Membrane Proximal Region of HIV gp41 Anchored to the Lipid Layer of a Virus-Like Particle Vaccine

Technology Summary

The HIV-1 envelope glycoproteins (gp120-gp41), which mediate receptor binding and entry, are the major targets of neutralizing antibodies. Although the envelope glycoproteins are immunogenic and induce a variety of antibodies, the neutralizing antibodies that are induced are strain-specific and the immune response is mostly diverted to non-neutralizing determinants. Broadly neutralizing antibodies have been isolated only from natural HIV infection, and rarely, as only five broadly-neutralizing antibodies have been identified to date. Three of these antibodies are gp41-directed (2F5, 4E10 and Z13) and the other two (b12 and 2G12) are gp120-directed. The three gp41 neutralizing antibodies recognize the membrane proximal region (MPR) of the HIV-1 gp41 glycoprotein. The membrane proximal region (MPR) region includes a series of amino acids that lie on the HIV virus surface, just before gp41 crosses the viral membrane. The MPR is highly hydrophobic (50% of its residues are hydrophobic) and is highly conserved across many HIV clades. Recently, the hydrophobic part of MPR and the presence of lipid membrane were shown to bind to 2F5 and 4E10 antibodies. To date, immunization with conserved membrane proximal elements or the core 2F5 epitope has failed to elicit broadly neutralizing antibodies.

Available for licensing is a technology that uses the immunogenic hepatitis B surface antigen (HBsAg) platform to array epitopes from the conserved, neutralization-sensitive MPR of HIV-1, and use of these constructs to induce an immune response to HIV-1. The replacement of a membrane spanning domain of HBsAg with a membrane spanning domain of gp41 anchors gp41 into HBsAg in virtually the same orientation as on HIV virions and correctly orients the nearby MPR on the lipid layer. HBsAg variant compositions with one or more transmembrane domains of the HBsAg replaced with a gp41 transmembrane domain and one or more gp41 MPRs are available for licensing.

Potential Commercial Applications

- Development of Human Immunodeficiency Virus (HIV) vaccines, therapeutics and diagnostics

Competitive Advantages

- Novel vaccine candidate
- Technology applicable to diagnostics and therapeutics

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Publications: Ira Berkower, Angelo Spadaccini, Hong Chen, Danah Al-Awadi, Jacqueline Muller, Yamei Gao, Dino Feiglestock, Konstantin Virnik, Yisheng Ni. Hepatitis B Virus Surface Antigen Assembly Function Persists when Entire Transmembrane Domains 1 and 3 are Replaced by a Heterogenous Transmembrane Sequence, Journal of Virology Feb 2011, 85 (5) 2439-2448.

Intellectual Property: United States Patent: US 9,005,631 issued 04.14.2015, United States Patent: US 9,897,645 issued 02.20.2018

Product Area: HIV vaccine, HIV therapeutic, HIV diagnostic

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