FINAL PROJECT REPORT

Date: 24 November 2015

Name:

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Project Title:

Understanding how food leads to fat: the effect of dietary modification on the development of the metabolic syndrome

Research Aim: To elucidate the effect of fat, fructose and salt on the molecular mechanisms influencing the development of the metabolic syndrome (MetS) and its progression to cardiovascular disease (CVD) and type 2 diabetes (DM2) in a unique mouse model.

Research Objectives:

Objective 1. To investigate whether diets rich in fat, salt or sugar (fructose) contribute to the development of either DM2 or CVD in a genetically susceptible mouse model of metabolic syndrome.

Objective 2a. To determine the specific molecular pathways augmented in response to dietary manipulation with overloads of fat, salt or fructose in the context of the metabolic syndrome.

Objective 2b. To identify overlapping molecular pathways activated by these dietary stimuli.

Briefly describe how successful you were in achieving the stated objective(s). If the objective(s) was not achieved, explain why that is the case and describe what you did manage to achieve.

In the first year of this project we successfully completed the 8-week dietary interventions in both wild-type and metabolic syndrome susceptible mice (n=40 per genotype group). During the feeding period physiological data was collected including, weekly body weight changes, blood pressure, cardiac function (via echocardiography), insulin and glucose tolerance testing and monitoring of food and water consumption throughout the study period. As expected animals given either a high fat or high fructose diet gained weight at a greater rate than those animals on either a control diet or high salt diet, irrespective of genetic background. However metabolic syndrome mice gained greater amounts of weight compared to wild-type animals. All three experimental diets resulted in increased mean arterial blood pressure. We are analysing the changes in cardiac function (determined by echocardiography) between the different genotypes and diets.

During the second year we have successfully extracted RNA from the hearts, kidneys and livers of all animals and synthesised cDNA for gene expression analysis. To date we have completed data collection from 15 different genes in the liver samples, 6 genes in the heart samples and a further 7 genes in the kidney samples. We are currently analysing the gene expression data in preparation for publication.

In conjunction with the RNA/cDNA studies, histological investigation of features of pathology associated with metabolic syndrome such as increased fibrosis (liver, kidney and heart), hypertrophy (heart) and increased adiposity (liver, kidney) have been catalogued.

We are currently analysing all data collected to prepare a manuscript for publication, we expect to be able to provide the scientific committee with a full report of all results obtained from this study in February 2016.

Briefly describe any interesting outcomes which might not have been considered in your original objectives (if any).

We decided to run a second study in parallel to high fat diet of this study using beneficial fats from walnuts to compare with the animal derived fats of the commercially sourced diet. We were able to demonstrate a significant improvement in the features of the metabolic syndrome, reduced blood pressure, weight management, improved glucose tolerance in the transgenic animals. We are currently analysing the gene expression data from this study to include in a manuscript which we hope to submit for publication in early 2016.