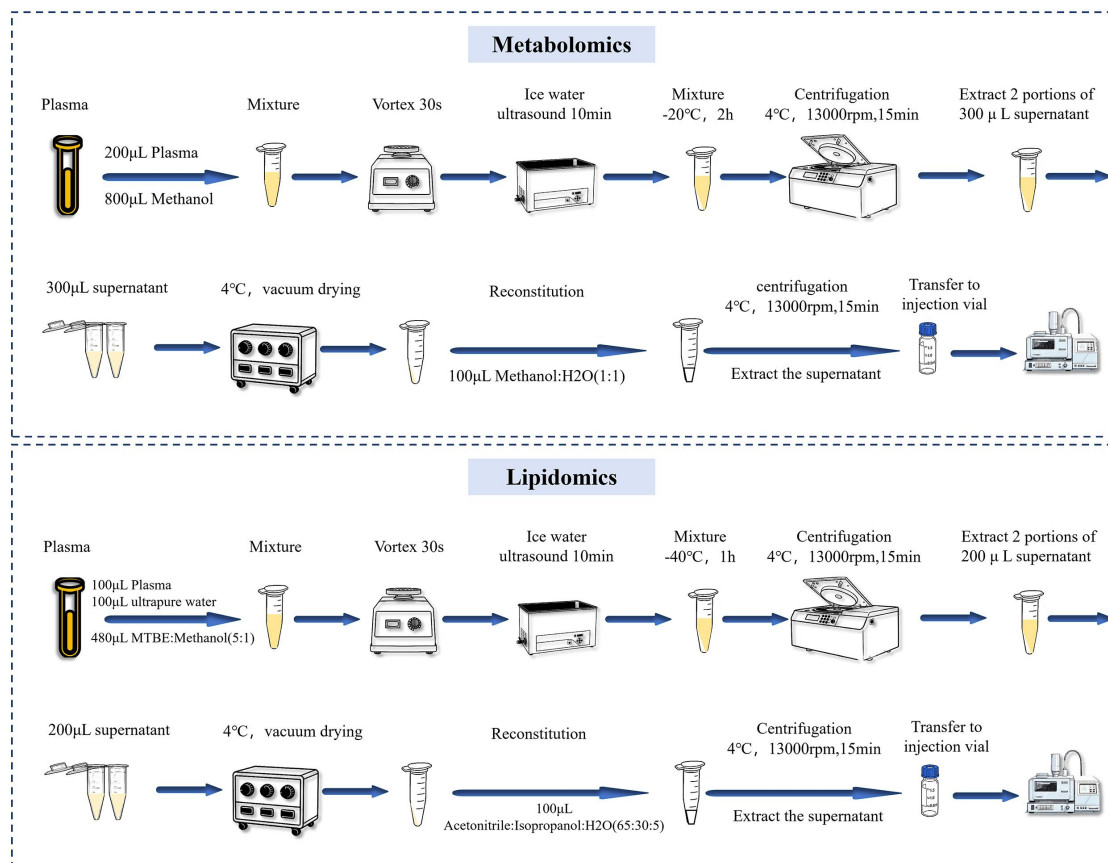
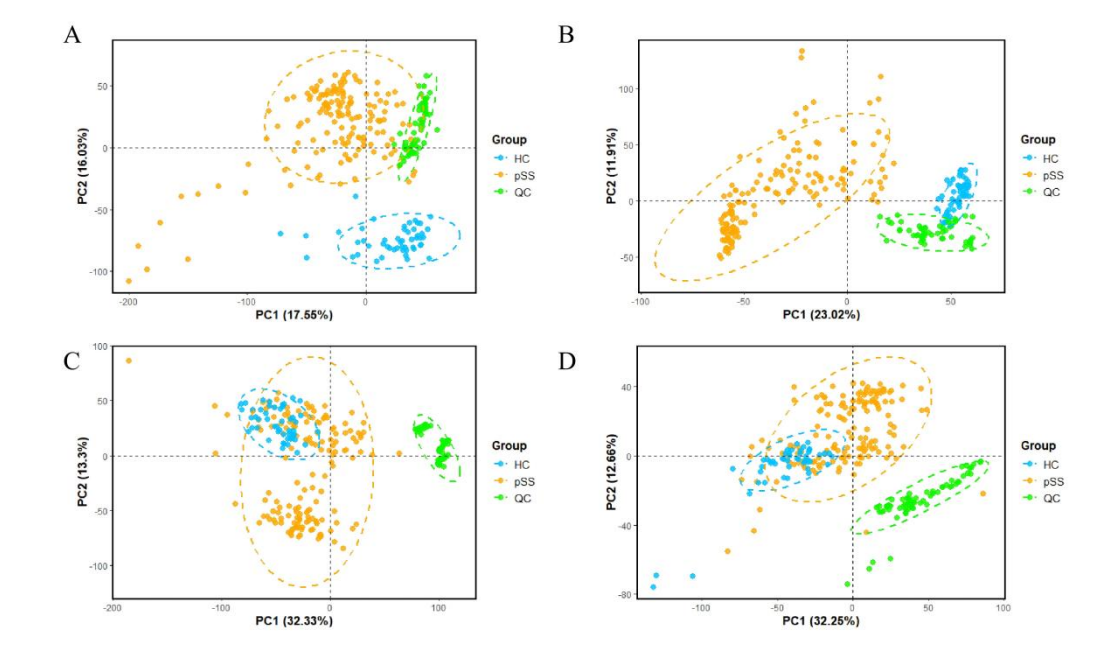




