**Preterm Neotal Urinary Renal Development and Acute Kidney Injury Metabolic Profiling**

Metabolomic Analysis: RTI RCMRC

PI, RTI RCMRC P&F Study: Patrick D. Brophy MD, University of Iowa

David Askenazi MD, University of Alabama

**Abstract:** Metabolomics is an emerging field in analytical biochemistry that is increasingly being recognized as the functionally most relevant discipline in personalized health care. Given the rapid advancement of genomics and proteomics in the identification of renal disease markers, the next logical step would be to evaluate the role of metabolomics as a diagnostic and experimental paradigm in the renal disease setting. The possibility that urine may be an important source of disease biomarkers in enticing because it is a complex, yet easily obtained body fluid particularly in the Neonatal population where blood draws can be problematic. There is currently a national strategy being devised in pediatrics in order to evaluate the effect of medication induced Acute Kidney Injury (AKI) and its relationship to morbidity, mortality and cost to the to the individual and the health care system as a whole. Within the realm of Pediatrics, Neonatology represents an at risk population in that little in understood about the potential development and impact of AKI. Standard codification of stages of AKI have been developed and validated in both pediatric and adult populations yet these criteria do not exist in neonatology (particularly pre-term infants). Creatinine as a measure of renal dysfunction suffers from considerable confounders and new proteomic-based biomarkers are being investigated in the Pediatric and adult patient population. The evaluation of these newer proteomic biomarkers has just begun in the neonatal population. Given the paucity of data available for neonatal patients, the proposal herein outlines a pilot project, metabolomics based strategy, to define a normative (no AKI) data set for preterm infants and identify changes in the urinary metabolic profile in preterm infants who have developed creatinine defined AKI based on commonly used birth weight indices (500-750 gm, 750-1000 and 1000-1500 gm). The results of these data will provide the basis for future multicenter studies whereby urinary metabolomics analysis can identify, in real time, the evolution of renal dysfunction in an early diagnostic, monitoring and prognostic fashion. This will be done in the context of renal developmental changes which metabolomics wikll be particularly valuable at determining. The use of metabolomics profiles in this population will help define early AKI prior to changes in serum creatinine and therefore all0ow early intervention that will positively impact on health outcomes in the Neonatal population.

**Goals**

Brophy and Askenazi hypothesize that postnatal renal maturation results in specific identifiable patterns of urinary metabolites and that these profiles will be altered in the presence of AKI. Their long-term goal is to identify novel metabolomics urinary profiles that can provide real-time evidence of evolving neonatal renal injury thereby allowing earlier diagnosis and treatment.

**Sample Description**

This study includes 40 pre-term infants age 2 days. Twenty infants were identified as not having AKI (11 females, mean gestational age=182.8 days, mean birth weight=834.0 grams) and 20 infants were identified as having AKI (13 females, mean gestational age=183.9 days, mean birth weight=815.8 grams). There are no statistical differences between the two groups based on gender, gestational age, and birth weight.

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

Procedures: 1. NeonatalAKI Metabolomics Procedure

Study Design Table: 2. NeonatalAKI Study Design Table

Metadata: 3. NeonatalAKI METADATA

Processed Data: 4. NeonatalAKI Normalized Binned Data

Raw Data (folders): 5. NeonatalAKI\_Raw\_NMR\_Data

**Notes:**

Each of the bin integrals were normalized to the total integral of each of the NMR spectrum (for more details, see accompanying Procedures file, **1. NeonatalAKI Metabolomics Procedure.docx**).

Descriptions of abbreviations for factors are available in the Variable Dictionary in the accompanying Study Design Table files, organized by sub-study i.e. **2. NeonatalAKI Study Design Table.xlsx**.

The normalized binned NMR data are available in the accompanying Processed Data files for each matrix per sub-study (i.e. **4. NeonatalAKI Normalized Binned Data.xlsx)**. Sample ID and factors can be found in the first 2 columns in the file no. 4. 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.

Sample ID serves as the unique identifier of the individual samples and is used as the NMR folder name in the raw NMR data file.