Developmental study of epitopes-presenting synthetic vaccine to induce specific Abs able to prevent infection of SARS-CoV-2 variants.

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Based on the identified RBD-epitopes of ACE2-binding and HR2-epitope of membrane fusion in SARS-CoV-2 Spike molecule, we produced a prototype of multivalent epitopes-conjugated vaccine that can induce IgG and IgA Abs recognizing Spike protein in mice by its priming via subcutaneous and sublingual boosting. These data indicated that convenient sublingual administration can enhance Ab-titers and induce class-switch to IgA Abs critical of mucosal immunity.

In this project, we will select appropriate adjuvants with the aim of further increase of neutralizing Abs (nAbs) and examine formulations that maximize the inhibitory ability against live virus infection. In addition to the epitope-conjugated vaccine development, we will develop a novel technology that utilize chemical ligands able to efficiently help Abs production from B cells, and that present the nAb-epitope structure to bind to the chemical ligands. It is a fully synthetic vaccine that induces the actions of both chemical ligand and epitope-Abs production.

This synthetic epitope vaccine (multivalent epitopes-conjugated carrier protein or fully synthetic epitope-conjugated chemical ligand) has the following features compared to existing LNP-mRNA vaccines and the like.

1) Synthetic epitope vaccines, in particular the fully synthetic epitope vaccines utilizing chemical ligands, can be produced in combinations of the existing coupling reactions and can be produced at usual manufacturing facilities for small molecule drugs.
2) It is very likely this synthetic epitope vaccine is useful as a booster vaccine to enhance, maintain and induce neutralizing ability for convalescents and healthy people vaccinated with S antigen mRNA, especially for low Ab- and poor Ab-titer population by the sublingual administration.
3) The identified neutralizing epitopes do not contain any epitopes of Abs-dependent infection enhancement, so that this synthetic epitope vaccines can minimize to produce Abs unrelated to the infection-neutralizing ability.

The fully synthesized vaccine antigen containing the defined epitopes including universal epitope will be assessed nAbs production with optimized sublingual administration condition. Then, this booster vaccine will be tested in in vivo infection model for confirming pharmacological POC.