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Oral presentation

Toward a glycopeptide-based HIV-1 vaccine

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A major difficulty in HIV-1 vaccine development is to identify conserved neutralizing epitopes. We hypothesize that conserved HIV-1 glycopeptides, a partial structure of the envelope glycoproteins, represent new types of neutralizing epitopes for several reasons: 1) certain HIV-1 glycopeptides are highly conserved and are well accessible; 2) a novel glycan cluster has been identified as the neutralizing epitope for the broadly neutralizing antibody 2G12, indicating N-glycan itself could serve as target of vaccine; and 3) the interactions of the carbohydrate and peptide epitope may generate new conformational epitope that could not be achieved by peptide or carbohydrate alone. To test this hypothesis, we have been exploring HIV-1 V3 domain glycopeptides that combine the conserved N-glycans as an essential epitope in immunogen design. Toward this end, we have developed a novel chemoenzymatic method for constructing large homogeneous HIV-1 V3 glycopeptides that are hitherto unavailable. Preliminary studies have revealed that the glycosylation affects the global conformation of the V3 domain and can protect the V3 domain against protease digestion. The binding of the synthetic HIV-1 glycopeptides with neutralizing antibodies (2G12, 447-52D) and other V3-specific antibodies is in progress and the implications of the results for effective immunogen design will be discussed.