

Figure S1. Diversity analysis between healthy cattle and cattle with respiratory disease. (A) The OUT clusters and annotation of each sample. **(B)** The evolution tree displays the similarity of whole samples. **(C)** Principal coordinate analysis (PCoA) using the weighted-UniFrac algorithm of beta diversity. **(D)** PCoA using Weighted-UniFrac of beta diversity. **(E)** PLS-DA analysis on the OUTs classification information of each sample. OUT, operational taxonomic unit.

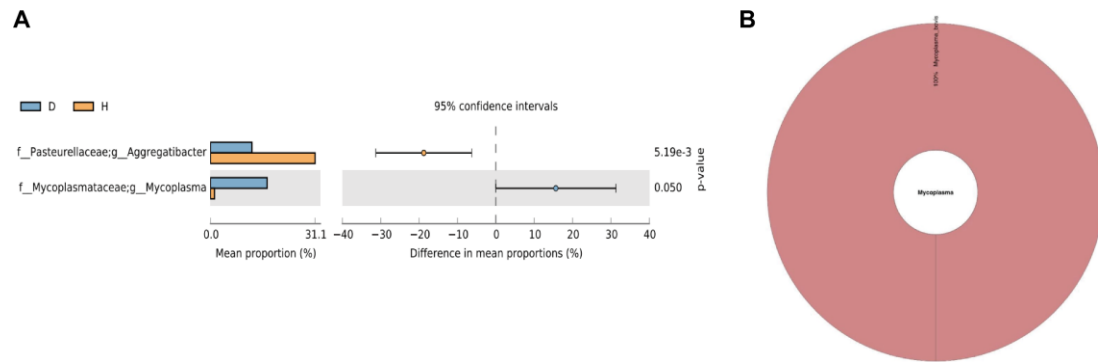


Figure S2. Identification of key pathogenic bacteria. (A) Student's t-test analysis of key bacterial types with significant differences between diseased D and healthy H groups. (B) Species annotation of the whole samples by Metagenomic sequencing.

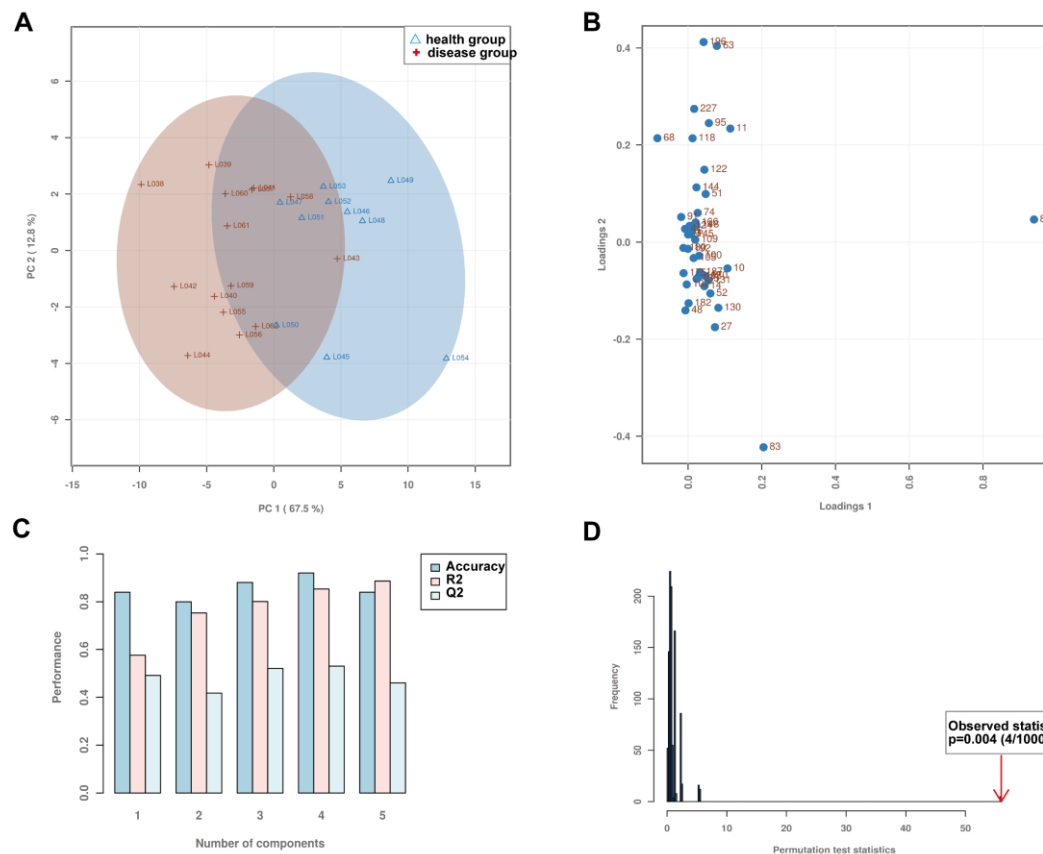


Figure S3. Unsupervised principal component analysis (PCA). Scores plot (A) and Loading plot (B) of GC-MSD profiled plasma from healthy and BRD cattle. (C) Cross-validation diagram of PLS-DA model. In this model, R2: 0.8535, Q2: 0.5300. (D) Permutation test compared with PLS-DA model. GC-MSD, gas chromatography/mass selective detector; BRD, bovine respiratory disease; PLS-DA, partial least-squares discriminant analysis.