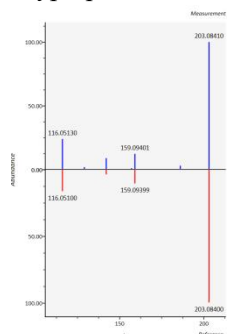
Supplementary figure 1. Schematic diagram of plasma metabolomics/lipidomics pretreatment workflow.



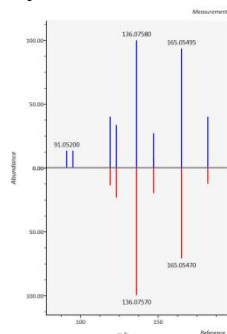
Supplementary figure 2. Two-dimensional PCA score plot of all samples

Scores were derived from log-transformed, mean-centered data. Percentages of variance explained by PC1 and PC2 are indicated in parentheses on the axes. (A) Metabolomics, positive ion mode; (B) Metabolomics, negative ion mode; (C) Lipidomics, positive ion mode; (D) Lipidomics, negative ion mode.

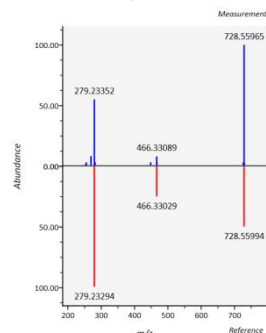
Tryptophan,  $C_{11}H_{12}N_2O_2$ ,  $m/z$  203.084,  $[M-H]^-$ , RT 2.7876min, Rev.prod.:0.9321, HMDB0000929



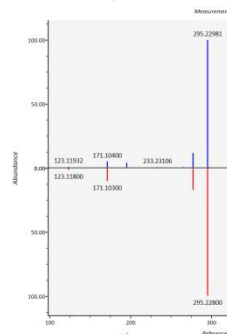
Tyrosine,  $C_9H_{11}NO_3$ ,  $m/z$  182.0812,  $[M+H]^+$ , RT 1.2368min, Rev.prod.:09676, HMDB0250803



