**Regulation of Metabolism by LSR**

Metabolomics Analysis: NIH Eastern Regional Comprehensive Metabolomics Resource Core (RTI RCMRC)

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**Abstract:**

Breast cancer is a global crisis, accounting for nearly one quarter of all cancers in women. In the U.S., African-American (AA) women suffer disproportionately from breast cancer mortality compared to other racial/ethnic groups. Both social (socioeconomic factors, diet, obesity) and biological hypotheses (gene polymorphisms, gene expression profiling) have been advanced to explain these discrepancies, but the differences remain poorly understood. Multiple aspects of tumor aggressiveness have been identified in the AA population, including a high proportion of basal-like tumors. Basal-like tumors are clinically the most aggressive, characterized by enhanced cancer stem cell-like features. Currently, no effective molecular therapies exist for these highly aggressive cancers and patient survival is poor. Escalating this disparity is the disease promoting effects of obesity and metabolic syndrome, which are significantly higher in AA women. Obesity and its associated inflammation have been attributed to poor patient outcomes, resistance to chemotherapeutics, and/or cancer risk. A meta-analysis of 43 studies of obesity and breast cancer

revealed that obese patients were 33% more likely than non-obese patients to die of breast cancer. Yet apart from correlative studies, no reports have combined these factors with cancer disparities to ascertain their molecular interactions and physiology on breast tumorigenesis. We tested the integration these factors, with focus on a specific molecule, Lipolysis Stimulated Lipoprotein Receptor (LSR), in the promotion of aggressive cancer behaviors. LSR is a cell surface molecule that regulates post-prandial lipid uptake in the liver, is sensitive to high fat diets, and is regulated by metabolic cues, including leptin. By testing each of these factors as well as their dynamic interactions on breast cancer tumorigenesis, we will gain valuable insight into biological mechanisms that influence cancer risk/disparities, response to therapy, and ultimately patient outcome. We recently reported LSR is overexpressed in breast tumors, directs aggressive breast cancer cell behaviors including proliferation and migration, and enhances cancer stem cell-like and chemotherapeutic resistance features in breast cancer cells. Our aim is to identify the LSR-driven metabolomics profile of breast cancer cells in lean and obesogenic environments. Breast cancer cell models with high or undetectable levels of LSR, including drug resistance models, were cultured in lean and obesogenic environments and comprehensive metabolomics profiling, including lipidomics-focused sub-analyses were performed. The metabolomics analyses using both approaches will help us determine if LSR enhances aggressive breast cancer phenotypes via modulation of cellular bioenergetic metabolism, ultimately contributing to poor patient outcome.

**Sample Description:**

Samples were 20 breast cancer cell pellets. Four cell lines and five replicate sample/line. The cell lines are paired for expression of LSR [MCF7 parental (LSR+), MCF7 Crisper (LSR-), Hs578t parental (LSR-) and Hs578t (LSR++)]. Samples were stored at -80˚C until sample preparation for metabolomics analyses.

The data obtained for the LCMS lipidomics analysis can be found in the accompanying files:

Procedures: 1. Fleming Lipidomics LCMS Procedures.docx

Study Design Tables: 2. Fleming Lipidomics LCMS Study Design Table.xls

Metadata: 3. Fleming Lipidomics METADATA.xlsm

Processed Data: 4. Fleming Lipidomics Positive LCMS Normalized Data.xlsx

Raw Data: 5. Fleming Lipidomics LCMS Raw Data.zip

**Notes:**

Full sample preparation and analysis procedures are available in the accompanying document entitled **1. Fleming Lipidomics LCMS Procedures**.

Descriptions of abbreviations for factors are available in the Variable Dictionary in the accompanying file no. **2. Fleming Lipidomics LCMS Study Design Table.xls**.

The phenotypic and normalized data are available in the accompanying file no **4. Fleming Lipidomics LCMS Normalized Data.xlsx**.

The Sample identifier serves as the unique ID (graphical ID) of the individual samples and is used as the LCMS file name in the raw LCMS data file **5. Fleming Lipidomics Positive LCMS Raw Data.zip.**