Osteoarthritis Research Unit, Montreal, Canada; J. P. Pelletier1, J. P. Raynauld1, F. Abram2, M. Dorais3, P. Paiement4, J. Martel-Pelletier5.

Methods: Participants were selected from the Osteoarthritis Initiative database. In this nested case-control design study, participants who received one treatment with IACI and had MRI exams available at the yearly follow-up visits before (pre-treatment), during (treatment), and after (post-treatment) were defined as “cases”. Each case was matched with one control for age, gender, body mass index (BMI), height, joint space width (JSW), cartilage volume, bone marrow lesion (BML), bone curvature), X-rays (JSW), and symptoms Osteoarthritis Index (WOMAC) pain at baseline. Ninety-three (93) patients from healthy people, as well as RA patients, would be extremely helpful for early diagnosis and treatment of these two diseases. Based on the hypothesis that each disease state may cause specific changes to the metabolome, metabolomics is becoming a powerful tool for biomarker discovery. In this work, we applied a high-performance chemical isotope labeling (CIL) LC-MS platform to search for biomarker candidates of PsA and AS in human serum samples.

Objectives: We aimed to identify metabolite biomarkers with high specificity for PsA and AS.

Methods: Serum samples were collected from 331 subjects, including 100 healthy controls, 48 PsA patients, 52 AS patients and 131 RA patients. The average age of each group was: 52.6 (control), 50.7 (PsA), 51.8 (AS) and 53.1 (RA) years. After pre-treatment, each sample was incubated with 12C-dansyl chloride, which can label the amine/phenol-containing metabolites. The reference sample for relative quantification was prepared by mixing all individual samples and then labeled with 13C-dansyl chloride. With this normalization, the individual samples and the reference sample were treated as an equal amount. Finally, we used the LC-QTOF-MS platform to analyze the mixtures and measure the 13C/12C peak pairs.

Results: We detected 1,149 peak pairs commonly existing in the serum samples. Using our dansyl-library of 700 dansyl-labeled standards and a prediction library, which contains the predicted retention times and masses of 3,431 dansylated human metabolites, we identified 134 and 141 peak pairs, respectively. The relative concentrations are calculated from the intensity ratios of 13C/12C peak pairs. We visualized the entire amine/phenol-submetabolome for all phenotypes using the partial least squares discriminant analysis (PLS-DA). We found that the most significant between-group separation was between healthy controls and all the patients. No significant sex or age effect was observed. Furthermore, among the three diseases, PsA and AS samples were closely clustering, while the RA group was well separated from them. Therefore, we chose a two-step diagnosis approach that first differentiates PsA patients from controls/RA patients and then filters out the AS patients wrongly classified as PsA in the first step. The same strategy was conducted for AS. Stipulating a fold change larger than 1.5 with the false discovery rate lower than 5%, we found 74 metabolites having significantly