

## Unveiling Urinary Metabolites as Potential Biomarkers for Seronegative Rheumatoid Arthritis Using Mass Spectrometry

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### Abstract:

**Objective:** Seronegative rheumatoid arthritis (negRA) is characterized as RA in which there are no circulating autoantibodies, including anti-citrullinated protein antibodies or rheumatoid factor antibodies. Diagnosing seronegative RA early can be challenging. In the present study, we explored urine metabolic profiles of seronegative RA.

**Methods:** We analyzed urine samples from 35 negRA patients and 25 healthy controls (HC) by applying untargeted metabolomic analysis. Metabolomic profiles were assessed using LC-QTOF-MS and GC-MS methods. We constructed a machine learning-based multivariate classification model, identified discriminating metabolites, and examined the relationships between metabolomic profiles and clinical variables.

**Results:** The urine metabolome profile of seronegative RA was distinguishable from HC. We identified the most significant differences in a panel of seven urine metabolites in the discovery cohort.

**Conclusion:** We developed a model based on urine metabolic markers that may be useful for diagnosis. Our findings suggest that comprehensive, integrative urine metabolomic profiling is an efficient system biology method for finding indicators that help diagnose seronegative RA.

**Keywords:**

Seronegative autoimmune diseases, Metabolic profiling, Oxidative stress, Joint inflammation, Partial least squares-discriminant analysis.