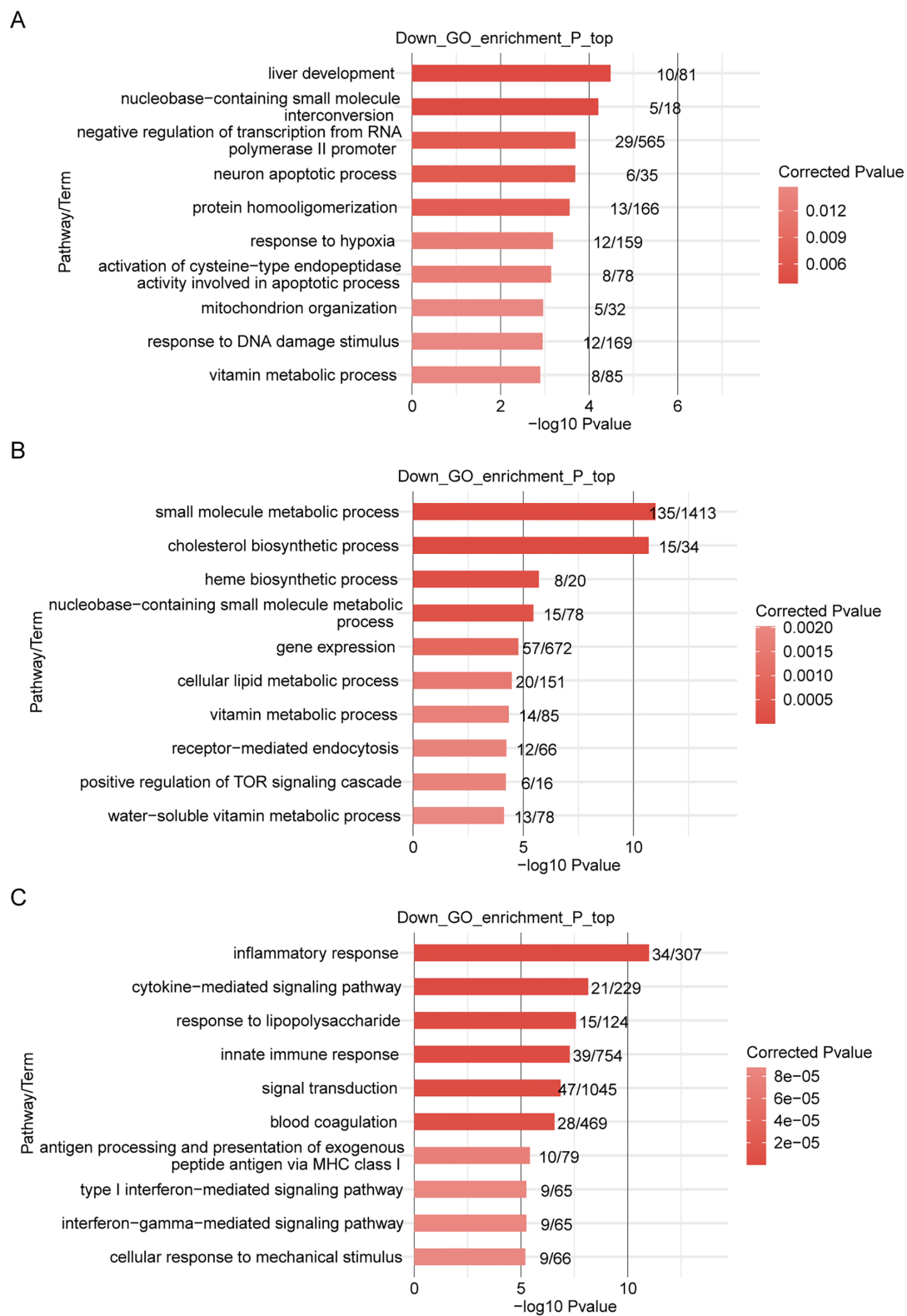
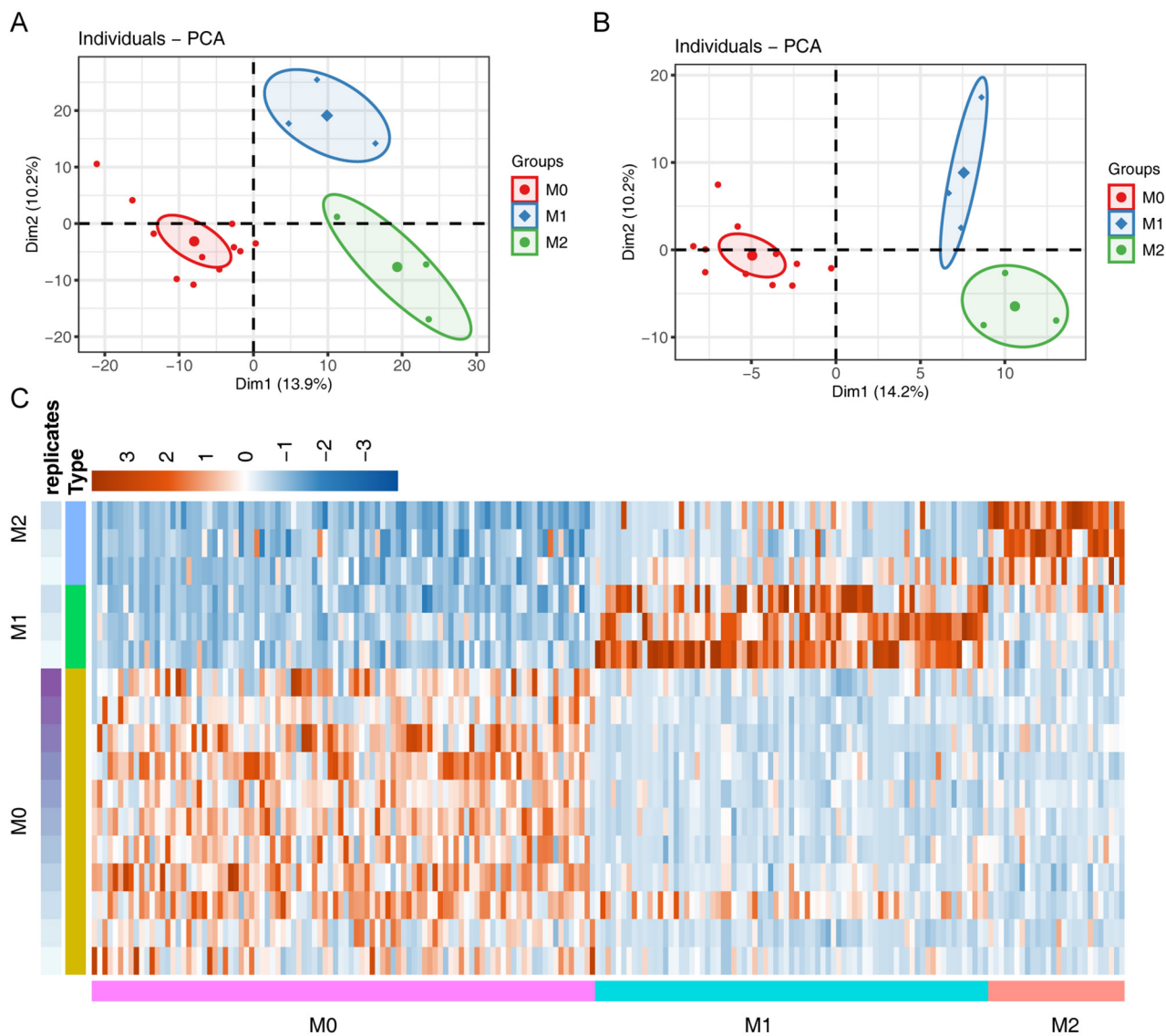


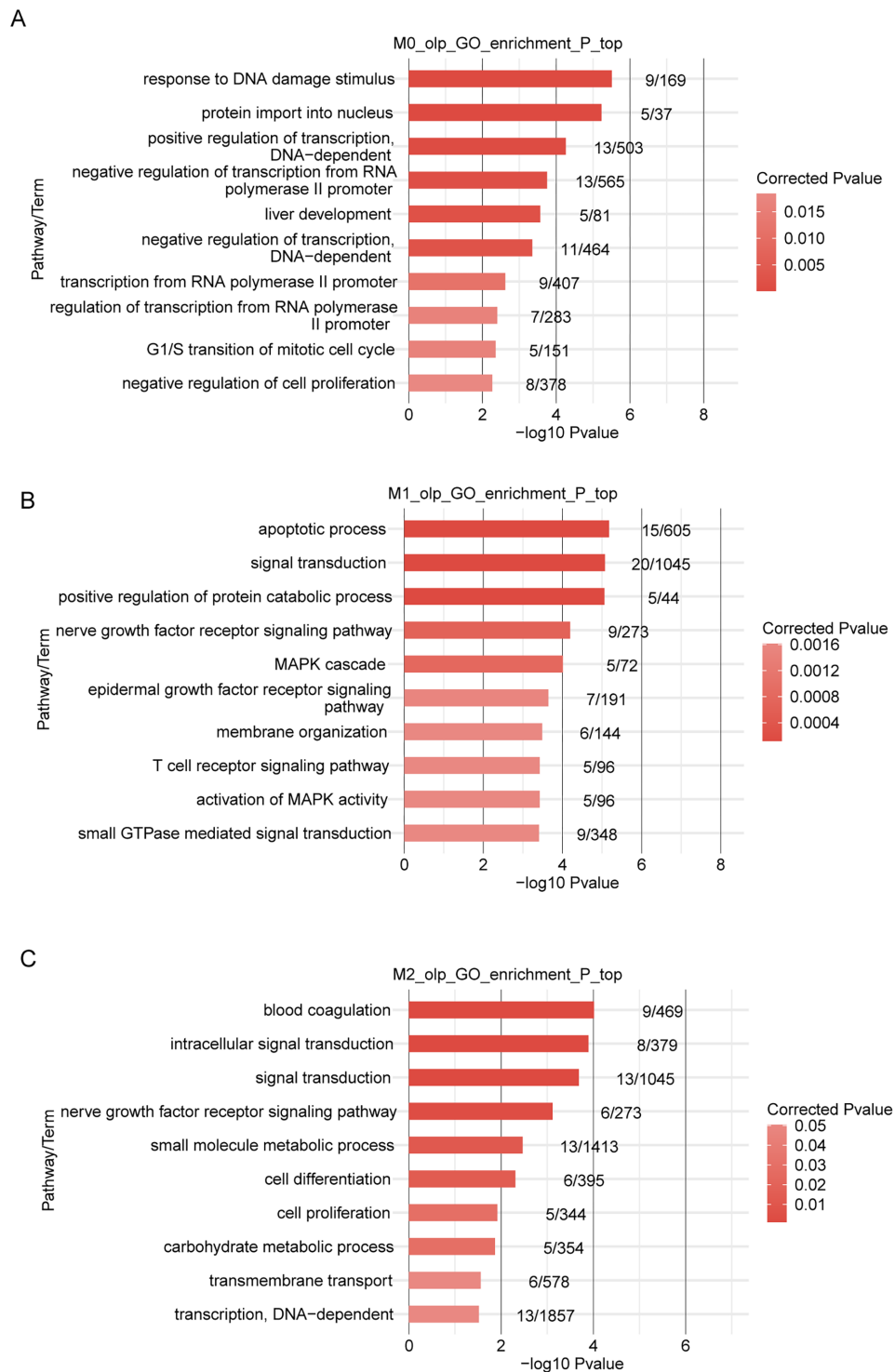
**Figure S1** The DE mRNA expression levels in clinical samples of COPD, Smoke, and Never. (A) The PCA of COPD, Smoke, and Never samples based on the non-normalized mRNAs expression level. (B) Boxplots showing the cellular immune components in COPD, Smoke, and Never samples. (C, D) The top ten mostly enriched GO terms of the down-regulated genes in COPD and Smoke specific samples. DE, differentially expressed; GO, Gene Ontology; PCA, principal component analysis; COPD, chronic obstructive pulmonary disease; Smoke, healthy smokers; Never, never smokers.



