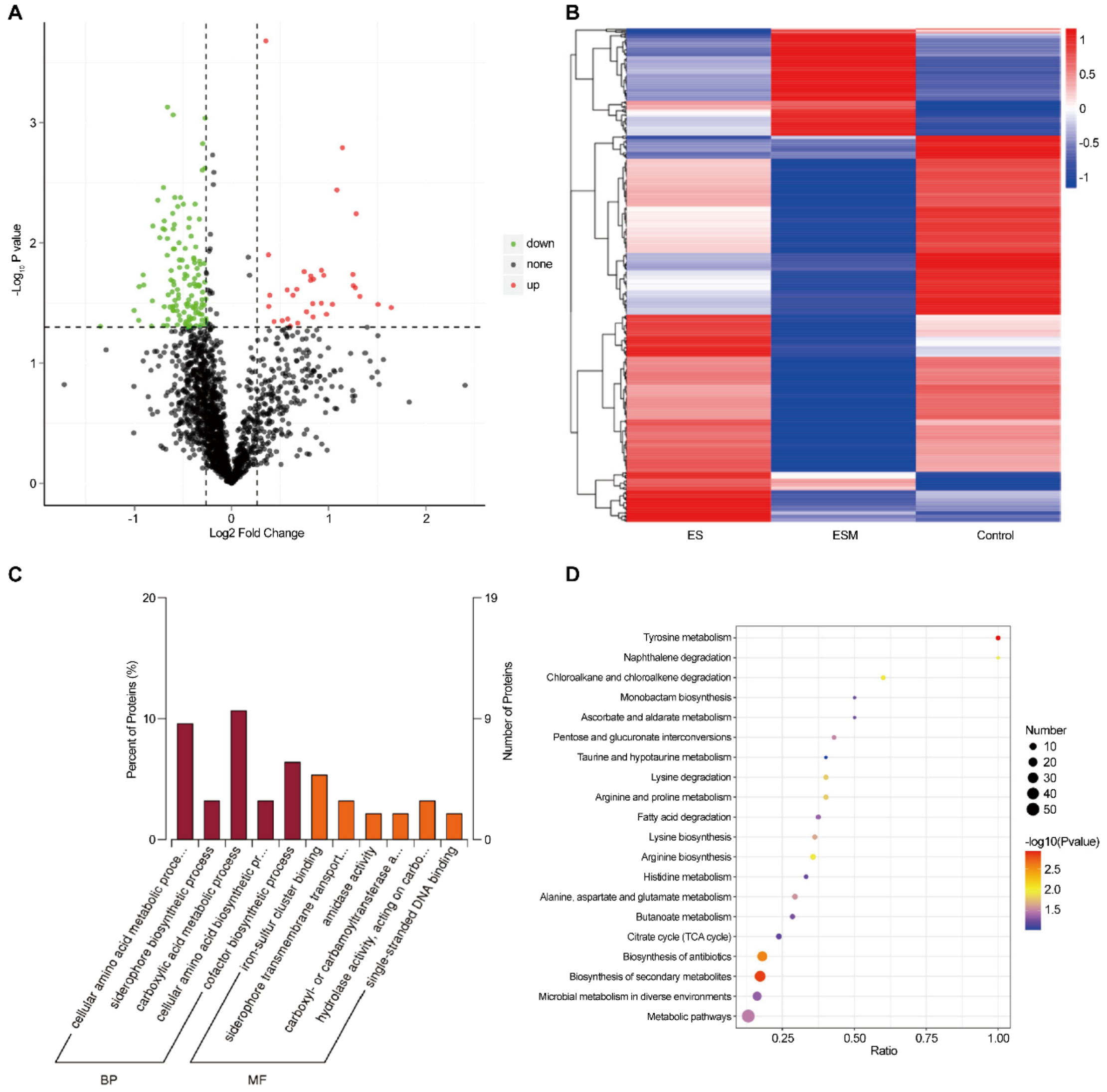

Fig. S7. ESM and ES proteomics data. (a) Volcano plot of differentially expressed proteins (DEPs) between **ESM** and **ES**. The plots revealed that the **ESM** treatment group had 158 significant changes in protein expression levels, of which 33 were downregulated and 125 were upregulated; (b) clustering heatmap of DEPs revealed that the expression levels of three histones—**ES**, Control, and **ESM**—dispersed significantly; (c) GO enrichment analysis of DEPs revealed that the **ESM** treatment group significantly outperformed the **ES** treatment group in biological processes (BP) with respect to iron carrier biosynthesis, carboxylic acid metabolism, and cellular amino acid metabolism; in molecular function (MF), there was a noteworthy enrichment of iron sulfur cluster binding and iron carrier transmembrane transport protein activity; and (d) KEGG enrichment analysis of DEPs. The **ESM** treatment group significantly enriched process, such as cellular amino acid metabolism, iron carrier biosynthesis, carboxylic acid metabolism, in BPs compared with those of the **ES** treatment group. A significant enrichment of iron sulfur cluster binding and iron carrier transmembrane transport protein activity was observed in MF.

ES, esculetin; ESM, esculetin-manganese complex.