**Metabolomics Analysis of Triple Negative Breast Cancer Cell Lines** Metabolomic Analysis: RTI RCMRC

PI, RTI RCMRC Core Collaboration: Delisha Stewart, Ph.D., RTI International

**Abstract:** To date there are no clinically approved targeted therapies for triple negative breast cancer (TNBC). In addition to the absence of estrogen, progesterone, and HER2/neu receptors, TNBCs possess characteristics that make them some of the most aggressive forms of breast cancer (BCa). In terms of epidemiology, breast cancers with the triple negative profile present at a higher prevalence in premenopausal women under the age of 40, usually with a BMI greater than 30, and have higher incidences of mutations in BRCA1 or BRCA2 genes. Additionally, several studies have shown a higher prevalence in African American women, demonstrating a health disparity. In spite of this knowledge and the fact that most people respond to initial chemotherapeutic treatment, lasting treatment modalities used for the cure and maintenance of other BCa subtypes generally fail to significantly increase disease-free survival or diminish the rates of recurrence within the first five years after initial detection of TNBC. We used untargeted metabolomic profiling to distinguish this form of BCa from estrogen receptor positive (ER+) subtypes (+/- HER2/neu) and determine that may explain why a commonly used chemotherapeutic, paclitaxel, is generally ineffective at eliciting long-term cytotoxic and/or cytostatic responses in cell line models of TNBC. Our ultimate goal is to identify novel biomarkers which may be leveraged for initiating prevention strategies in high risk populations, earlier detection, or targeted treatment of this disease.

This metabolomics study used broad spectrum 1H NMR to compare Luminal A (BT474, MCF-7) and triple-negative (MDA-MB-231, MDA-MB-468) BCa cell lines, to determine differences in the two subtypes as well as distinguish therapeutic treatment responses for identifying new targets for drug discovery.

The data required for the metabolomics analysis can be found in the accompanying files:

Procedures: 1. DS\_Cells Metabolomics Procedure.docx

Study Design Table: 2. DS\_Cells Study Design Table.xlsx

Metadata: 3. DS\_Cells MetaData.xlsx

Processed Data: 4. DS\_Cells Normalized Binned Data.xlsx

Raw Data(zip): 5. DS\_Cells NMR Raw Data.zip

**Notes:**

Full sample preparation and analysis procedures are available in the accompanying document entitled **1. DS\_Cells Metabolomics Procedure.docx**.

Descriptions of abbreviations for factors are available in the Variable Dictionary in the accompanying file no. **2. DS\_Cells Study Design Table.xlsx**.

The phenotypic and normalized data are available in the accompanying files: **4. DS\_Cells Normalized Binned Data.xlsx** for normalized binned NMR data. Sample ID and factors can be found in the first 3 columns and other columns in the spreadsheet contain the normalized binned data.

If the statistical program does not allow variable names to begin with a number then add a prefix to the column names, for example, bin\_8.98 instead of 8.98.

The Sample ID serves as the unique identifier (Graphical ID) of the individual samples and is used as the NMR folder name in the raw NMR data file **5. DS\_Cells NMR Raw Data.zip**.