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Filovirus Immunogen Display Platform

Researchers at the La Jolla Institute for Immunology (LJI) have engineered the ebolavirus glycoprotein (EBOV-GP) by replacing the mucin-like domain (MLD) with heterologous immunogens which could be developed as multiple-valent vaccines against emerging and re-emerging pathogens.

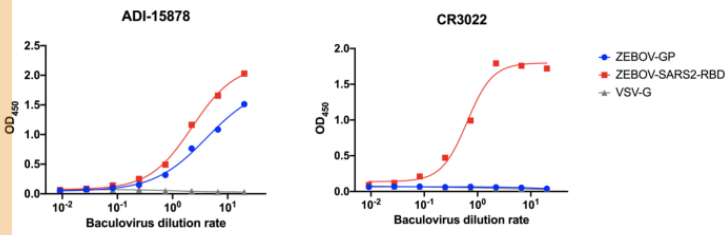
The glycoprotein (GP) of ebolavirus (EBOV), which sufficiently elicits protective immune response in animals and human beings, is the key immunogen of the licensed vaccine against EBOV (Ervebo®). The mucin-like domain (MLD) of EBOV-GP is a highly variable domain and structurally independent from the main GP trimer. It is one of the immunodominant regions that is exposed on the surface of EBOV-GP trimer; however, the antibodies elicited by MLD are usually non-cross-reactive and less protective.

As such, the researchers at LJI have engineered with EBOV-GP to display heterologous immunogens, using the RBD of SARS-CoV-2 and mCherry fluorescent protein as two examples. Particularly in the first example, the novel immunogen combines the key neutralizing determinant of SARS-CoV-2 with Ebola virus to make a single immunogen for use in Africa. Display of only the RBD allows steering of the antibody response to the predominant neutralizing epitope and limits risk of antibody dependent enhancement by complete spike protein-containing immunogens. Placement of the SARS-CoV-2 RBD within a flexible upper display region of EBOV-GP enhances its presentation and allows trivalent display of the RBD within the framework of a vaccine backbone already shown to be safe and efficacious in over 200,000 people in west Africa. Fusion of the SARS-CoV-2 key neutralizing determinant into the EBOV-GP may allow immunization against two serious diseases at once.

ADVANTAGES:

- Applicable for multiple-valent vaccine development against emerging and re-emerging pathogens
- Allows trivalent display of immunogen within the framework of a vaccine backbone already shown to be safe and efficacious in over 200,000 people in west Africa

Novel Filovirus Immunogen Display Platform Created by Replacing EBOV-GP MLD with Heterologous Immunogens



ELISA binding assay of baculovirus and monoclonal antibodies. Anti-Ebola neutralizing antibody (ADI-15878) and anti0SARS-CoV-2 RBD confirmational antibody (CR3022) were used to verify the conformation of ZEBOV-GP and RBD.

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La Jolla Institute for Immunology | Business Development
+1 (858) 752-6500
bd@lji.org
https://www.lji.org/research/licensing-opportunities/