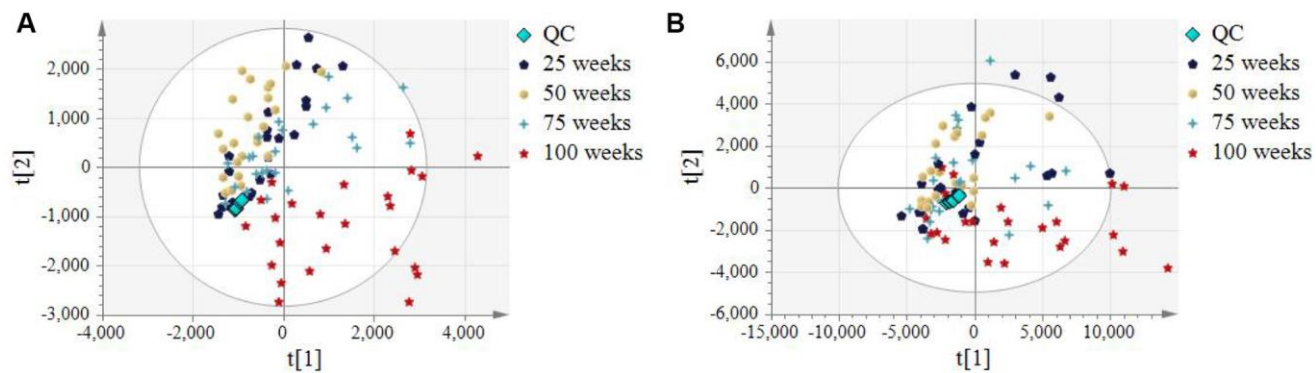
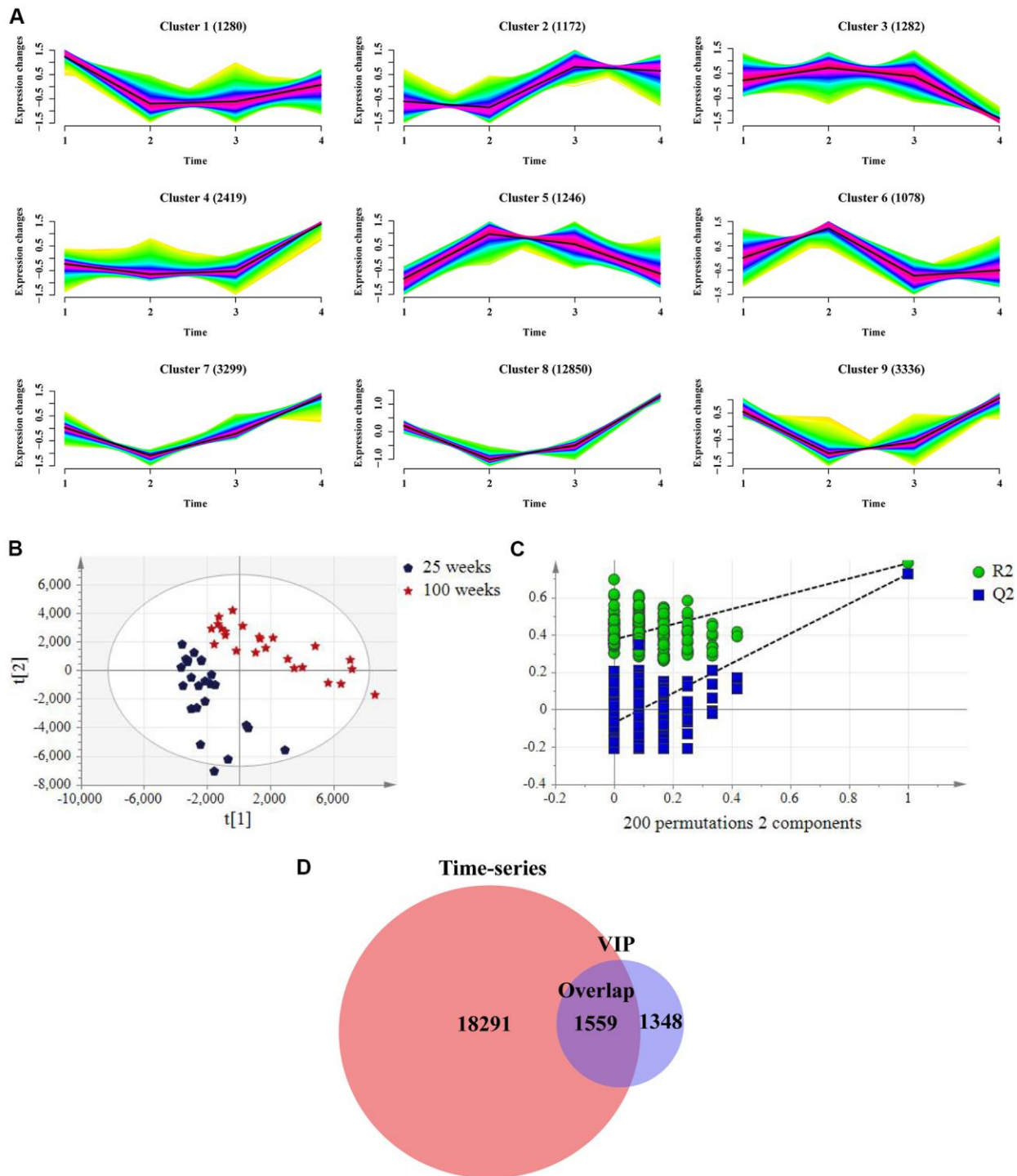


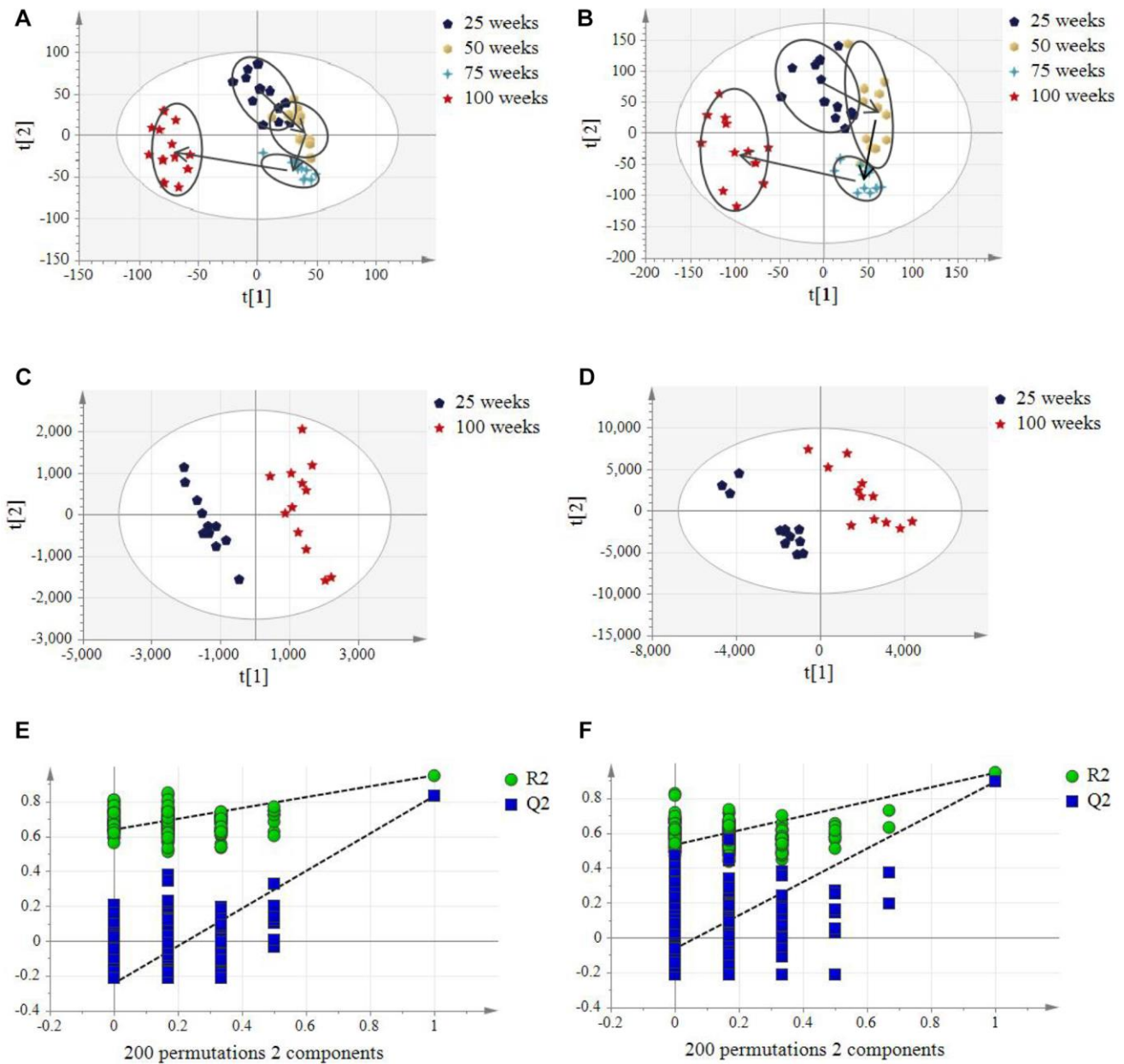
SUPPLEMENTARY FIGURES



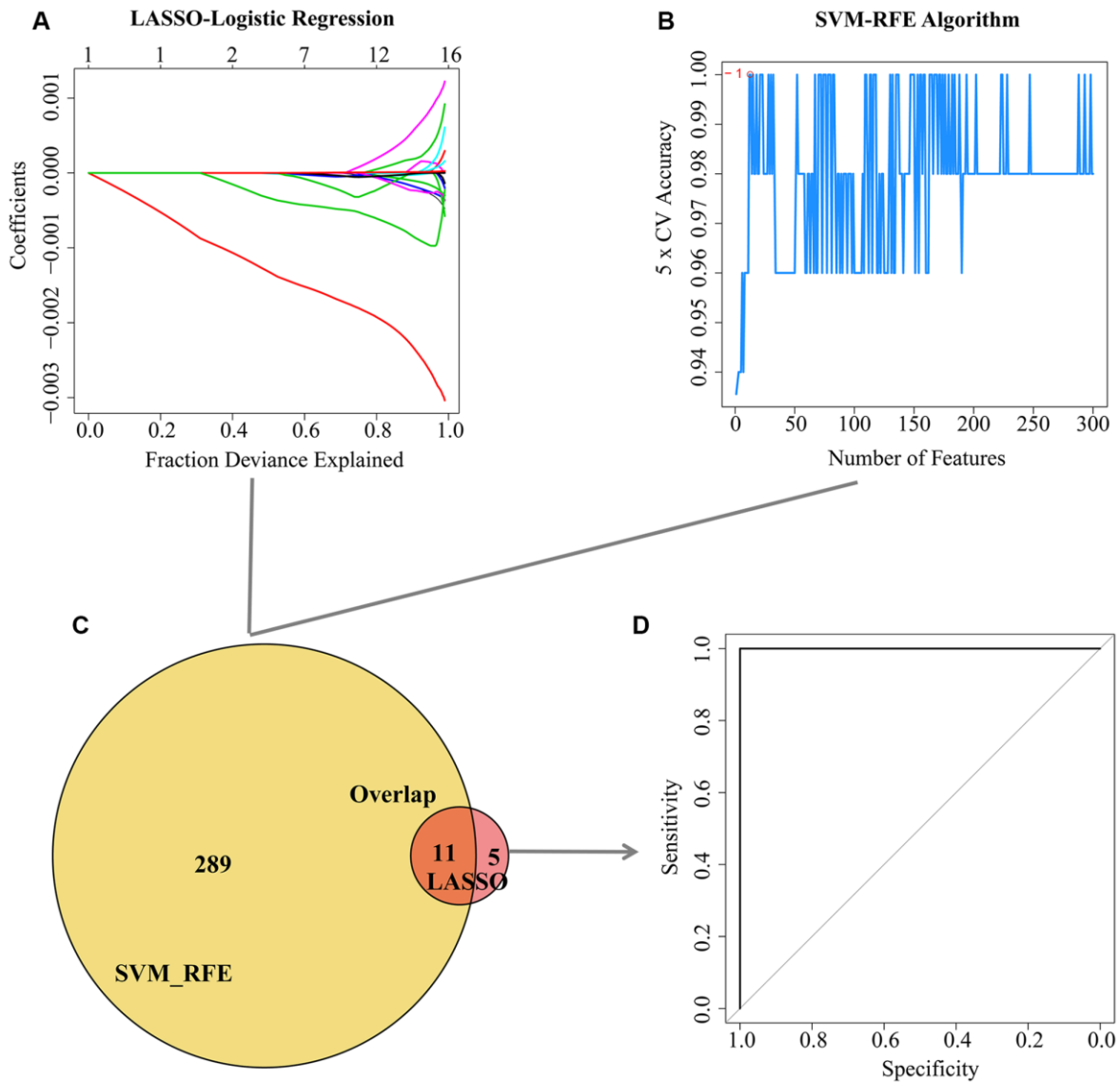
Supplementary Figure 1. PCA scores plots of urine obtained from the UPLC-Q-TOF-MS. PCA score plots including quality control (QC) samples and experimental samples of time data in (A) the positive mode and (B) the negative mode.



Supplementary Figure 2. Screening metabolites in combination with time-series analysis and variable importance in the project (VIP) value in the positive