Single-cell RNA sequencing analysis of SARS-CoV-2 conventional and moonlighting receptors in human organoids

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Abstract

Background and Purpose: Lack of suitable experimental models hinders SARS-CoV-2 research. Reports denote SARS-CoV-2 uses ACE2, TMPRSS-2 as its primary receptors. However, SARS-CoV-2 clinical symptoms were also related to organs with poor or no expressions of primary receptors. Hence, using single-cell RNA sequencing data of human organoids, we analyzed expression levels of primary receptors and array of RNA receptors for their involvement in SARS-CoV-2 pathogenesis. Experimental Approach: From the gene expression omnibus (GEO) or array express database, normalized cell counts of human intestine coventional, intestine improved, prostate, kidney morizane, kidney takasato, brain, retinal, lung organoids were obtained. Individual cell types, RNA receptor expressions in ACE2 (+) and ACE2(-) cells were analyzed. Using immune enrichment analysis, immune pathway activation in ACE2(+) and ACE2(-) cells were determined. Key Results: ACE2 expression is abundant in all organoid, except prostate and brain, while TMPRSS2 is omnipresent. Innate immune component pathways are upregulated in ACE2 (+) cells in all organoids, except lung. Besides, expression of low-density lipoprotein receptor (LDLR) is highly enriched in ACE2 (+) cells in intestinal (conventional and improved), lung, and retinal organoids, with highest expression in lung organoids. Other than primary receptors, LDLR and HDLR might also exert crucial role SARS-CoV-2 pathogenesis. Conclusion and Implications: Mimicing Invivo niche, with array of cell types expressing primary and RNA receptors, immune pathways activation, human organoids will be suitable model for rapid SARS-CoV-2 translational research. Other than ACE2 and TMPRSS2, LDLR and HDLR with moonlighting functions can be useful targets in SARS-CoV-2 clinical management.

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