Higher Dietary Carbohydrates Detrimentally Impact Obesity-Associated Breast Cancer Chemoresistance

Metabolomic Analysis: Metabolomics and Exposome Laboratory, Nutrition Research Institute, UNC Chapel Hill

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**Abstract:**

Epidemiologic and experimental studies have established that obesity is an important risk and/or prognostic factor for most cancer types, but the mechanisms underlying the obesity-cancer link have not been clearly elucidated. The goal of this project is to address questions on the mechanisms of (and potential solutions to) obesity that results directly from diet exposures and the associated chemotherapeutic resistance. In a mouse model of basal-like breast cancer (BLBC), we compared a high protein (HP) diet to a high carbohydrate plus high fat (HCHF) diet and determined their comparative impacts on body weight, fatty liver development, tumor growth acute chemotherapy response to doxorubicin, profiled 80 inflammatory markers and performed untargeted metabolomics. Briefly, female C57BL/6 mice were fed either the HP or HCHF diet for 15 weeks, orthotopically implanted with MMTV-Wnt-1 mammary cells for tumor formation and growth (up to six weeks), then treated with a single dose of doxorubicin (or saline vehicle control) for 24 hours prior to study completion. Mice were euthanized and biospecimens were collected at the following study endpoints: **1-**baseline (following 1-week quarantine); **2-**after the 15 weeks of differential diet exposure; **3-**after 5 weeks and 5.5 weeks of tumor growth; and **4-**after 24 hours of treatment, corresponding to 6 weeks of tumor growth. Untargeted metabolomics analysis was performed by UPLC high resolution mass spectrometry (LCMS) on liver samples at the four study endpoints described above. Liver tissues were sectioned into three discrete lobes (right, left and median=caudate + quadrate) prior to analysis.

The data obtained for the LCMS metabolomics analyses can be found in the accompanying files:

Procedures: 1. DS-Liver-LCMS Metabolomics-Procedures.docx

Study Design Table: 2. DS-Liver-LCMS Metabolomics-Study Design Table.xlsx

Metadata: 3. DS-Liver-LCMS Metabolomics-METADATA.xlsx

Processed Data: 4. DS-Liver-LCMS Metabolomics-Normalized Data.xlsx

Raw Data: 5. DS-Liver-LCMS Metabolomics-Raw Data.zip