SARS-CoV-2 co-receptors: What they do and how they do it?

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Cell surface receptors are crucial entry points for viruses into host cells. Viruses often bind to these receptors and undergo conformational changes to facilitate internalization. During the SARS-CoV-2 pandemic, angiotensin-converting enzyme 2 (ACE2) was identified as the primary receptor, but SARS-CoV-2 also interacts with other cell surface proteins, including neuropilin-1 (NRP-1), leucine-rich repeat-containing 15 (LRRC15), transmembrane serine protease 2 (TMPRSS2), and transmembrane protein 106B (TMEM106B)[1-6]. While ACE2's interaction with the virus is well-studied, the structural details of how SARS-CoV-2 engages with these co-receptors, particularly NRP-1 and LRRC15, remain unclear, as well as the downstream effects of these interactions.

In my research, I am characterizing NRP-1 and LRRC15 using structural, biochemical, and biophysical methods. Mass photometry reveals that NRP-1 forms monomers, dimers, trimers, and tetramers, whereas LRRC15 exists as a monomer. Negative stain electron microscopy (EM) shows that NRP-1 has secondary binding sites that overlap with ACE2 on the SARS-CoV-2 Omicron spike surface. However, no binding of LRRC15 to the intact spike or receptor-binding domain of the Omicron variant was detected. Preliminary pull-down assays suggest that NRP-1 can bind to furin cleavage site-deficient spikes of MERS and HKU1 coronaviruses.

Overall, my findings indicate that NRP-1 could serve as a potential pan-receptor for coronaviruses, while the role of LRRC15 as a bona fide co-receptor remains uncertain.

References

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