**Figure S2** The GO analysis of specific down-regulated DE mRNAs in different periods of polarization cells (M0, M1, and M2). (A-C) Down-regulated genes in M0, M1, and M2 specific cells, respectively. GO, Gene Ontology.



**Figure S3** Different miRNA expression in different periods of polarization (M0, M1, and M2). (A) PCA of M0, M1, and M2 samples based on the normalized known miRNAs expression level. (B) PCA of M0, M1, and M2 samples based on normalized novel miRNAs expression level. (C) Expression heatmap of all significant up-regulated DE miRNAs among M0, M1, and M2 samples. DE, differentially expressed; GO, Gene Ontology; PCA, principal component analysis.



**Figure S4** The GO analysis of the up-regulated genes targeted by miRNAs in M0, M1, and M2 specific cells. (A) The top 10 most enriched GO terms of overlapped DE mRNAs by M0 specific down-regulated genes and the M0 samples specific up-regulated miRNA targeted DE mRNAs. (B) The top 10 most enriched GO terms of overlapped DE mRNAs by M1 specific down-regulated DE mRNAs and the M1 samples specific up-regulated miRNA targeted genes. (C) The top 10 most enriched GO terms of overlapped genes by M2 samples specific down-regulated genes and the M2 samples specific up-regulated miRNA targeted genes. GO, Gene Ontology; DE, differentially expressed.