MS02-1-3 Structural bases for the higher adherence to ACE2 conferred by the SARS-CoV-2 spike Q498Y substitution
#MS02-1-3

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Abstract
A remarkable amount of SARS-CoV-2 variants and other yet unmonitored lineages harbour amino acid substitutions with potential to modulate the interface between the spike receptor binding domain (RBD) and its receptor ACE2. The naturally-occurring Q498Y substitution currently present in circulating SARS-CoV-2 variants has drawn the attention of several investigations[1-4], and recent studies have detected this substitution in previously unidentified SARS-CoV-2 lineages found in wastewater samples of New York City[5].
To decipher the structural bases that underlie the enhanced affinity attributed to this substitution, I have crystallized the RBD Q498Y mutant bound to its human ACE2 receptor. Compared to the structure with its wild type counterpart, the RBD Q498Y:ACE2 complex reveals conservation of major hydrogen-bond interactions and a more populated, non-polar set of contacts mediated by the bulky side chain of Tyr498, as well as one additional π-π stacking interaction, that collectively lead to this increase in the binding affinity.
Our studies contribute to a deeper understanding on the impact of a relevant mutation present in current SARS-CoV-2 circulating variants and which might lead to stronger host-pathogen interactions.

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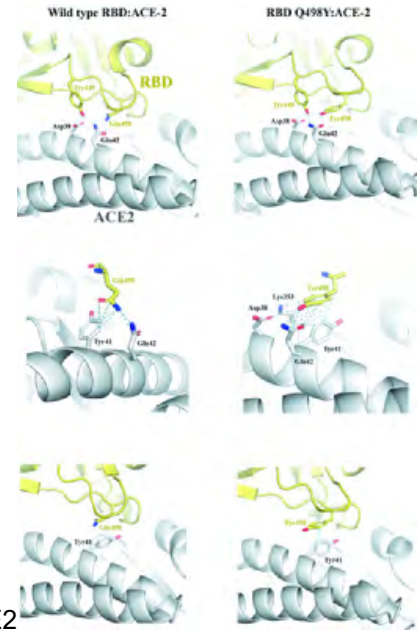

Interatomic contacts between RBD Q498Y and ACE2