE-47 in hepatic metabolism. We hypothesize that the drug will cause increased cell injury, inflammation and accumulation of fat within the liver (hepatic steatosis) and will have significant effects on individuals predisposed to disruption in insulin signaling. In order to disrupt insulin signaling in vivo, we have generated mouse models with liver-specific deletion of Tsc1 and Pten, negative regulators of mTORC1 and Akt respectively. Both of these complexes play critical roles in the cell cycle and insulin metabolism within the liver. Cohorts of Tsc1-/-, Pten-/-, and control mice were exposed to BDE-47 or placebo for six weeks within their first 10-12 weeks of life. During exposure, the mice were tested for insulin sensitivity and glucose tolerance. Liver tissue was also tested for several markers of hepatic insulin signaling post-mortem. Differences in impacts on these genetic mutants could indicate if the BDE-47 targets the Akt or mTOR cascades differently and if those predisposed to aberrations in insulin signaling may be more sensitive to the toxic effects of BDE-47. This study will determine if a significant interaction between the environmental influence of BDE-47 and the genetic deregulation of insulin signaling occurs, which could have deleterious implications for the use of these compounds in consumer products in the future.

POSTER SESSION 3

Balcony, Easel 121
2:30 PM to 4:00 PM

Diabetes, Obesity, and Ossabaw Pigs
Kristin Nancy Kontogianis, Senior, Biochemistry, Business Administration (Human Resources Management)
Mary Gates Scholar
Mentor: David Flum, Surgery
Mentor: Yuki Aoki, Surgery

Obesity is a growing epidemic. Consequently, the percentage of Americans living with Type 2 Diabetes Mellitus (T2DM) has increased; 25.8 million Americans suffer from diabetes, and 90-95% of adult diabetes is T2DM. Bariatric surgeries–gastrointestinal operations designed to encourage weight loss by rerouting and reconnecting various parts of the stomach and small intestine–have been developed in response to increased obesity. A ramification of these surgeries is the elimination of T2DM; 84% of patients with T2DM experienced complete remission of diabetes after bariatric surgery. At RYGB Mechanisms (RYGBM) Animal Lab, we seek to understand the mechanisms of weight loss and T2DM remission in bariatric surgery through the development of an animal model. The animal models selected for this research are Ossabaw pigs. These pigs, raised on high fat diets, are obese and naturally develop insulin intolerance similar to T2DM in humans. There are two leading hypotheses for the causal relationship of bariatric surgery and the elimination of T2DM: the Lower Intestinal Hypothesis and the Upper Intestinal Hypothesis. To test these hypotheses, we perform five variations of bariatric surgery on the animal models: Gastrojejunostomy (GJ), GJ with Duodenal Exclusion, Roux-En-Y Gastric Bypass (RYGB), RYGB with Vagotomy, and Sham operation. We perform these variations of surgeries in attempts to identify which procedures will decrease T2DM while being the least invasive and most recoverable. Pre-operative and post-operative weights indicate if the surgery worked as a weight loss mechanism, while the pre-operative and post-operative changes in insulin sensitivity and gut peptide hormones–

ghrelin, PYY, GLP1–indicate if the procedure succeeded as a T2DM loss mechanism. Since the start of the study, survival rates have improved, and RYGBM compilation of data has increased, thus enhancing conclusive findings, though data to support either hypothesis is still in progress.