



**Control/Tracking Number:** 16-A-1050-OARSI

**Activity:** Abstract

**Current Date/Time:** 11/16/2015 7:42:15 PM

# **METABOLIC PROFILES ASSOCIATED WITH RADIOGRAPHIC KNEE OSTEOARTHRITIS IN A POPULATION-BASED COHORT OF MIDDLE-AGED WOMEN**

**Author Block:** J. Bacardit<sup>1</sup>, A. Mobasher<sup>2</sup>, S. Kluzek<sup>3</sup>, M. Edwards<sup>4,5</sup>, T. Spector<sup>6</sup>, D. Hart<sup>7</sup>, C. Cooper<sup>3,5</sup>, N. Arden<sup>3,5</sup>; <sup>1</sup>Newcastle Univ., Newcastle upon Tyne, United Kingdom, <sup>2</sup>Univ. of Surrey, Guildford, United Kingdom, <sup>3</sup>Univ. of Oxford, Oxford, United Kingdom, <sup>4</sup>Univ. of Southampton, Southampton, United Kingdom, <sup>5</sup>MRC Lifecourse Epidemiology Unit, Southampton, United Kingdom, <sup>6</sup>King's Coll. London, London, United Kingdom, <sup>7</sup>King's Coll. London, London, United Kingdom

## **Abstract:**

**Purpose:** Osteoarthritis (OA) is associated with significant risk of cardiovascular disease, dyslipidaemia, type 2 diabetes and central obesity, suggesting early metabolic dysregulation. The exact mechanism underlying those associations is unknown, but recent literature points towards deregulation of several metabolic pathways. Understanding those links could open new avenues advancing biomarker discovery and future targeted intervention. Systemic metabolomic profiling, also called metabolomics, gives a comprehensive snapshot of metabolic activity by measuring levels of molecules involved in different metabolic pathways.

The aim this project was to screen the comprehensive metabolomics data, and identify possible metabolic pathways associated with radiographic knee osteoarthritis in a homogenous cohort of middle-age women.

**Methods:** The Chingford 1000 Women study is a population-based cohort of middle-aged women recruited from a single general practice. This cohort has been shown to be representative of women in England.

Out of 1,003 recruited, 861 attended year 5, and 872 year 6 of follow-ups. 477 serum samples were collected at year 6 follow-up and later analysed by the Metabolon, Biotechnology Company specialising in metabolomics, using the tandem mass spectrometry platform for metabolomics. Levels of 711 biochemicals, associated with different metabolic pathways, have been analysed.

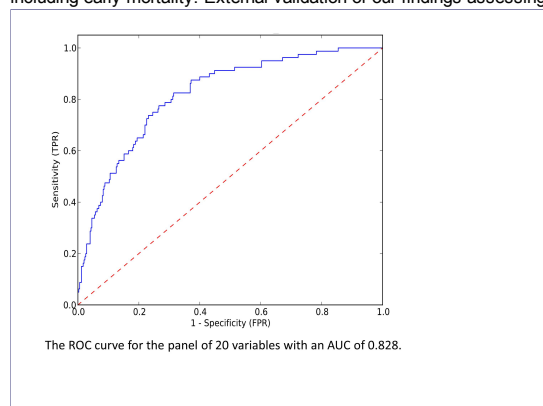
A weight-bearing anteroposterior radiographic knee examination was performed at year 5 to assess the Kellgren-Lawrence (K/L) OA grade of each knee. Women were classified as having radiographic KOA (RKO) if they had a Kellgren-Lawrence (K/L) OA grade of 2 or more in at least one knee.

431 women (mean  $\pm$  SD age:  $53.2 \pm 5.8$  yrs, body mass index:  $26.4 \pm 4.4$ ) had both serum samples analysed and knee x-ray performed. 80 participants from that group had an evidence of RKO in one or both knees.

We used our RGIFE algorithm, a machine learning heuristic method, to identify reduced panels of variables strongly associated with RKO. The RGIFE algorithm builds a classification model using the RandomForest algorithm to estimate the relevance of a panel of variables. The quality of a model is estimated by computing the area under the curve (AUC) for the receiver operating characteristic (ROC) curve. Finally, the permutation tests were used to rule out spurious associations. In each permutation, the outcome variable for each participant (RKO or not) was scrambled, and the prediction model was trained and tested again. This process was repeated 100 times and the permutation results were compared with the results obtained from the original dataset.

**Results:** RGIFE was able to identify several reduced panels of variables with varying trade-off between AUC and number of variables. The best panel had 20 variables (out of 713) and an AUC of 0.828. The ROC curve for this model is shown at the right. The biochemicals most frequently appearing in these reduced panels were X15694, xylolate, X12244 and lactate. A model containing only age and BMI obtained an AUC of 0.662. None of the permutations had an AUC higher than what was obtained from the original data (mean AUC  $0.645 \pm 0.03$ ).

**Conclusions:** The analysis of the metabolomics data generated from the Chingford cohort that some of the measured biochemicals, especially those linked with the carbohydrate metabolism, are associated with RKO. We propose to use this information to construct analyses of metabolic pathways in KOA and try to link them with clinically relevant outcomes, including early mortality. External validation of our findings assessing correlation between identified biochemical and RKO is needed.



**Category (Complete):** Biomarker

**Keyword (Complete):** Knee Osteoarthritis ; Mass Spectrometry ; Metabolism ; Biochemical Marker

**Presentation Preference (Complete):** Poster Preference

**Additional (Complete):**

**Payment (Complete):** Your credit card order has been processed on Monday 16 November 2015 at 7:40 PM.

**Status:** Complete

[Osteoarthritis Research Society International](http://www.oarsi.org)

1120 Rt. 73, Ste. 200

Mt. Laurel, NJ 08054, USA

[mrvan@oarsi.org](mailto:mrvan@oarsi.org)