

Review of: "Omicron Variant Could be an Antigenic Shift of SARS-CoV-2"

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Potential competing interests: No potential competing interests to declare.

The review provides a compelling exploration of the impact of the SARS-CoV-2 Omicron variant on immune system evasion and its implications for the diminished effectiveness of various immunization approaches. While the information presented in the review is pertinent, there is room for improvement in the rewriting, and the following suggestions aim to enhance the manuscript.

Sections that should be improved to be more clear:

"The overall mutational landscape of Omicron shows a drift from other variants, lowering potency. "- lowering potency of what?

"This is the fourth year since the COVID-19 pandemic erupted, which continues to be fueled by the emergence of many variants and recombinants around different geographies of the world. " many variants and recombinants, what is the difference here for variants and recombinants?

"Mutants and recombinants of the virus are more transmissible and virulent" I do not agree that all mutants and recombinants increase virulence.

"The variants of concern are depicted in the figure" which figure and panel, describe better.

"who can get infected and become resistant to drugs, which could lead to not only long COVID or post-acute COVID syndrome but also the birth of more contagious variants. The Omicron variant appears to have evolved separately from all the previous mutational variants. "- which drugs?, and confused the last sentence.

"Theories to support Omicron's birth are explained as follows:" I suggest to change the word birth;

"Most of the mutations in the RBD region are reported to increase transmissibility and infection rate. The NTD region is also linked to increased transmissibility and virus binding affinity, S1/S2 increase infectiousness and transmissibility, and S2 has immunogenic response development significance (Dhawan et al., 2022). Some known mutations, such as D614G (B.1), N501Y, E484K (Eek), K 417, and L452R, allow the virus to bind more tightly to human cells and help spread the virus faster than ever."- confused

"These mutations in the RBD region were investigated via $\Delta\Delta G$ score" $\Delta\Delta G$ score of what assay?

“SARS-CoV-1 and SARS-CoV-2 “ should be SARS-CoV and SARS-CoV-2

“exhibited enhanced fusogenicity and S-processing”confused

“The neutralizing antibody level was reported as weakest in unvaccinated, convalescent, and naïve individuals who have received two doses of mRNA vaccine. Therefore, two doses of the vaccine were not sufficient to build the effective humoral response that was regained during reinfection or with a booster dose, still providing short-term protection.”
missing reference

“However, the prospects of primary immunization against the symptomatic disease of COVID-19 Omicron remain limited (Chavda et al., 2022). This can be defined as antigenic drift.”confused

“Anti-RBD IgM (297 mAbs) protects against pseudovirus beta and Omicron BA.1. It was also effective against SARS-CoV-2 WA 1 when the infection was given to epithelial cells in vitro (Hale M. et al., 2022). A cocktail of monoclonal antibodies (297) used with Regeneron REGN 10987/10933 mAbs didn’t neutralize Omicron. However, mAbs 297 possess neutralizing activity against Omicron BA.1 and BA.2 but is eventually reduced in the case of BA.4 and BA.5. Monoclonal antibodies are effective only if the prevalence of the respective variant is active (Huo et al. 2023). Therefore, it gives clues to develop pan-variant monoclonal antibodies that can be potent against RBD, NTD, and S2 conserved regions to boost immunity in the human body. There are 11 relevant mutations: 6 deletions and 1 insertion with N211Δ, ins 214 EPE are unique in the NTD region. “the text should be improved

“At approximately 22 dissociation constants, these nanomolecules can neutralize the virus in plaque reduction assays. The biparatropic nanobodies were more efficient and effective against SARS-CoV-2, irrespective of known virulent mutations. “ confused

“Myxomonas Xanthus” should be *Myxomonas xanthus* (italic)

“with Cys5p8 to Cys 538 disulfide bridge” what is Cys5p8?

“the RBD motif – site IV-V, and the rare antibodies sites I-II partially overlap the RNB also involved to some extent” what is antibody sites I-II and RNB?

“ tRNA in low abundance can enhance translation in rich conditions. “confused

“which was a result of antigenic shift and reassortment of antigens among avian, human, and swine viruses “confused

- Some regions of the review are used sub-lineages, variants and subvariants, I suggest reviewing the correct use for each of them;
- Abbreviations should be in described correctly in the first time that are written.

Some times Omicron variant and mutations as together and should be better described such as in this

