Statistical genetics is a research field that evaluates causality of human genetic variations on diseases. Recent developments of sequencing technologies have successfully identified comprehensive catalogues of genetic susceptible loci. Integration of large-scale human genome data with diverse biological resources should elucidate biology of human complex traits including infectious diseases. We launched Japan COVID-19 Task Force, where >100 hospitals joined and DNA, RNA, plasma, and clinical information of >6,000 COVID-19 patients of Japanese. The GWAS of severe and young COVID-19 patients identified a population-specific risk variant of DOCK2. Single cell RNA-seq (scRNA-seq) identified non-classical monocytes and COVID-19-specific eQTL effects of the DOCK2 risk variants. Inhibition of DOCK2 function increased the severity of pneumonia in a Syrian hamster model of SARS-CoV-2 infection (NamKoong H. Nature 2022). By constructing whole blood RNA-seq data, we found the limited but non-zero effect of COVID-19 phenotype on eQTL discovery, and highlighted the presence of COVID-19 severity-interaction eQTLs (Wang Q. Nat Commun 2022). Large-scale COVID-19 scRNA-seq of Japanese with host genetics highlighted critical roles of innate immune cells in severe COVID-19. Putative disease genes identified by COVID-19 genome-wide association study showed cell type-specific expressions in monocytes and dendritic cells (Edahiro R. Nat Genet 2023). Our results should empirically show the value of statistical genetics to dissect disease biology.

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