Glycopeptide vaccine: Study of an innovative vaccine modality targeting invariant glycosylation sites

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A major challenge to developing effective vaccine is the extensive genetic diversity in the targeted protein antigens. Our interest was focused on the presence of invariant glycosylation sites that have critical roles in protein folding and regulation/maintenance of functional three-dimensional structures, even though genetic diversity plays a major role in immune evasion and is a barrier to the development of vaccine-induced protective immunity.

The purpose of this study is to establish an innovative vaccine morality targeting invariant glycosylation sites distributed in the disease-relevant glycoproteins, namely glycopeptide vaccines. Recently we developed a novel method for the creation of antibodies recognizing glycopeptidic epitopes based on the specific antigen presentation mechanism without lysosomal degradation of the target glycopeptides as antigens. Our findings facilitated generation of monoclonal antibody SN-343 to SARS-CoV-2 spike protein, in which SN-343 binds tightly (Kd = 1~10 nM) to the spike protein of Omicron sub-variants such as BA2.75 and XBB by interacting specifically with glycosylated peptide region involving Asn343 residue. In the present study, we develop efficacious glycopeptide vaccines for SARS-CoV-2, HIV-1, and Malaria Plasmodium falciparum by targeting 9 potential peptide regions with an invariant glycosylation site identified in the spike protein of SARS-CoV-2, gp-120 of HIV-1, and PfRH5 of malaria, respectively. The study is composed of 5 key projects: (1) Identification of glycosylated peptide regions as candidates for glycopeptide vaccines, (2) Construction of highly efficient processes for the production of glycopeptide vaccines, (3) Assessment of biological activities of glycopeptide vaccines such as potentials for generation of broadly neutralizing antibodies including the optimization of adjuvants and carrier materials, (4) Characterization and validation of neutralizing monoclonal antibodies for obtaining non-clinical Proof-Of-Concept (POC), and (5) Studies on the mechanism in the immunological activities by glycopeptide vaccine modality.