Methods and compositions for the treatment or prevention of human immunodeficiency virus infection

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摘要

It is widely accepted that the heavily glycosylated glycoprotein gp120 on the surface of HIV-1 shields peptide epitopes from recognition by the immune system and may promote infection in vivo by interaction with dendritic cells and transport to tissue rich in CD4 T cells. A conserved cluster of oligomannose glycans on gp120 has been identified as the epitope recognized by the broadly HIV-1-neutralizing monoclonal antibody 2G12. Oligomannose glycans are also the ligands for DC-SIGN, a C-type lectin found on the surface of dendritic cells. Multivalency is fundamental for carbohydrate–protein interactions, and mimicking of the high glycan density on the virus surface has become essential for designing carbohydrate-based HIV vaccines and antiviral agents. An efficient synthesis of oligomannose dendrons, which display multivalent oligomannoses in high density, and characterize their interaction with 2G12 and DC-SIGN by a glycan microarray binding assay is disclosed. The solution and the surface binding analysis of 2G12 to a prototype oligomannose dendron clearly demonstrated the efficacy of dendrimeric display. These glycodendrons inhibit the binding of gp120 to 2G12 and recombinant dimeric DC-SIGN with IC50 in the nanomolar range. A second-generation Man9 dendron was identified as a potential immunogen for HIV vaccine development and as a potential antiviral agent.

技術優勢

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應用範圍

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