Review of: "M-cell targeting acid-resistant oral vaccine delivery for immunization against Hepatitis B infection using cationic solid lipid nanoparticles"

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Potential competing interests: No potential competing interests to declare.

This study, if modified to improve clarity, is an impressive effort towards addressing the burden caused by Hepatitis B (HB) infection. If the efficacy can be demonstrated, this vaccine can be a very promising and a painless solution to immunize against HB infection.

The article needs to be re-written/revised to improve the clarity of expression and grammatical correctness.

Title must be edited appropriately. The items below need to be addressed/clarified:

- there is no evidence shown for the claim that this vaccine targets M-cells.
- HB virus neutralizing assays are needed to confirm that this vaccine immunizes against HB infection.
- the claim for ‘acid-resistance’ of the vaccine does not seem to be proven with data or citations.

Method: Specifics of the mice (e.g., age and weight), and the sample collection methods (e.g., for intestinal lavage) must be included.

Fig 1, Abstract, and in the body: The phrase ‘cSLNs encapsulated in LPS’ may be better than ‘LPS anchoring with cSLNs’. Also, after defining cSLNs in the abstract, that abbreviation must be used in place of ‘nanoparticles’ and ‘prepared nanoparticles’, etc., throughout the rest of the article.

Fig 3: The molecular weights of the markers A to F must be stated.

Figs 4 and 5: Fold-changes in IgA and IgG, compared with blanks, must be indicated.

Tables 3 and 4: If the particles remained stable,

- why did the particle-size of the formulations change over time?
- why did the protein content of the formulations decrease over time?

Interpretation: The basis behind the claim that LPS-HB-cSLNs are non-toxic must be stated.