**Manuscript title:** Regulation mechanism of Hanshi Zufei formula in COVID-19: Identification of a network pharmacology analysis

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Supplementary material for the manuscript including compounds and potential targets of Hanshi Zufei formula (HSZF), targets of COVID-19, and bioinformatics analysis result of the manuscript.

It is being made public to act as supplementary data for publications in order for other researchers to use this data in their own work.

**Description of the data in this data set:**

**Supplementary material lists:**

**01 compounds of HSZF formula**

Herb Name: represents the name of the Chinese herbal medicine;

Mol ID: represents the compound number of the compound in the Chinese herbal medicine in the TCMSP database (DOI:10.1186/1758-2946-6-13);

OB: oral bioavailability; DL: Drug Likeness; OB and DL are the most common pharmacokinetic parameters for drug screening; we used OB ≥ 30% and DL ≥ 0.18 as the screening conditions for active constituents of HSZF.

**02 targets of HSZF formula**

The SwissTargetPrediction database (http://www.swisstargetprediction.ch/) can accurately predict targets of active constituents based on the similarity between the two- and three-dimensional structures of the molecule and the known ligand. We imported the SMILES format file into the SwissTargetPrediction database. Using humans as the research species, we obtained the targets of the compounds and saved them in. CSV format. Potential targets of HSZF were obtained after integration and deduplication.

**03 Network topology analysis**

We introduced potential targets of HSZF in the treatment of COVID-19 into the Search Tool for the Retrieval of Interacting Genes/Proteins (STRING; http://stringdb.org/). For species, we selected humans. We analyzed PPI between targets, imported the results into Cytoscape via the Cytohubba plug-in for network topology analysis, and used Cytoscape for visual processing.

**04 GO BP, 05 GO CC, 06 GO MF, and 07 KEGG**

We used the org.Hs.eg.db and ClusterProfiler data packages of R language software version 3.5.2 to perform gene ontology (GO) enrichment analysis of gene function [18] and Kyoto Encyclopedia of Genes and Genomes (KEGG) signaling pathways[19] of the common targets obtained. We retained results for which *P* ≤ 0.05 and obtained GO and KEGG signaling pathway histograms.

**08 COVID-19 related targets**

There is no clear therapeutic target for COVID-19 at present. It is reported that the mechanism by which SARS-CoV-2 infects type II alveoli is the interaction of spike (S) protein with human renin and angiotensin-converting enzyme 2 (ACE2), thereby infecting type II alveolar cells and resulting in the occurrence of pneumonia. Therefore, based on single-cell sequencing results of colon epithelial cells in a previous study, we extracted genes co-expressed with ACE2 and performed standardized conversion of gene names in the original files to match human-related targets. By mapping these genes to the abovementioned potential targets of HSZF, we obtained the potential targets of HSZF in the treatment of COVID-19.