

# Review of: "Christ Bearing the Cross: the original antigenic sin of the immune system and its potential role in emerging diseases"

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This is a very interesting article where the authors have started with a religious notion for explaining the term 'original antigenic sin or OAS'. Although I believe there was no need to do that in this particular article because the authors basically are trying to justify the basic concept of antigenic sharing between related viruses and the immunological cross-reactivity. These concepts are fairly well understood now for many years, that old exposures to some of virus goes on to generate both T- as well as B- memory cells, which remain in the host for many many years and in some instances life long. These are the cells which are responsible for recall responses during the subsequent exposures to same or related viruses due to sharing of some antigenic components with the original viruses. The authors have nicely connected this with 'immune imprinting', which has been coined recently more frequently in context of response to SARS CoV2 vaccines which have been made using the gene-sequencing of original Wuhan strain of SARS CoV2, while the subsequent waves of pandemic were caused by mutated variants of virus like 'delta' and 'omicron' etc. There were obvious concerns raised about the possibility of reduced protective efficacy of these vaccines against mutated variants of virus due to the rapidly mutating nature of this virus. But the interesting part in this article is that the authors have tried to bring in the concept of 'antibody-dependent enhancement or ADE', which the authors have explained well with various examples of influenza, dengue and HIV viral infections in context of enhancement of viral replication after a second exposure or vaccination. The concept of ADE is relatively recent and is shown to occur due to preexisting antibodies having lower affinity or low neutralising capacity, which leads to weak binding of live viral particles and facilitating their uptake by the host cells via Fc or Complement receptors, further leading to release of live virus inside the cells causing enhanced replication. This being a very interesting immune phenomenon, which is contrary to the belief that the vaccines should always induce a protective response and the pre-existing memory cells should always facilitate a more rapid protective response.

Overall, the article is well written and generates interest with the readers, so I fully endorse the paper.