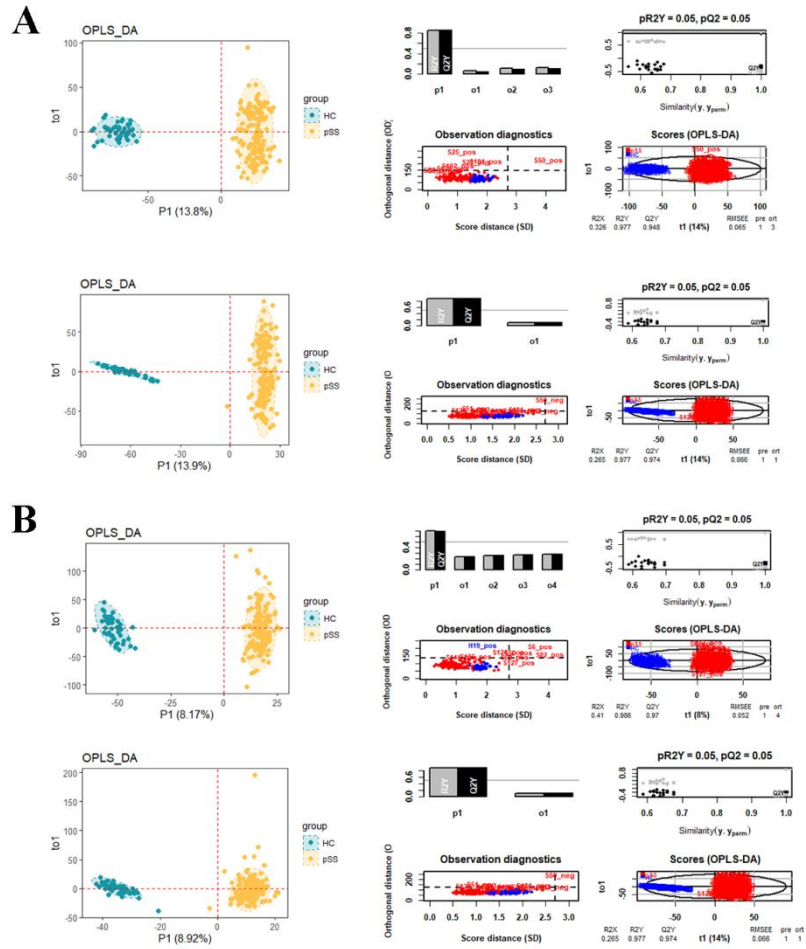
PE O-36:2,  $C_{41}H_{80}NO_7P$ ,  $m/z$  728.5599,  $[M-H]^-$ , RT 15.1361min, Rev.prod.:0.8425



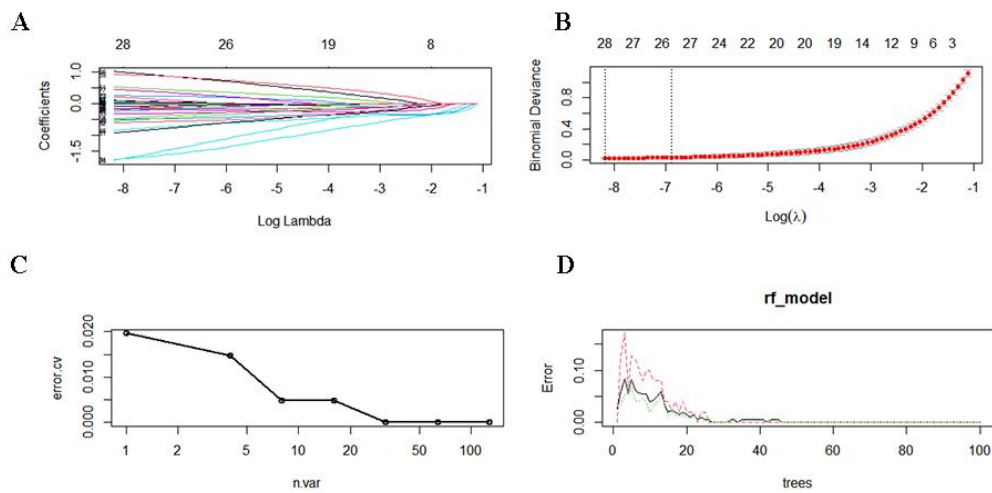
9-HODE,  $C_{18}H_{32}O_3$ ,  $m/z$  295.228,  $[M-H]^-$ , RT 19.3867min, Rev.prod.:0.9312, HMDB0004677



Supplementary figure 3 Characteristics and reference spectra of typical metabolites identified in human plasma.



Supplemental figure 4 (A) Metabolomics and (B) lipidomics profiling analysis for human serum OPLS-DA score plots from the pSS and HC.



