Pantaleo: Poxvirus-Based Vaccine Development

OVERVIEW

The primary goal of the Pantaleo-led research consortium is to generate highly attenuated replication-competent poxvirus vectors that would substantially improve the breadth of HIV-1-specific vaccine induced immune responses. This strategy is also combined with the deletions of certain poxvirus genes known to interfere with the induction of the immune response. These newly generated vectors, in addition to improving the magnitude and the quality of the vaccine-induced HIV-1-specific T cell response, may serve as potent priming strategies for envelope protein-based vaccines, and thus for the induction of potent antibody responses.

Furthermore, Pantaleo/CHUV was awarded with a 2nd grant to develop the DNA/NYVAC platform. The DNA/ NYVAC platform has been tested in multiple phase I and II clinical trials in Europe and has shown to be highly immunogenic. This part of the project represents further development of the DNA/NYVAC platform targeted to improve both the magnitude of the T-cell response (particularly the CD8 T cell response) and breadth of the response. The primary goal of the project is to investigate whether the 2nd generation DNA-C/NYVAC-C vaccine combination, together with novel immunization strategies, is able to increase response magnitude and breadth and induce balanced Env (versus Gag, Pol and Nef) HIV-1-specific T cell responses in humans.

RESEARCH OBJECTIVES

1.) Development of poxvirus-based vaccine candidate(s) with at least a 10-fold increase in immunogenicity, as measured by the frequency of vaccine-induced T-cells when compared to the current poxvirus vectors; development of novel formulation/delivery strategies.

2.) Conduct NHP studies as well as a phase I safety and immunogenicity study with the 2nd generation DNA and NYVAC vaccine candidates, to generate data for the phase IIB study in sub-Saharan Africa.

PROGRESS

At present, the research consortium has:

1.) Completed several NHP studies:

   a.) Demonstrated that the new NYVAC and DNA vaccines developed within PTVDC are highly immunogenic, both in terms of T-cell and B-cell responses

   b.) Evaluated and compared different vaccine combinations, inserts, and regimens which have provided pivotal data for the design of future clinical studies

2.) 2. In collaboration with HVTN, a number of phase I/II trials have been completed evaluating the safety and immunogenicity of different vaccination regimens combining DNA, NYVAC, and protein vaccines in the US and sub-Saharan Africa. The more recent effort has been focused on the evaluation of a DNA and protein combination, and results have demonstrated that the combination elicits robust antibody and T-cell responses. A comparative analysis with the ALVAC/protein combination has shown that the DNA/protein regimen induces potent V1V2 responses, greater than the ALVAC/protein regimen. These responses were shown to be immune correlates of reduced risk from HIV infection in the RV144 trial. The DNA/protein is now planned for a phase IIB efficacy trial in Africa, supported by a European program.

3.) 3. In collaboration with the Haynes and Felber groups, a NHP SHIV challenge study has been initiated, evaluating the protective efficacy of different homologous prime-boost regimens combining NYVAC-KC, DNA-HIV-PT123, and sequential CH505 DNA gp145s co-administered with gp120 proteins (the EnvSeq-2 vaccine).

Grant at a Glance

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Grantee Institution
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Project Title
Poxvirus Vaccine Regimen Design

OPPID
38599 & 52845

Grant Award
Up to $21.1 Million, awarded August, 2006
Up to $5.7 Million, awarded November, 2009

Collaborating Institutions
- Arizona State University, USA
- Biomedical Primate Research Centre, The Netherlands
- CHU Henri Mondor, University Paris 12, France
- Consejo Superior de Investigaciones Cientificas, Spain
- Fred Hutchinson Cancer Research Center, USA
- Imperial College London, UK
- Institute for Research in Biomedicine, Switzerland
- IPPOX Foundation, Switzerland
- Leiden University Medical Centre, The Netherlands
- Murdoch University, Australia
- Oregon Health Sciences University, VGTI, USA
- Sanofi Pasteur, Canada
- University of Cambridge, UK
- University of Montreal, Canada
- University of Regensburg, Germany
- University of Washington, USA

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