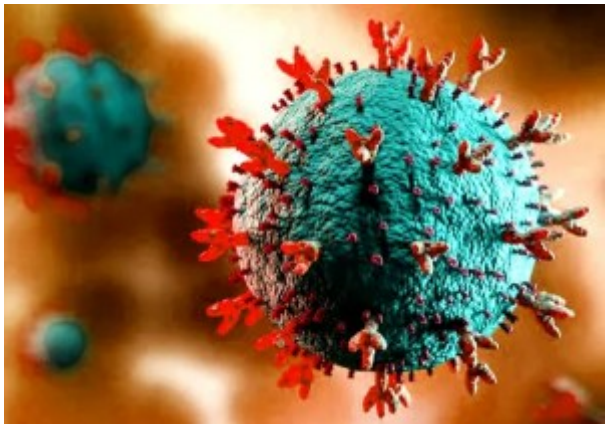
A recent study conducted by Chinese researchers proposes the classification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants into five serotypes based on the antigenicity of the receptor-binding domain (RBD), with all pre-Omicron variants classified as serotype-I, and Omicron sub-variants classified as serotype-II, III, IV, and V according to their stages of evolution.

With the continuous evolution of the SARS-CoV-2, a significant number of variants have emerged, particularly with the emergence of Omicron with many subvariants. These variants, which have been classified as variants of concern (VOCs) or variants of interest (VOIs) by the World Health Organization, carry an unprecedented number of mutations in the receptor-binding domain (RBD) of the spike (S) protein. These variants have been shown to be able to evade the herd immunity induced by natural infection, and have led to the loss or reduction in efficacy of most previously approved vaccines and monoclonal antibodies. This led to a major wave of breakthrough infections worldwide.

RBD of SARS-CoV-2 plays a crucial role in determining the efficiency of viral entry into host cells, as it directly interacts with the human angiotensin-converting enzyme 2 (ACE2) receptor. SARS-CoV-2 variants with more RBD mutations tend to be more immune-evasive, while still being highly transmissible.

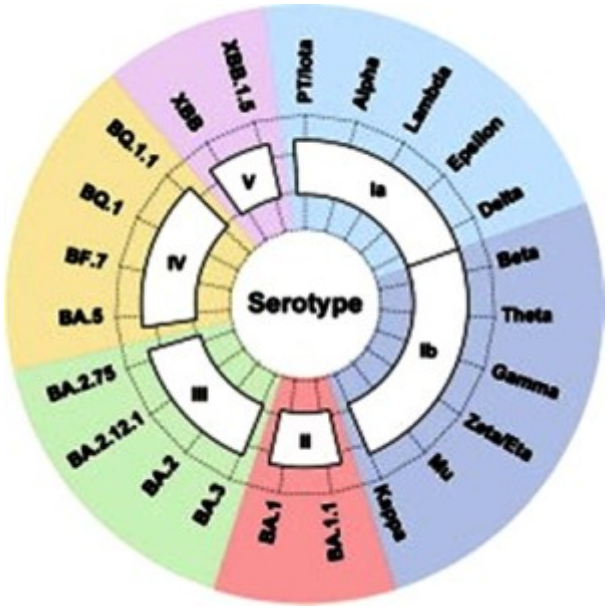
The authors have emphasized that the classification of viral serotypes has proven to be pivotal in the preventing and controlling viruses. They explained that dengue virus, for example, is classified into four serotypes, each encompassing multiple diverse genotypes. The immunogenicity of vaccine candidates for dengue virus has always been evaluated based on their ability to neutralize the four serotypes. The establishment of distinct serotypes could provide a foundation for a rapid evaluation of the antigenicity of newly emerged variants.



About the study

The researchers inoculated a mouse model with RBD-based vaccines to simulate the infection of a single variant. With cross-neutralization of antisera they conducted a systematic characterization of the antigenicity of 23 representative SARS-CoV-2 variants, which encompassed the prototype (PT), pre-Omicron VOCs, pre-Omicron VOIs, and Omicron sub-variants including BA.1, BA.2, BA.5, XBB, and their derivatives.

These data enabled the classification of the 23 variants into five distinct serotypes based on a systematic assessment of the antigenicity of their RBD in the S protein. The five distinct serotypes were designated as serotype-I, II, III, IV, and V. Each serotype contains several genetically distinct SARS-CoV-2 variants.



The ilustration from the original article by Hu S, Wu C, Wu X et al. Science Bulletin. In press.2023

All the pre-Omicron variants were classified as serotype-I (with two subtypes), since they all potently cross-react with each other. Two subtypes, serotype-Ia (PT, Alpha, Lambda, Epsilon, or Lambda) and serotype-Ib (Beta, Theta, Gamma, Zeta, Mu, and Kappa), were classified within serotype-I. All the serotype-Ib variants possessed the E484K/Q mutation in RBD, while all the serotype-Ia variants (PT, Alpha, Lambda, Epsilon, and Delta) did not. These results suggest that the additional immunogenicity of serotype-Ib may be attributed to the presence of the E484K/Q mutation.

The remaining four serotypes are all comprised of Omicron sub-variants at various stages of evolution. The BA.1 and BA.1.1 subvariants were classified as serotype-II because they only cross-react with BA.1 and BA.1.1, which was unique among the all selected variants. Based on the similarity of their neutralization spectra, the remaining Omicron subvariants were classified into three serotypes, with BA.3, BA.2, BA.12.1, and BA.2.75 being serotype-III, BA.5, BF.7, BQ.1, and BQ.1.1 being serotype-IV, and XBB, XBB.1.5 being serotype-V.

The Omicron sub-variants showed a consecutive antigenic shift, with variants in serotype-III evading variants in serotype-II, which in turn were evaded by serotype-IV variants, and further evaded by serotype-V variants. Each Omicron subvariant exhibited specific cross-reaction with the variants in the preceding serotype, indicating that evading the previously dominant variant was the primary driving force behind the evolution of the Omicron

subvariants.

However, no such a consecutive antigenic shift was observed during the transition from serotype-I to serotype-II, suggesting that Omicron was not a direct decedent of the prevalent variants immediately prior to its emergence. This observation is consistent with previous analyzes of the mysterious origin of Omicron.
https://discovermednews.com/omicron-variants-may-have-been-artificially-synthesized-rather-than-naturally-formed/

The authors pointed out that this classification of serotypes was based on the assessment of cross-neutralization of antisera using RBD-based mRNA vaccines to simulate infection with different SARS-CoV-2 variants. They emphasized that the antigenicity of SARS-CoV-2 could be influenced by proteins other than the S protein, or by domains of the S protein other than RBD, although RBD is the most antigenic domain in SARS-CoV-2.

In summary, this work proposes to classify SARS-CoV-2 variants into five serotypes based on RBD antigenicity, with all pre-Omicron variants classified as serotype-I and Omicron subvariants classified as serotype-II, III, IV, and V according to their stages of evolution. The authors suggested that this classification could facilitate the rapid determination of the serotype of newly emerged SARS-CoV-2 variants.

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