

Figure S1. Statins significantly inhibit colony formation in a concentration-dependent manner. The cancer cells were treated with various concentrations of statins (Control, 0, 5, 10, 15, 20 and 25  $\mu\text{M}$ ) for 72 h. Three independently cultured replicates were performed per experimental condition.

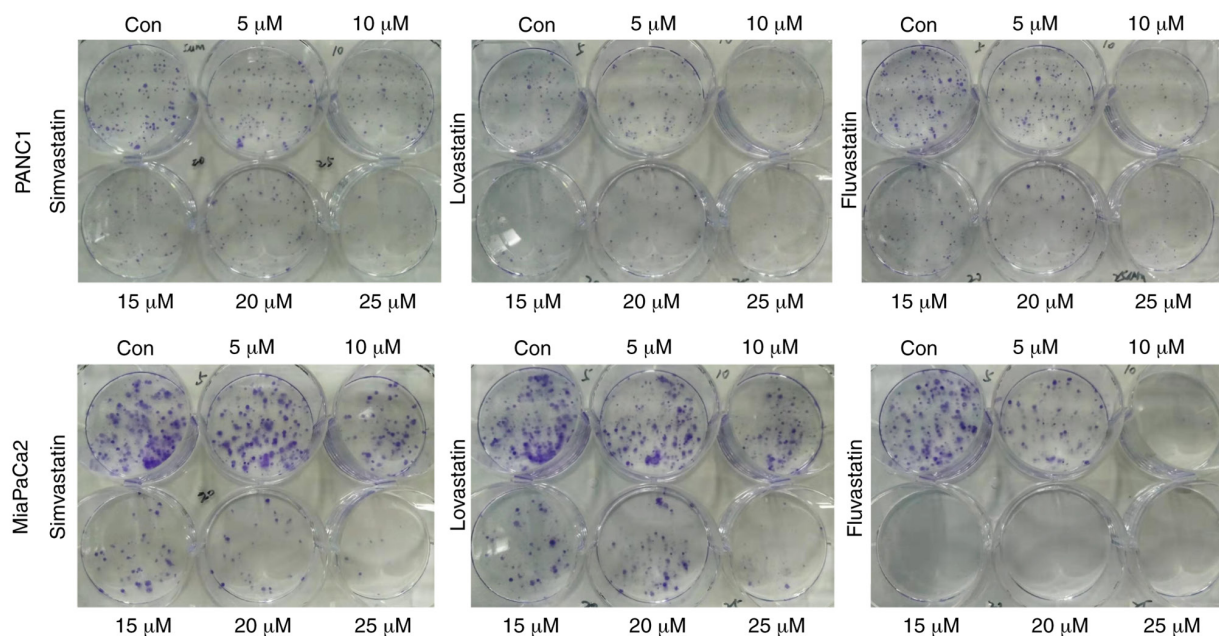


Figure S2. Volcano analysis revealing various expression genes in different groups.

