Pantaleo: RepliVax Vaccine Platform

OVERVIEW

Pantaleo's RepliVax VDC focuses on the development of novel replication competent platforms for optimal priming of antibody responses. The overarching goal of the work performed for this grant is to develop a replication competent self-limiting single cycle flavivirus vector based HIV vaccine candidate, ie RepliVax®, for use in a prime-protein boost regimen with a strong emphasis on eliciting optimal, robust and durable/boostable antibody responses. In parallel to the RepliVax® development, the VDC will also focus on the development of novel delivery systems for Env proteins and generation of novel Env immunogens. Two main approaches to this end are planned: (i) target ENV antigen(s) to dendritic cells (DCs) using a DC-specific antibody and (ii) use bioinformatics to generate ENV immunogens (ENV) with improved epitopes selected basd on binding to broadly neutralizing antibodies.

RESEARCH OBJECTIVES

1.) To develop a RepliVax® based viral vector platform for delivering HIV antigens

2.) To generate novel Env immunogens and delivery systems for Env proteins

3.) Immunological characterization of the RepliVax® vectors and prime/boost immunization strategies

PROGRESS

The VDC has completed a series of in vitro and in vivo (mice and NHP) immunogenicity studies with RepliVax in different prime-boost regimens combining with DNA, and/or NYVAC, and/or protein, and have demonstrated that:

- RepliVax is highly attenuated in sensitive 2-3 day old suckling mouse neurovirulence studies and has shown to be safe and well tolerated in NHP studies
- RepliVax vectors can be used in combination with other vectors to elicit HIV specific cellular and humoral immune responses as a potentially effective vaccination strategy.

In collaboration with Inserm, the VDC has also conducted several NHP studies with DC-targeting based vaccines. Meta-analysis across several NHP studies has been performed by VISC comparing DC-targeting vaccines bearing Env gp140 with the gp120 protein formulated with MF59 adjuvant, and the outcome indicated portential advantages for DC-targeting via CD40 for more durable cellular and humoral responses.

Last but not least the VDC has successfully generated a number of novel Env proteins which have exhibited potentially improved antigenic properties. Results from the rabbit immunogenicity study has shown that these variants induced robust binding antibody responses and high neutralization against the Tier 1A isolate.

Grant at a Glance

Principal Investigator

Giuseppe Pantaleo, MD

Grantee Institution

Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

Project Title

A novel replication competent flavivirus-based HIV vaccine platform, i.e. RepliVax, as a priming component for improving antibody response

OPPID

1040705

Grant Award

Up to $8.8 Million, awarded September, 2012

Collaborating Institutions

- Arizona State University, USA
- Baylor Research Institute, USA
- Consejo Superior de Investigaciones Cientificas
- Fred Hutchinson Cancer
- Institut Nationaal de la Sante et de la Recherche Medicale, France
- Sanofi Pasteur, Canada
- University of Regensburg, Germany