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Editorial

Identification of Several Genome-Wide-Associated-Genetic Variants in Critical COVID-19

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A recent study using genome-wide association study (GWAS), a monocyte transcriptome-wide association study (TWAS) models, and Mendelian randomization revealed association of the critical COPVID-19 with genes related-host factors required for viral replication and entry, immunometabolism, monocyte-macrophage activation and endothelial permeability, and inflammatory signalling; RAB2A and TMPRSS2 (Figure 1) [1], AK5 and SLC2A, PDE4A, and JAK1, respectively [1]. There was critical correlations between predicted gene expression in monocyte [2], blood [3], and lung (Figure 2) [1,4,5].

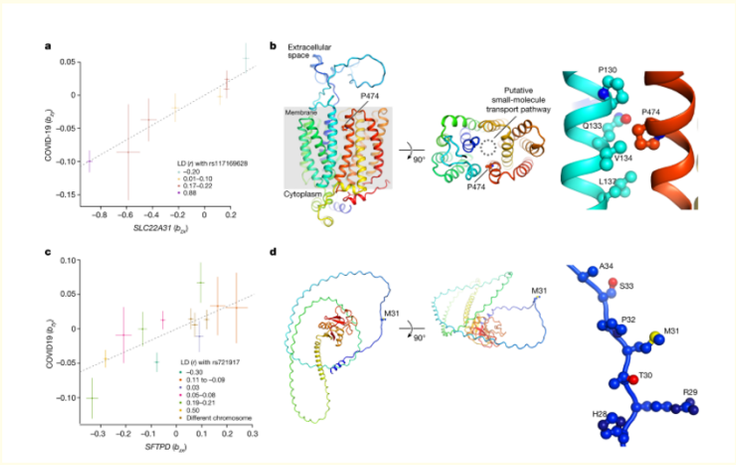

Figure 1: *a, Demonstrating the critical COVID-19 increasing susceptibility against by the effect-size plot for the effect of multiple variants on SLC22A31 expression (eQTLgen, x axis) ($\beta_{xy} = 0.11$; $P_{xy} = 1.3 \times 10^{-9}$). The missense variant rs117169628 with linkage disequilibrium (LD) is demonstrated by coloring. b, An AlphaFold model of putative solute carrier family member (SLC22A31; UniProtKB: A6NKX4) is demonstrated by three cartoon views. Connected spheres represent the side chains of Pro474 and interacting amino acids. Indicating a dashed circle is a putative channel for small-molecule transport across the cell membrane. Pro474 is predicted to be located in the transmembrane helix and point towards a putative transport pathway of a small molecule. P474L (Ala at rs117169628), a risk variant to the introduction of more flexibility to the transmembrane helix with possible affecting the transport properties of SLC22A31. A tightly packed environment by Pro474 may contribute to affecting the folding of SLC22A31. c, Against increasing susceptibility to critical COVID-19 ($\beta_{xy} = 0.16$; $P_{xy} = 9.7 \times 10^{-6}$) could be from effect-size plot for the effect of multiple variants on SFTPD expression (eQTLgen, x axis). Color demonstrates linkage disequilibrium with the missense variant rs721917. d, An AlphaFold model of pulmonary surfactant-associated protein D (SFTPD; UniProtKB: P35247) is demonstrated by three cartoon views. The connected spheres represent the side chain of the variant Met. Considering the secondary-structure-lacking region of SFTPD, Met is predicted to be located in this site. Sulfur atom, oxygen and nitrogen atoms are colored yellow, red and blue respectively in the diagram on the right [1].*

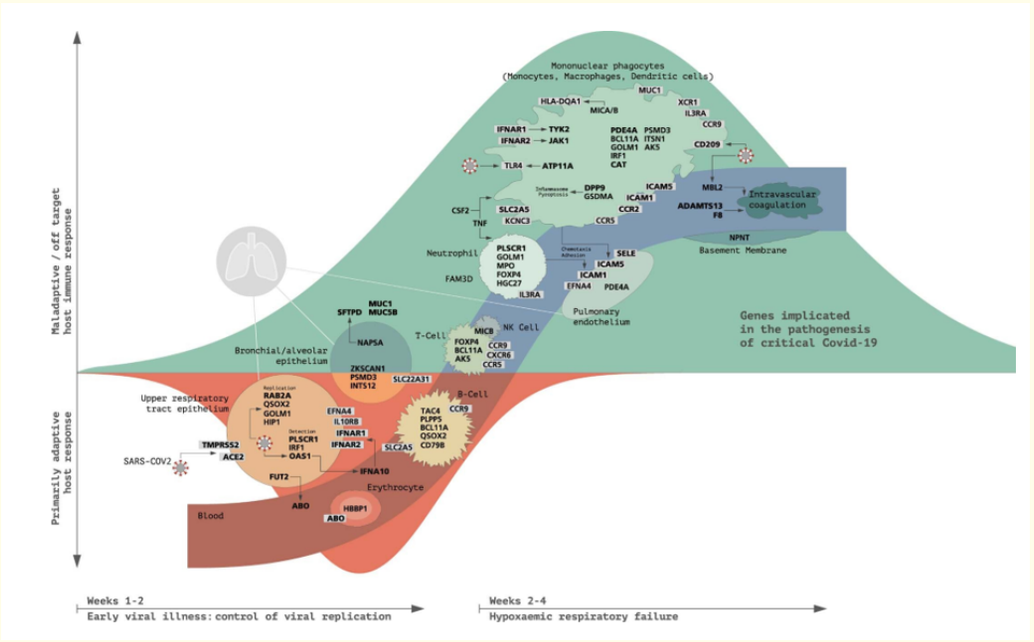

Figure 2: *Demonstrating the postulated roles for genetic variants are demonstrated in a highly simplified format to illustrate potential roles in pathogenesis, with the shaded background indicating the hypothetical impact of the host immune response over time. Playing a role in controlling viral replication and those implicated in driving hypoxemic respiratory failure later in disease (green section, demonstrating "maladaptive" response) are functioned by dived host-immune process. A higher level of confidence in both the gene identification and the biological role are indicated by the bold-type-gene names [1,4,5].*

In conclusion, therapeutic targeting for critical COVID-19 could have potential by highlighting novel disease-biological mechanisms and critical COVID-19-pathogenesis understanding.

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