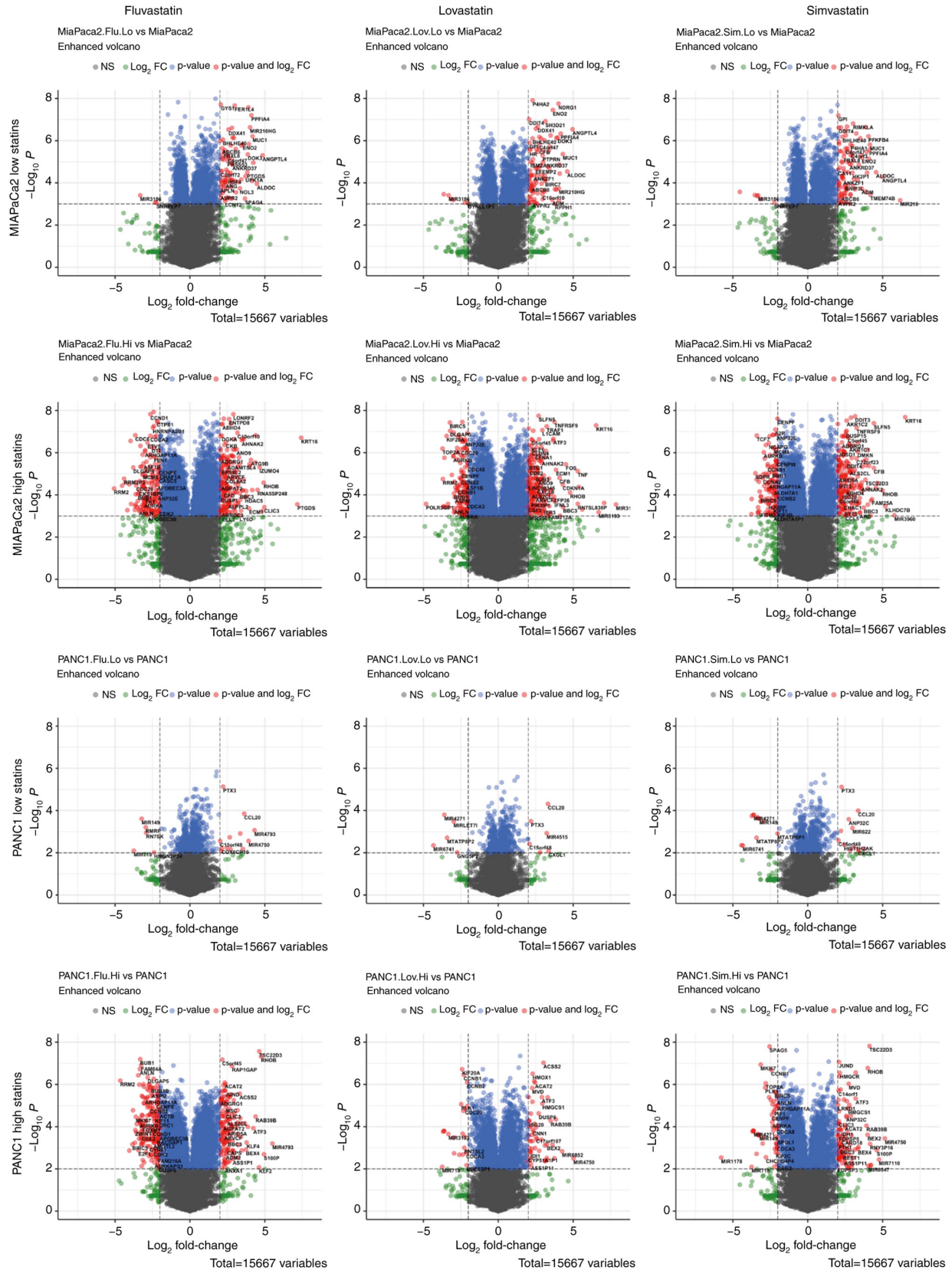


Figure S3. Module-trait relationships in the statin-treated pancreatic cancer cells. (A) Module-trait relationships of MiaPaCa2. (B) Module-trait relationships of PANC1. The blue box indicates that the modules were significantly affected by low-concentration statins. The red box indicates that the modules were significantly affected by high-concentration statins.