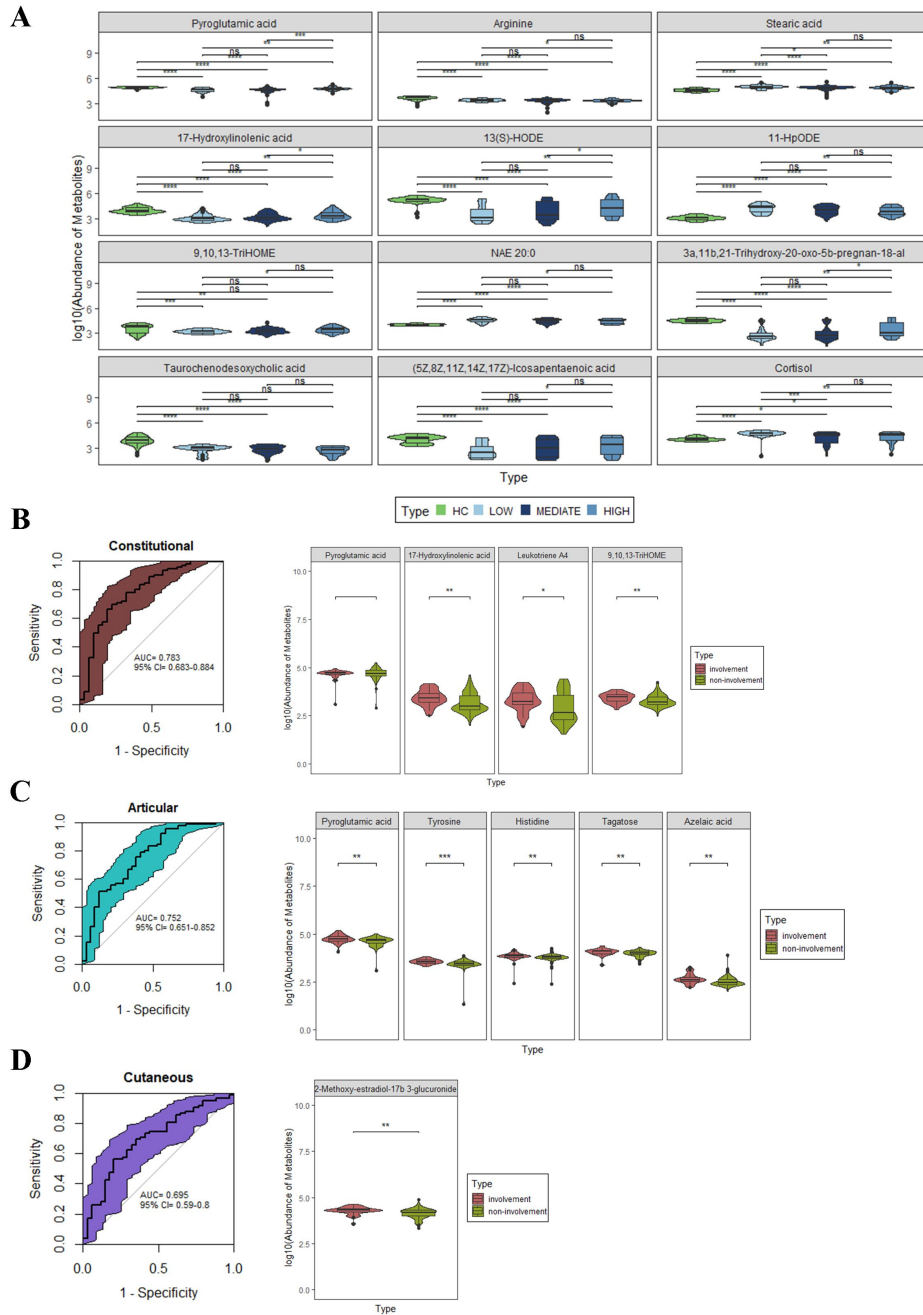
Supplemental figure 5 Biomarker selection via LASSO regression and Random Forest.

(A) Variable coefficient paths. The vertical line indicates the optimal  $\lambda$  where a subset of features is selected.

(B) Cross-validation for determining the optimal penalty parameter ( $\lambda$ ) in LASSO regression.

(C) Error rate of the Random Forest model versus the number of features.

(D) Error rate stabilization as the number of trees increases, indicating model robustness.



Supplemental figure 6 Stratification of disease activity and organ involvement in pSS based on metabolomic and lipidomic profiles.

(A) Violin plots displaying the expression levels of metabolites associated with ESSDAI across different disease activity groups (e.g., low, mediate and high). Each group is represented by a distinct color.

(B) Left: ROC curve for distinguishing constitutional involvement, with the AUC highlighted in purple. Right: Violin plot showing the distribution of a specific metabolite related to constitutional involvement.

(C) Left: ROC curve for distinguishing articular involvement, with the AUC indicated in green. Right: Violin plot illustrating the distribution of a metabolite associated with articular involvement.

(D) Left: ROC curve for distinguishing cutaneous involvement, with the AUC shown in teal. Right: Violin plot depicting the distribution of a metabolite relevant to cutaneous involvement.