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Single cell analysis involving host genetics elucidates COVID-19

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Zoom

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Zoom:

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.

Yukinori Okada, M.D., PhD is the Professor of Graduate School of Medicine, the University of Tokyo, and Osaka University Graduate School of Medicine, and the team leader of RIKEN Center for Integrative Medical Sciences. He received the M.D. and PhD from the University of Tokyo. His research theme is the elucidation of mechanism where genetic variants affect biological and clinical phenotype. He has multiple professional backgrounds as a rheumatologist, a statistician, and a bioinformatician. Through active collaborative partnerships among the researchers of human genetics, Prof. Okada has conducted large-scale genomics studies of a variety of human complex traits. His interests are now moving towards statistical genetics and bioinformatics analysis generated by the latest omics technologies, such as single cell sequencing and microbiome metagenomics, and its application to novel drug discovery and personalized medicine.