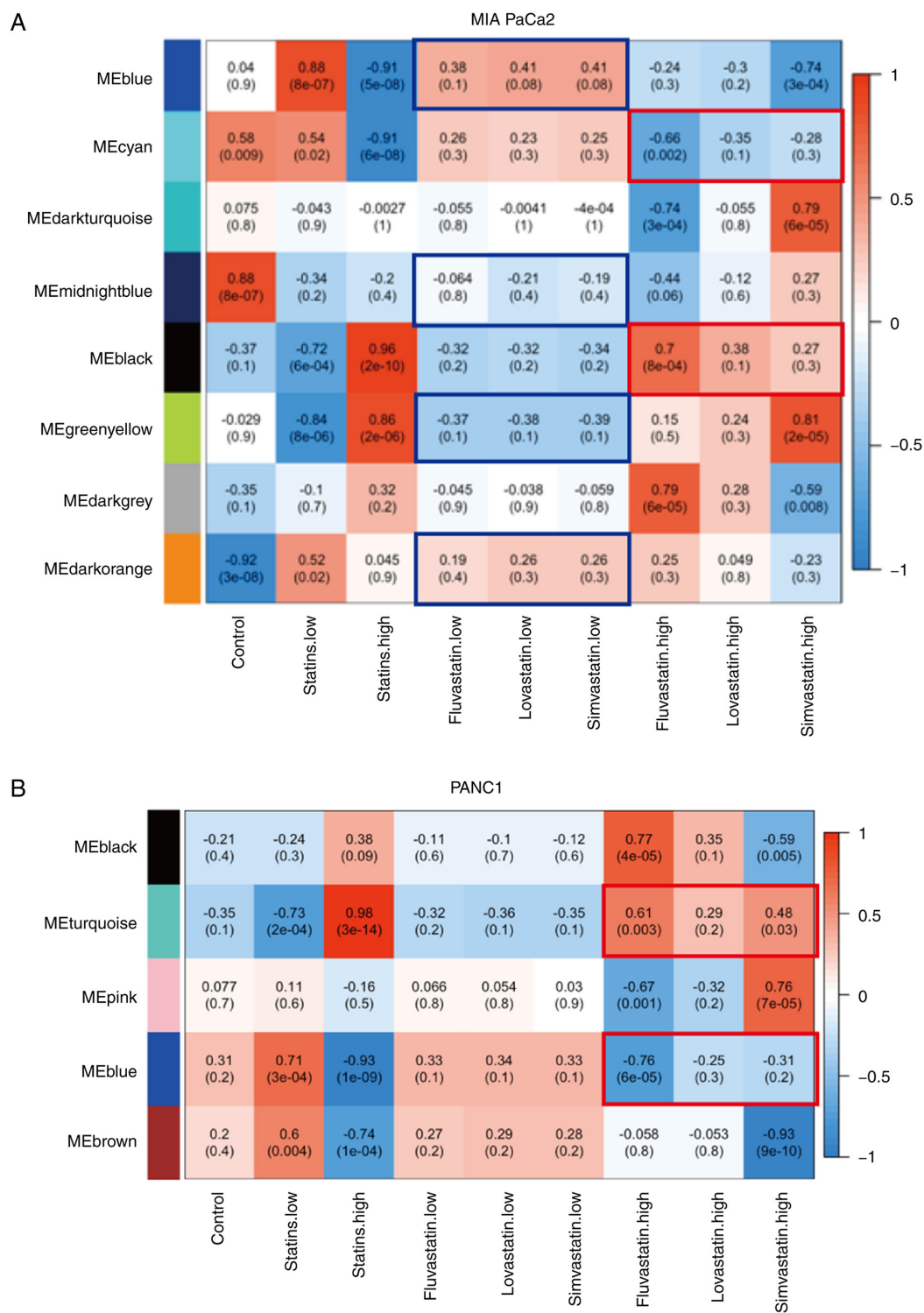


Figure S4. DEGs between MiaPaCa2 and PANC1 cells. (A) Volcano analysis revealing DEGs in MiaPaCa2 and PANC1 cells. (B) Heatmap of DEGs in MiaPaCa2 and PANC1 cells. (C) DAVID-KEGG analysis of high expression genes in MiaPaCa2. (D) DAVID-KEGG analysis of high expression genes in PANC1. DEGs, differentially expressed genes; DAVID, Database for Annotation, Visualization and Integrated Discovery; KEGG, Kyoto Encyclopedia of Genes and Genomes.

