**Biomarker Discovery in Knee Osteoarthritis**

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

PI, RTI RCMRC P&F Study: Richard F. Loeser Jr., MD, Wake Forest University

Joanne M. Jordan, MD, MPH, UNC-Chapel Hill

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**Abstract:** Collaboration with Richard Loeser at Wake Forest University and Joanne Jordan at UNC-Chapel Hill (original sample collection was performed under the Johnston County Osteoarthritis Project funded by Centers for Disease Control and Prevention [CDC]1UO1DP003206-01, **CDC/Association of Schools of Public Health S043, S1733, and S3486, and the National Institute of Arthritis and Musculoskeletal and Skin Diseases [NIAMS] 5-P60-AR30701 and P60-AR49465;** Joanne M. Jordan, MD, MPH, PI). The Johnston County Osteoarthritis Project (JoCo) is a 20+ year ongoing, population-based, prospective cohort study of knee and hip OA designed to be representative of the civilian, non-institutionalized, African American or Caucasian population aged 45 years and older, who were residents of one of 6 townships in Johnston County NC for at least 1 year, and who were physically and mentally capable of completing the study’s protocol. All participants had an initial home interview, a clinic examination with radiographs, and a subsequent second home interview. Approximately 3,200 individuals were recruited into the baseline evaluation between 1991 and 1997 (T0); the first follow up visit (T1) occurred from 1999-2004, and the second follow up visit (T2) from 2006-2010. Cohort enrichment (T1\*) occurred from 2003-4, allowing new participants to be enrolled; the first follow up for these individuals was at T2. At T0, the sample was approximately 38% men and one-third African American. Between T0 and T1, radiographic knee OA, defined as Kellgren-Lawrence grade 2-4, developed in 12% of knees without knee OA at T0.

This metabolomics pilot and feasibility (P & F) study was conducted to provide data to be used to gain a better understanding of metabolic alterations in people with knee osteoarthritis (OA) and to discover novel biomarkers of the disease. The goal of the metabolomics study was to determine if metabolic differences, detected by a comprehensive metabolomics analysis, can be used to distinguish people who will develop symptomatic knee OA from those who will not.

For this metabolomics study, individuals participating in T1 or T1\* with 5-year follow-up at T2 were selected. At T2 subjects were on average 68.1(±9.12) years old with an average BMI of 31.4(±7.01) with 32% men and one-third African American. All had weight-bearing posterior-anterior knee films obtained with the Synaflexer positioning device at both time points and read paired for Kellgren-Lawrence grade and minimum joint space. Urine samples (second morning void) collected from 36 overweight or obese participants in the JoCo at T1 or T1\* were selected from two subgroups (a group that developed radiographic osteoarthritis (n=16) and an age, race, sex, and BMI matched group that did not develop osteoarthritis (n=20). Radiographic knee OA was defined as Kellgren-Lawrence grade 2-4 at T2 in a person with Kellgren-Lawrence grade 0 or 1 at T1 or T1\*.

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

Procedures: 1. WOA\_JC Metabolomics Procedure.docx

Study Design Table: 2. WOA\_JC Study Design table.xlsx

Metadata: 3. WOA\_JC Metadata and Analytical Metadata.xlsm

Processed Data: 4. WOA\_JC Phenotypic and Normalized Binned Data.xlsx

Raw Data: 5. WOA\_JC Raw NMR Data.xlsx

**Notes:**

Each of the bin integrals were normalized to the total integral of each of the NMR spectrum (for more details, see accompanying file no. **1. WOA\_JC Metabolomics Procedure.docx**)

Descriptions of abbreviations for factors are available in the Variable Dictionary in the accompanying file no. **2. WOA\_JC Study Design table.xlsx**.

The phenotypic and normalized binned NMR data are available in the accompanying file **4 (WOA\_JC Phenotypic and 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.

**Reference:**

Nelson AE, Braga L, Renner JB, Atashili J, Woodard J, Hochberg MC, Helmick CG, Jordan JM. Characterization of individual radiographic features of hip osteoarthritis in African American and white women and men: The Johnston County Osteoarthritis Project. 2010. Arthritis Care and Research, 62(2):190-7.PMCID: PMC2846079

Braga L, Renner JB, Schwartz TA, Woodard J, Helmick CG, Hochberg MC, Jordan JM. Differences in radiographic features of knee osteoarthritis in African-Americans and Caucasians: The Johnston County Osteoarthritis Project. 2009. Osteoarthritis & Cartilage,7(12),1554-61.