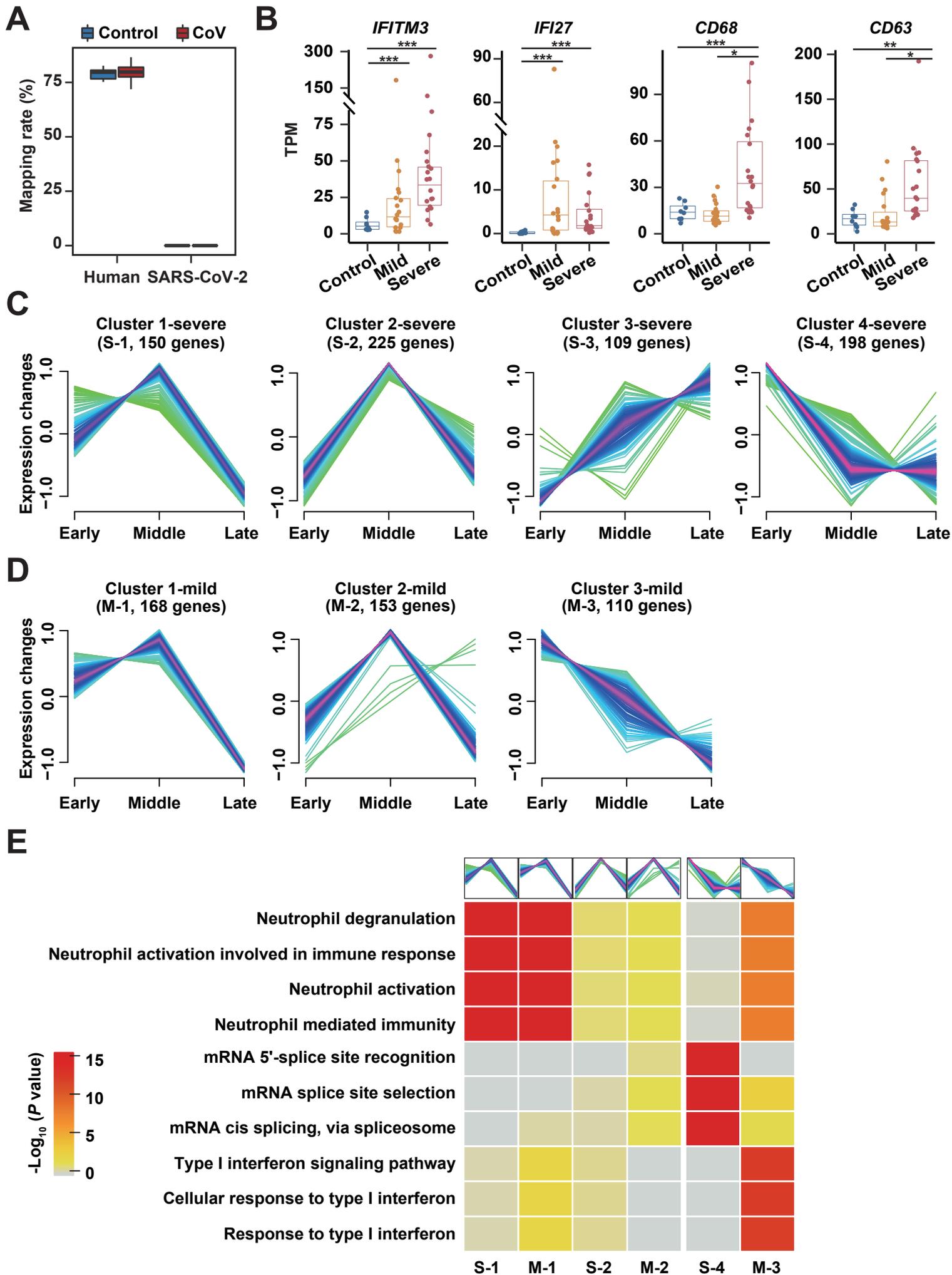


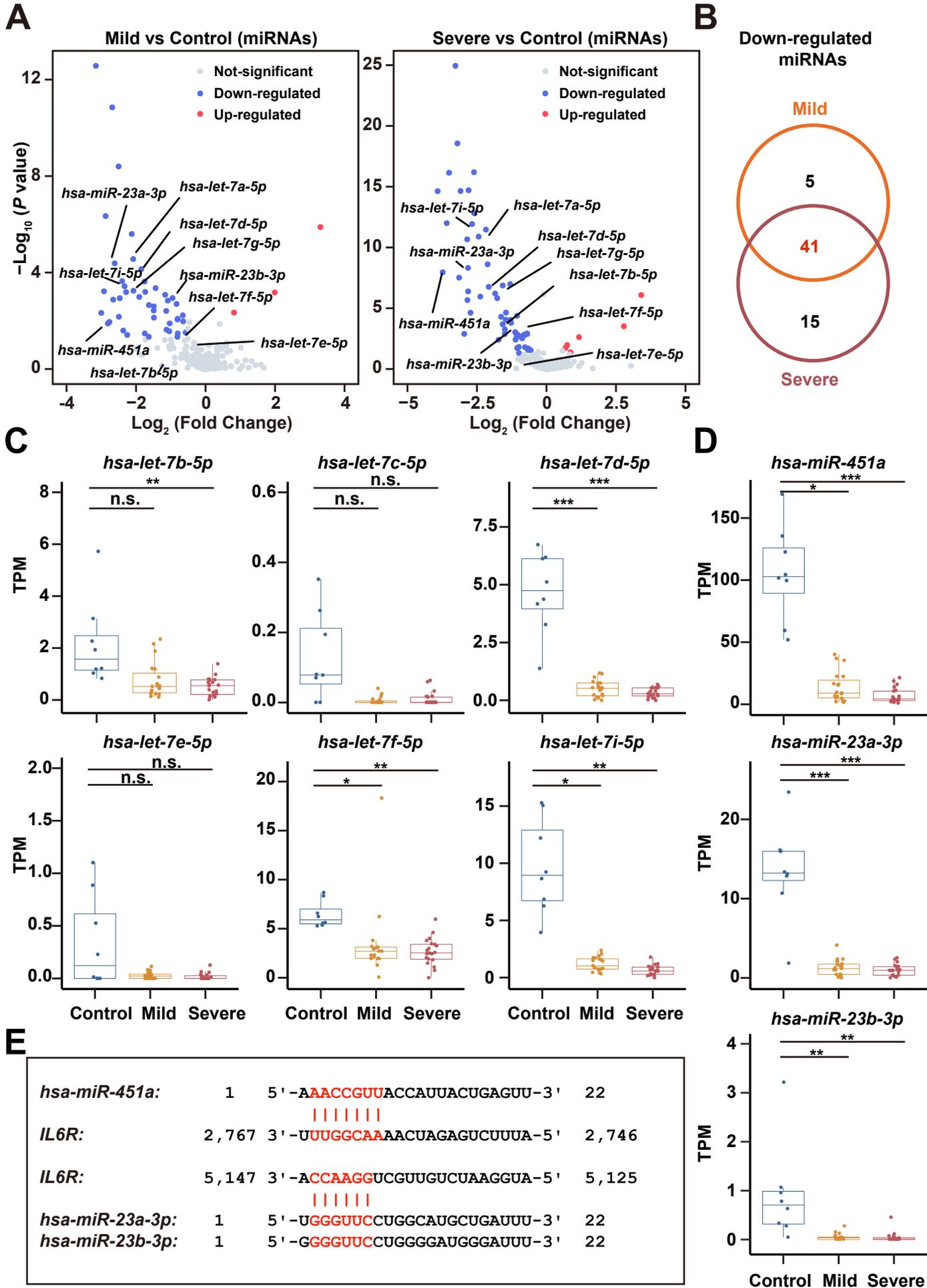
Figure S1



Supplemental Figure S1. Time-course analysis of cfRNA profiles during therapy, Related to Figure 1

(A) Box plot showing the mapping rate against human and SARS-CoV-2 genome (n=156). Control, healthy donors. COV, COVID-19 patients (including mild and severe COVID-19 patients). **(B)** Box plot showing the expression levels (TPMs) of *IFITM3*, *IFI27*, *CD68* and *CD63* in healthy donors, mild and severe COVID-19 patients. **(C)** Gene expression patterns of severe COVID-19 patients during therapy. **(D)** Gene expression patterns of mild COVID-19 patients during therapy. **(E)** GO enrichment analyses of genes of clusters in (B) and (C). Asterisks indicate statistically significant differences (* P < 0.05, ** P < 0.01; *** P < 0.001).

Figure S2



Supplemental Figure S2. Functional analysis of differentially expressed miRNA genes, Related to Figure 2

(A) Volcano plots showing differentially expressed miRNA genes in mild (left) and severe (right) COVID-19 patients relative to healthy donors. **(B)** Venn diagram of down-regulated miRNA genes in mild and severe COVID-19 patients. **(C)** Box plot showing the expression levels (TPMs) of *hsa-let-7b-5p*, *hsa-let-7c-5p*, *hsa-let-7d-5p*, *hsa-let-7e-5p*, *hsa-let-7f-5p* and *hsa-let-7i-5p*. **(D)** Box plot showing the expression levels (TPMs) of *hsa-miR-451a*, *hsa-miR-23a-3p* and *hsa-miR-23b-3p*. **(E)** Base-pairing interaction between *IL6R* and *hsa-miR-451a* (top) or *hsa-miR-23a-3p*/*hsa-miR-23b-3p* (bottom). Target sites and seed sequences are highlighted in red. Asterisks indicate statistically significant differences (* $P < 0.05$, ** $P < 0.01$; *** $P < 0.001$). n.s., not significant.

Supplemental Figure S3. tRNA pool and codon disturbance in COVID-19 patients, Related to Figure 3

(A) Venn plot showing up-regulated tRNA genes in mild and severe patients relative to healthy donors. **(B)** ROC curve of 138 up-regulated tRNAs in COVID-19 patients. This set of tRNAs was predictive of COVID-19 patients with a sensitivity of 100% and a specificity of 100%. The green area under the curve (AUC) was 0.87. **(C)** Venn plot showing up-regulated codons in mild and severe patients relative to healthy donors. **(D)** Box plot showing the frequency of codons ending with A/T and G/C in human and SARS-CoV-2 genomes. **(E)** The line plot showing the z score of 14 increased codons in SARS-CoV-2 of COVID-19 patients during therapy. The red line is the average value for each period, and the gray lines represent 14 codons. **(F)** Relative codon usage frequency in SARS-CoV-2 and FLUAV genome of the 14 up-regulated codons which were more frequently used in the SARS-CoV-2 genome. Codon usage frequency of these codons in human genome was set to 1.