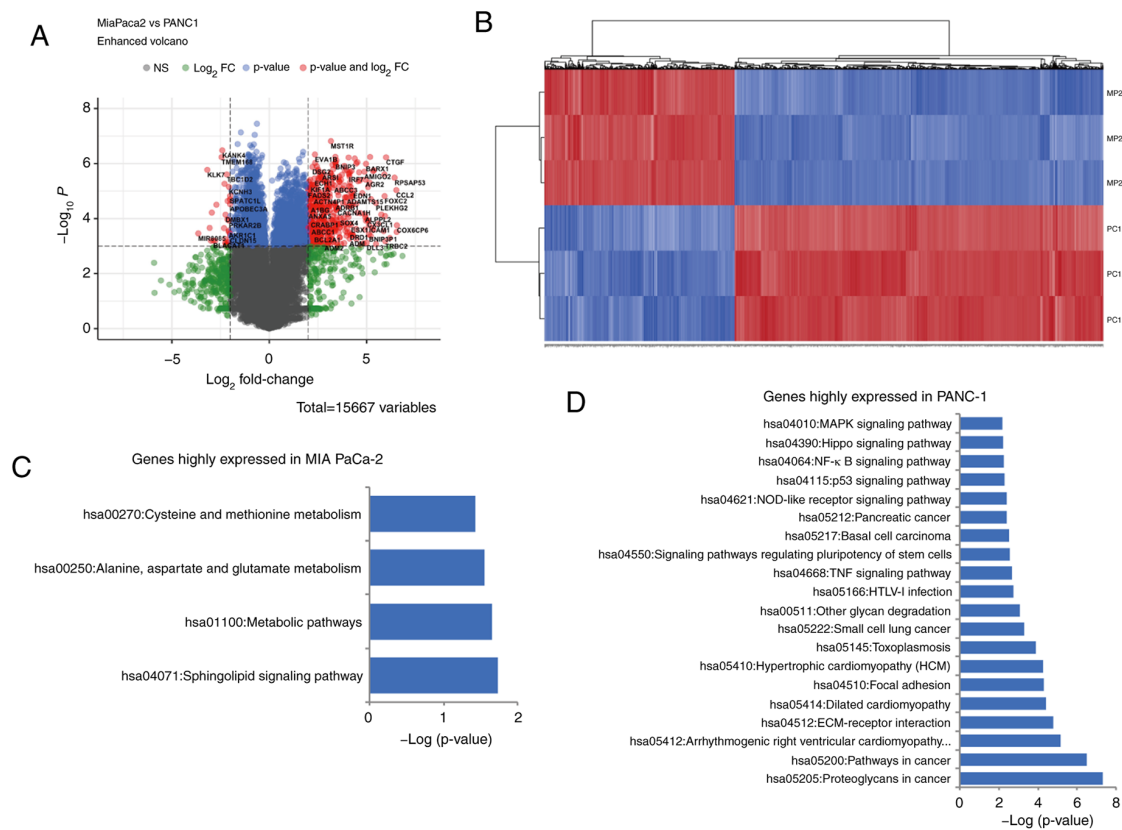


Figure S5. Expression of CCNA2 and LZTS3 in MiaPaCa2 and PANC1 cells with or without low/high-concentration statins treatment. (A) RNA-seq revealed suppressed expression of CCNA2 by high-concentration statins in MiaPaCa2 and PANC1 cells. (B and C) RT-qPCR analysis revealed suppressed expression of CCNA2 by high-concentration statins in (B) MiaPaCa2 and (C) PANC1 cells. (D) RNA-seq revealed induced expression of LZTS3 by high-concentration statins in MiaPaCa2 and PANC1 cells. (E and F) RT-qPCR analysis revealed suppressed expression of LZTS3 by high-concentration statins in (E) MiaPaCa2 and (F) PANC1 cells. Low-concentration, 2  $\mu$ M; High-concentration, 20  $\mu$ M. Compared with untreated control group, \*\*\*P<0.001. CCNA2, cyclin A2; LZTS3, leucine zipper tumor suppressor family member 3.