mode in the training group. (A) Metabolic aging trajectories. Fuzzy c-mean clustering of all 27962 metabolite abundances. Average trend of clusters is shown as a black line. **(B)** PLS-DA scores plots of rat urine at 25 weeks and 100 weeks. (ESI+, R2Y= 0.784, Q2 = 0.727). (n = 24 each time point). **(C)** Permutation test with 2 components of PLS-DA score plot. **(D)** Venn diagrams demonstrated the overlap of metabolites in combination with two algorithms.



Supplementary Figure 3. Aging trajectories in the negative and positive modes in the test group. (A–B) PLS-DA scores plots of urine obtained from the UPLC-Q-TOF-MS with aging in (A) left: the negative mode, and (B) right: the positive mode in the test group. ($n = 12$ each time point) (C–D) PLS-DA scores plots at 25 weeks and 100 weeks in (C) left: the negative mode, and (D) right: the positive mode in test group. (ESI–, $R^2Y = 0.95$, $Q^2 = 0.832$; ESI+, $R^2Y = 0.946$, $Q^2 = 0.895$). ($n = 24$ each time point). (E–F) Permutation test with 2 components of PLS-DA scores plots related to Figure C and D in (E) left: the negative mode, and (F) right: the positive mode in the test group.



Supplementary Figure 4. Two algorithms based on machine learning were used for feature selection in the positive mode. (A) Least Absolute Shrinkage and Selector Operation (LASSO) algorithm in the training group. **(B)** Support Vector Machine-Recursive Feature Elimination (SVM-RFE) algorithm in the training group. **(C)** Venn diagrams demonstrated the overlap of metabolites in combination with two algorithms. **(D)** 11 candidate metabolites detected in the training group were validated in the test group using receiver operator characteristic (ROC) curve analysis.