

OVERVIEW

Viral diseases such as measles, mumps, rubella, and yellow fever are controlled by immunization with live attenuated viral vaccines. The mild or asymptomatic infections caused by the attenuated vaccine viruses generates immunity that prevents disease after later natural exposure to the viral disease agents. Similarly, immunity induced by experimental live attenuated SIV vaccines has been shown to protect macaques from progressive SIV infection caused by highly pathogenic challenge viruses. Unfortunately, a vaccination strategy based on live attenuated strains of HIV for use in people is too risky, thus the objective of the program led by Dr. Chris Parks at The International AIDS Vaccine Initiative (IAVI) is to use viruses that do not cause serious human illness to generate replication-competent viral vectors to deliver HIV vaccine immunogens.

Vectors based on vesicular stomatitis virus (VSV) have been the primary focus of recent research because VSV can be used to generate chimeric viruses in which the natural VSV glycoprotein (G) is replaced with HIV Env. VSV-HIV chimeric viruses can be developed that express Env that incorporates in the infected cell membrane and VSV particle where it performs functions needed to support viral replication specifically in T lymphocytes that express the HIV co-receptors CD4 and CCR5. Therefore, vaccination with a live VSV-HIV chimera has the potential to mimic multiple important aspects of Env presentation that would occur during an HIV infection.

A lead chimeric VSV-HIV vaccine candidate (VSV Δ G-Env.BG505) has been developed based on clade A HIV Env from strain BG505. In the first preclinical vaccine efficacy study conducted in Indian rhesus macaques, 7 of 10 animals vaccinated with VSV Δ G-Env.BG505 resisted infection following repetitive rectal challenge with heterologous clade B SHIV SF162p3 while the 3 macaques that became infected were shown to have substantially lower Env antibody responses induced by vaccination. Efficacy also was shown to be associated with the chimeric virus design, as a group of macaques vaccinated with a more typical VSV vector that expressed both VSV G and Env developed Env antibodies but failed to resist SHIV infection.

The efficacy of VSV Δ G-Env.BG505 as well as the association between antibodies and protection support additional investigation and development of the vaccine platform. A grant was awarded to further develop the VSV Δ G-Env.BG505 vector, including advancement of processes to support vaccine manufacturing and analytical assessment of the vaccine product, manufacturing of the VSV Δ G-Env.BG505 vaccine material, preclinical safety assessment, and a phase 1 exploratory clinical trial.

RESEARCH OBJECTIVES

- 1.) Conduct a non-human primate study to further evaluate variable affecting VSV Δ G-Env.BG505 vector immunogenicity and efficacy that will inform the design of the exploratory phase 1 clinical trial
- 2.) Complete construction of the Vero CD4+/CCR5+ cell line and establish a qualified cell bank.
- 3.) Complete rescue and characterization of a VSV Δ G-Env.BG505 vector and establish a virus seed that will support vaccine manufacturing
- 4.) Conduct preclinical safety / toxicology assessment of the VSV Δ G-Env.BG505 vector
- 5.) Develop and transfer processes and analytical testing methods to support vaccine manufacturing a contract manufacturing organization. Manufacture VSV Δ G-Env.BG505 clinical trial material.
- 6.) Communicate with regulatory authorities and file an IND and other document as required to enable a phase 1 exploratory clinical trial
- 7.) Conduct an exploratory phase 1 clinical trial including immunologic assessment to determine if Env antibody responses associated with preclinical efficacy are observed in clinical trial volunteers.

Grant at a Glance

Principal Investigator
Chris Parks, PhD



Grantee Institution
International AIDS Vaccine Initiative,
New York, USA

Project Title
Live Attenuated VSV-HIV-Env Vaccine Candidate for Evaluation in a Clinical Trial

OPPID
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Grant Award
Up to \$21.8 Million, awarded October, 2016