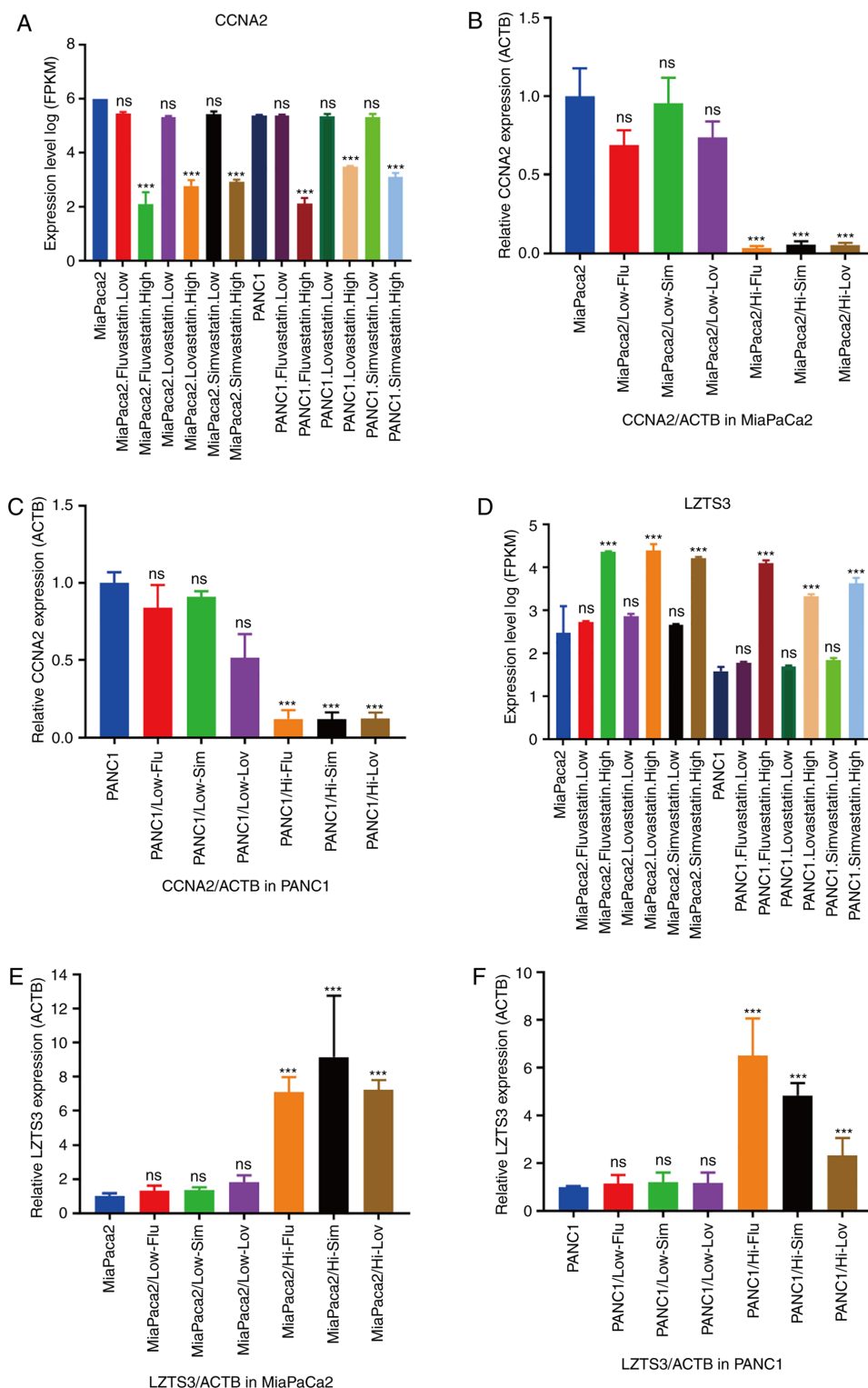




Figure S6. Upregulated genes by high-concentration statins in pancreatic cancer. (A) Genes in the black module of MiaPaCa2cells were significantly upregulated by high-concentration statins. (B) Genes in the turquoise module of PANC1cells were significantly upregulated by high-concentration statins. (C) Common genes in the black module of MiaPaCa2 cells and turquoise module of PANC1 cells.

