sex/age-matched healthy controls: 50 in Cohort 1, 50 in Cohort 2, and 100 in Cohort 3. Among these 446 subjects, 75% were females and the average age was 52.5 years. Amine/phenol-containing metabolites were labeled by 13C-dansyl chloride to improve the LC-MS detection. For each cohort, a pooled sample was prepared and labeled by 13C-dansyl group to serve as the reference sample for relative quantification. Then the individual samples and the pooled sample were mixed 1:1. Finally, an LC-QTOF-MS platform analyzed the mixtures and output the intensity ratios of 12C/13C peak pairs.

**Results:** 1,149 amine/phenol-containing metabolites were commonly detected across the three sample sets. Among them, 134 were positively identified by our dansyl-labeling standard library, and 141 were matched to predicted retention times and mass values of dansyl-labeled human metabolites. Visualized by the partial least squares discriminant analysis (PLS-DA), the overall amine/phenol-submetaabolome demonstrated clear and consistent differences between healthy controls and the RA groups, with cross-validation Q2 = 0.785, 0.745, 0.793, respectively. The selection of significant metabolites was conducted according to the fold change and false-discovery-rate-adjusted Welch's t-test. Cohort 1 demonstrated 85 metabolites having higher concentrations in the RA samples than the controls, and 89 metabolites with lower concentrations. The number of increased/decreased metabolites in Cohort 2 and 3 were 87/26 and 90/53, respectively. Importantly, there were 99 significantly discriminatory metabolites commonly found in the three data sets (49 increased and 9 decreased). We picked the top three with the highest univariate classification performance to form a biomarker panel. We implemented the linear support vector machine (SVM) to build the classifier and the receiver operating characteristic (ROC) analysis to measure the performance. The area-under-the-curve (AUC) values (95% confidence interval) were 1.000 (1.000-1.000), 0.992 (0.967-1.000) and 0.902 (0.858-0.945) for the three cohorts, respectively. These results revealed the importance of examining multiple sample sets and even in the worst case (Cohort 3), our biomarker candidates could differentiate RA at 82.5% sensitivity and 82.5% specificity. Particularly, in Cohort 3, there were 30 RA patients negative for anti-cyclic citrullinated peptide and rheumatoid factor, and our metabolite panel demonstrated consistently high performance for differentiating these specific subjects from healthy controls.

**Conclusion:** Metabolites showing significant and consistent changes associated with RA have been identified with high discriminative power.

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**OBESITY PREDICTS RESPONSE TO NOT ALL BUT CERTAIN BIOLOGICAL/TARGETED DISEASE MODIFYING ANTI-RHEUMATIC DRUGS FOR RHEUMATOID ARTHRITIS - RESULTS FROM KANSAI CONSORTIUM FOR WELL-BEING OF RHEUMATIC DISEASE PATIENTS (ANSWER COHORT)**

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**Background:** A number of previous reports suggested that obesity is one of the baseline factors indicating refractory to biologic disease-modifying antirheumatic drugs (bDMARDs). However, difference of the significant responses appears on obesity patients depending on each kind of drug is yet unclear. However, it is yet unclear how the significant responses on obesity patients vary on each kind of drug.

**Objectives:** To assess whether obesity affects clinical outcome in rheumatoid arthritis (RA) treated with each molecular-targeted agent including bDMARDs and tocafentin.

**Methods:** In Kansai consortium for well-being of rheumatic disease patients (ANSWER) cohort, which was the real-world retrospective cohort of clinical database for rheumatic diseases, RA patients who initiated biological / targeted disease modifying anti-rheumatic drugs were included and consecutively followed. Obesity was defined as BMI over than 25, and patients were divided between