HIV gp41-Membrane Proximal External Region Arrayed on Hepatitis B Surface Antigen Particles for HIV Diagnostic and Vaccine Application

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Technology description

Summary

This technology describes vectors encoding the membrane proximal external region (MPER) and select variants from HIV-1 gp41 linked to the hepatitis B surface antigen (HBsAg) and the resulting expressed particles for use in HIV diagnostic and vaccine applications. HIV-1 gp41 membrane proximal region contains two epitopes recognized by broadly neutralizing human monoclonal antibodies 2F5 and 4E10. However, immunization with gp41 MPER or the 2F5 or 4E10 epitopes have failed to raise neutralizing antibodies. In the subject technology, the particles were shown to bind antibodies from broadly neutralizing human sera and to the two known broadly neutralizing antibodies 2F5 and 4E10 with high relative affinities, demonstrating that the relevant epitopes are accessible for antibody binding and the potential utility of the particles in diagnostic applications. Additionally, these particles could be used to screen phage-display libraries for novel broadly cross-reactive neutralizing antibodies, of which only five are currently known. These particles could also be used for selection of MPER specific B cells. Lastly, these particles have been shown to be immunogenic and raise antibodies that recognize HIV-1 Env gp160 expressed on the cell surface. These immunogens can elicit neutralizing antibodies specific for HIV gp41 MPER, the MPER of gp41 is highly conserved across various HIV clades and therefore is likely to generate broadly neutralizing antibodies when administered in a proper presentation in a lipid context as is the case in HBsAg particles. Multiple copies of the MPER of HIV-1 gp41 arrayed on the particles could significantly increase the immunogenic potential compared to monomeric molecules. An increase of this nature has been observed with HBsAg and HPV virus-like particles in hepatitis B and cervical cancer vaccines, respectively, suggesting that particulate array may improve the presentation of selected epitopes to the immune system.

Application area

HIV vaccines; HIV diagnostics

Advantages

These immunogens can elicit neutralizing antibodies specific for HIV gp41 MPER, which is highly conserved across various HIV clades and therefore is likely to generate broadly neutralizing antibodies when administered in a proper presentation in a lipid context as is the case in HBsAg particles. Multiple copies of the MPER of HIV-1 gp41 arrayed on the particles could significantly increase the immunogenic potential compared to monomeric molecules.

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