Parks: HIV Vaccine Clinical Candidates based on Replication-Competent Viral Vectors that Preferentially Replicate in Lymphoid Tissues

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 coreceptors 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△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△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△G-Env.BG505 as well as the association between antibodies and protection support additional investigation and development of the vaccine platform and the immune responses it elicits. A grant to further develop the VSV△G-Env.BG505 vector was awarded to support a second preclinical efficacy study and to initiate activities required to advance a VSV△G-Env.BG505 vector for future evaluation in a phase 1 explor- atory clinical trial.

Grant at a Glance

Principal Investigator
Chris Parks, PhD

Grantee Institution
International AIDS Vaccine Initiative, New York, USA

Project Title
HIV Vaccine Clinical Candidates based on Replication-Competent Viral Vectors that Preferentially Replicate in Lymphoid Tissues

OPPID
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Grant Award
Up to $5.8 Million, awarded March, 2016

RESEARCH OBJECTIVES

1.) 1.) Evaluate the VSV△G-Env.BG505 vector in a non-human primate study to confirm efficacy observed previously and investigate variables affecting vaccine immunogenicity.

2.) Develop methods for further assessment of the immune response elicited in the non-human primates and detailed analysis of the composition of the vaccine vector

3.) Construct Vero CD4+/CCR5+ cell line, required to propagate the VSV△G-Env.BG505 vector, which complies with cGMP vaccine manufacturing

4.) Prepare VSV△G-Env.BG505 pre-Master Virus Seed that complies with cGMP vaccine manufacturing