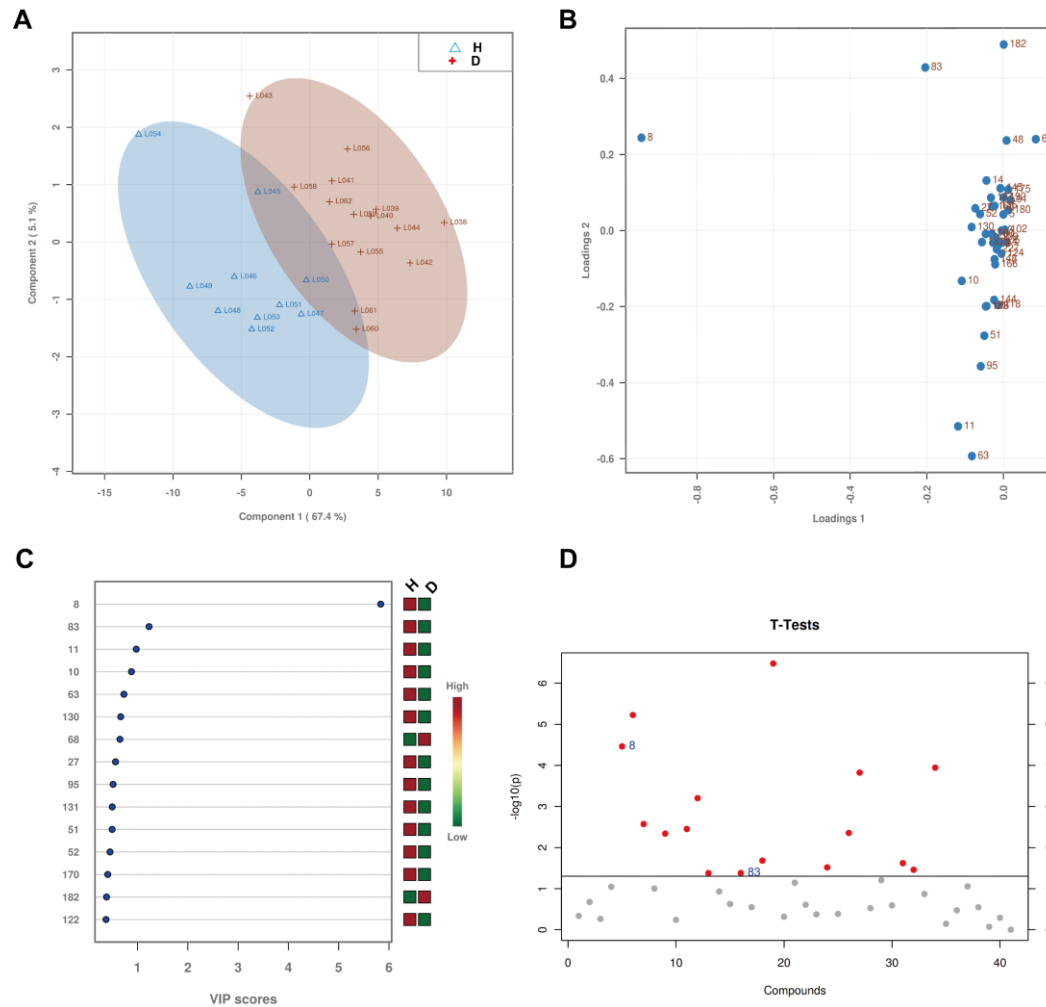


Figure S4. Evaluation of metabolites in bovine serum. Supervised PLS-DA scores plot (A) and loading plot (B) of GC-MSD profiled plasma from healthy and BRD cattle. (C) VIP of PLS-DA for different metabolites. Larger VIP scores are associated with a greater contribution to distinguishing the samples. The criteria for significance included VIP scores >1. (D) Statistical analysis (Student's t-test). Each dot represents a metabolite, and the solid line represents the threshold line of $P = 0.05$. Grey dots represent metabolites with $P > 0.05$, red dots represent metabolites with $P < 0.05$. The dots mark the VIP >1 metabolites obtained by PLS-DA analysis. PLS-DA, partial least-squares discriminant analysis; GC-MSD, gas chromatography/mass selective detector; BRD, bovine respiratory disease; VIP, variable importance in projection. D: bovines with respiratory disease, H: healthy bovines.