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**Supplementary Material**

**Association analysis of genetic variants in critical patients with COVID-19 and validation in a Chinese population**

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**Data collection**

We conducted a comprehensive search in the PubMed database and Google Scholar using the Key words “genetic variants of COVID-19 patients” and “GWAS” to identify large-scale studies investigating the association between SNPs and COVID-19 susceptibility or severity, published in or before January 2023 (Supplementary Table S1). We further validated these data in a Chinese GWAS dataset (Gong et al., 2022). As previous described, we enrolled a total of 632 patients diagnosed with critical COVID-19 and 3,021 normal controls. The cases samples were collected from the Sichuan Provincial People’s Hospital, and 474 patients were selected from the Zhongnan Hospital of Wuhan University and the Wuhan Leishenshan Hospital. All study procedures were conducted in accordance with the principles outlined in the Declaration of Helsinki. The DNA samples from the discovery cohort were genotyped by Jinneng Biotech (Shanghai, China) using HumanOmniZhongHua-8 Bead Chips (Illumina), according to the manufacturer’s protocol. A total of 900,015 SNPs were initially analyzed. SNPs with a call rate of less than 90% was excluded from further analysis. After quality filtering and cleaning, a total of 761,993 SNPs were retained for the association analysis. The selected SNPs for replication were genotyped using the Sequenom Mass ARRAY system. The association analysis of the replicated genotype data was conducted using PLINK 1.9, with adjustment for gender as a covariate.

**Statistical analysis**

For case–control comparisons, we tested for association by performing logistic regression using PLINK, assuming additive allelic effects for genotyped and imputed SNPs. Genotypes were exported in Genome Reference Consortium human build 38 (GRCHb38) and Illumina “source” strand orientation using the Genotype Studio PLINK input report plugin (Gong et al., 2022). To obtain further information regarding COVID-19-related SNPs in our Chinese cohort, we searched our Chinese cohort data and the 1000 Genomes Project Phase 1 East Asian population data for SNPs with identical linkage disequilibria (LDs; *r*2 ≥ 0.6). Finally, METAL was used for the meta-analysis of the previously reported SNPs and the SNPs in our Chinese cohort data (Willer et al., 2010).

**References**

Gong B., Huang L., He Y., Xie W., Yin Y., Shi Y., Xiao J., Zhong L., Zhang Y., Jiang Z., Hao F., Zhou Y., Li H., Jiang L., Yang X., Song X., Kang Y., Tuo L., Huang Y., Shuai P., Liu Y., Zheng F., Yang Z., 2022. A genetic variant in il-6 lowering its expression is protective for critical patients with covid-19. Signal Transduct Target Ther, 7: 112.

Willer C.J., Li Y., Abecasis G.R., 2010. Metal: Fast and efficient meta-analysis of genomewide association scans. Bioinformatics, 26: 2190-2191.

Table S1 The information of genome-wide association studies on genetic variants in patients with COVID-19.

Table S2 All the validated SNPs in the Chinese population.