Researchers discover novel receptors for SARS-CoV-2 and their age-dependent expression

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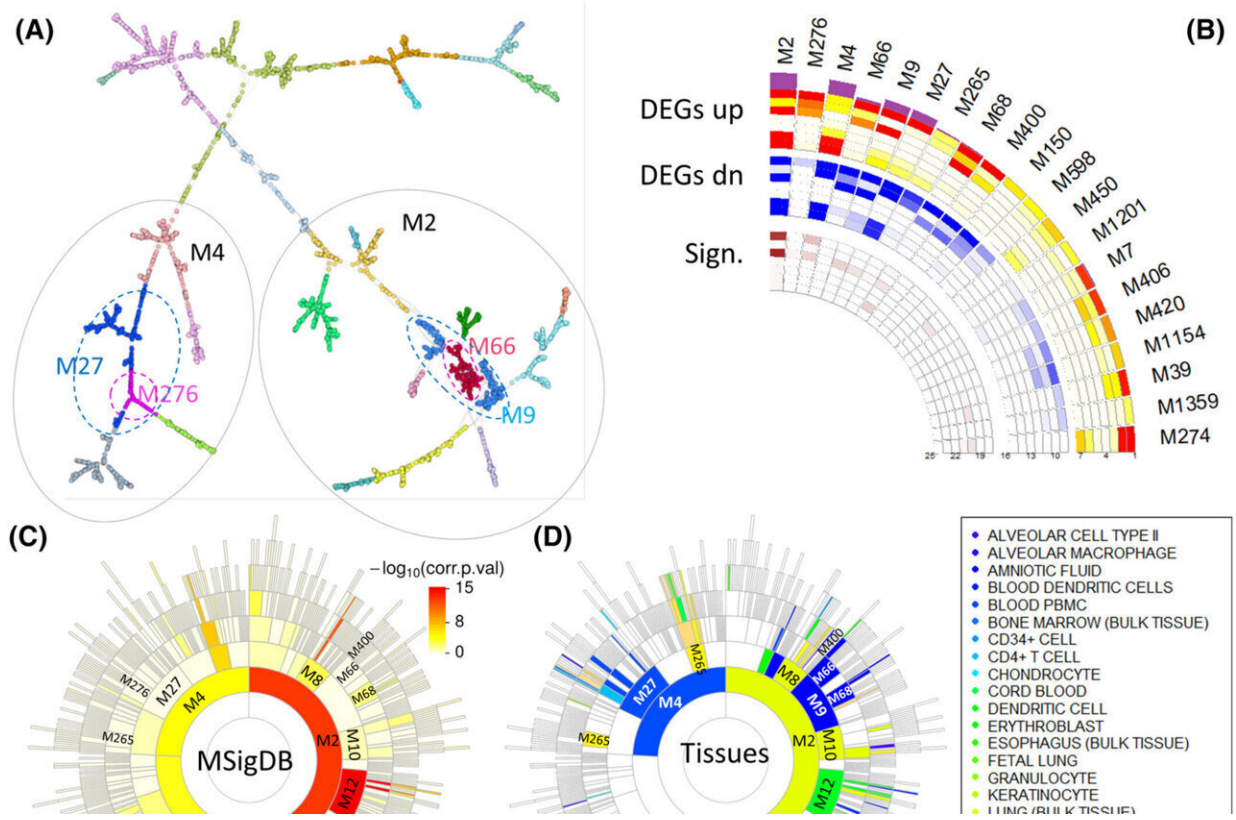

Credit: *FEBS Letters* (2023). DOI: 10.1002/1873-3468.14613

A study led by Mount Sinai researchers Dr. Bin Zhang, the Willard T.C. Johnson Research Professor of Neurogenetics, and Dr. Christian Forst,

an Associate Professor in the Department of Genetics and Genomic Sciences, has identified potential novel receptors for SARS-CoV-2 and unveiled their tissue-specific and age-dependent expression. The findings were published on March 23 in the *Federation of European Biochemical Societies Letters (FEBS Letters)*.

The study's multiscale network analysis suggests that SARS-CoV-2 utilizes multiple novel receptors, such as the TYOBP receptor CD300e, to facilitate its life cycle and trigger a unique response in the host system. This receptor activates IL-2 pro-inflammatory cytokine signaling, which is believed to contribute to the severity of COVID-19. Researchers identified a strong correlation between tissue age-dependency and SARS-CoV-2 infection-induced receptor expression in subcutaneous fat, tibial artery, brain substantia nigra, esophagus gastroesophageal junction, and liver.

These findings reveal that SARS-CoV-2 may exploit different receptors and pathways across various tissues and age groups, with older adults being more susceptible to severe outcomes. The study's results also provide valuable information about the host response to the virus, the hijacking of key cellular processes, and the age-dependence of these receptors in different tissues.

"These findings provide crucial insights into the gene regulatory organization during SARS-CoV-2 infection and the tissue-specific, age-dependent expression of cell receptors involved in COVID-19," said Dr. Bin Zhang. "This information is critical for public health as it allows us to better understand the molecular mechanisms of SARS-CoV-2 infection and develop new therapeutic interventions against COVID-19."

The study highlights the importance of understanding the host response to viral infections and how age can impact the severity of the disease. With these new insights, researchers can develop targeted therapies and

interventions to mitigate the impacts of COVID-19 on vulnerable populations, such as older adults and individuals with pre-existing conditions.

The methods employed in this study involved a multiscale network analysis utilizing bulk and single-cell omics data, which allowed the researchers to analyze the complex biological systems of SARS-CoV-2 infection. They integrated large-scale transcriptomic datasets from COVID-19 patients and healthy individuals, along with protein-protein interaction (PPI) data and protein expression data, to construct a comprehensive host-virus interactome.

This approach enabled them to identify key genes, proteins, and molecular pathways involved in SARS-CoV-2 infection and the host response, and the age-dependent expression patterns of novel receptors. The research team also validated the findings using a combination of in vitro and in vivo experiments, further substantiating the potential roles of the newly discovered receptors in SARS-CoV-2 infection and COVID-19 severity.

Dr. Christian Forst added, "The discovery of novel receptors that SARS-CoV-2 utilizes, and their age-dependent expression, offers new avenues for research and potential therapeutic strategies. This could be especially significant for older adults who have a higher risk of severe COVID-19 outcomes. Our research will help guide public health strategies and support targeted therapies for vulnerable populations."

More information: Christian V. Forst et al, Multiscale network analysis identifies potential receptors for SARS-CoV -2 and reveals their tissue-specific and age-dependent expression, *FEBS Letters* (2023). DOI: 10.1002/1873-3468.14613

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