Profectus Announces Publication of Preclinical Data Supporting the Effectiveness of Novel RALDH2 Mucosal Adjuvant for DNA Vaccines

BALTIMORE, Md., September 23, 2016 —Profectus BioSciences, Inc., a clinical-stage company developing novel vaccines for the prevention and treatment of infectious diseases and the treatment of cancer, announced today that the journal *Vaccine* has published preclinical efficacy data demonstrating that Profectus' mucosal homing adjuvant—a DNA plasmid encoding the gene Retinaldehyde dehydrogenase 2 (RALDH2)—enhances mucosal immunity when added to a DNA-based vaccine.

The paper, co-authored by researchers from Profectus and collaborators from the Arizona State University, reports that co-delivery of Profectus' mucosal homing adjuvant with a model DNA vaccine via electroporation significantly enhanced antigen-specific T cell responses in the mucosal compartments of mice and provided for dramatically superior protection from a vaginal viral challenge.

The publication, titled "Retinaldehyde Dehydrogenase 2 as a Molecular Adjuvant for Enhancement of Mucosal Immunity During DNA Vaccination," appeared online ahead of the print edition of *Vaccine*. The purpose of the published RALDH2 study was to provide proof of concept that the adjuvant, when added to a DNA-based vaccine, would enhance mucosal immunity. This was the first study of RALDH2 and compared an antigen plasmid alone, antigen delivered in combination with the RALDH2 plasmid, and antigen delivered along with systemic administration All-Trans Retinoic Acid (ATRA). It had previously been shown by collaborators that systemic ATRA administration during vaccination resulted in improved mucosal immune responses. The antigen/RALDH2 combination achieved better systemic and similar mucosal immune responses than the vaccine/ATRA combination. Perhaps most important, both RALDH2 and ATRA dramatically enhanced vaccine-mediated protection from a vaginal virus challenge, demonstrating the importance of mucosal immunity in vaccine-mediated protection. It is anticipated that RALDH2 will dramatically enhance the efficacy of Profectus' DNA and prime/boost vaccines by enhancing mucosal immunity, allowing the vaccine-elicited immune responses to combat invading pathogens directly at their points of entry at mucosal surfaces.

This study was funded by a Phase I Small Business Innovative Research (SBIR) grant (1R43AI089290-01) awarded to Profectus by the Division of AIDS, National Institute of Allergy and Infectious Diseases (NIAID). Profectus will next test the RALDH2 adjuvant in a macaque model of SIV infection under a recently funded follow-on Phase II SBIR grant (2R44 AI089290-02).

About the Profectus RALDH2 Mucosal Adjuvant for DNA Vaccines

Adjuvants are an agents that improve the effectiveness vaccines and are included in vaccines to enhance or otherwise modify the immune responses directed against the antigens contained in the vaccine. Adjuvants for conventional vaccines are composed of chemicals or pathogen components that are not usually found in the body. By contrast, adjuvants expressed by DNA plasmids can encode host genes such as cytokines, chemokines, co-stimulatory molecules, and signal transduction molecules that can stimulate potent anti-vaccine immune responses. Researchers at Profectus have exploited the ability of DNA vaccines to express host genes to create an adjuvant that can elicit mucosal immune responses from systemic intramuscular immunizations. The gene they used for this purpose is RALDH2, an enzyme that is crucial for the conversion of Vitamin A into retinoic acid. This represents a major breakthrough in vaccinology since mucosal immunity is highly desirable, but until now has only been achievable through the application of vaccines to mucosal surfaces, at technique that typically evokes much less robust immunity. Mucosal tropic chemokines have been previously reported to have similar mucosal homing adjuvant effects, but it has never been convincingly demonstrated that these DNA-expressed chemokines preferentially enhance mucosal immune responses over systemic responses. Likewise, a convincing mechanism of action for these chemokine adjuvants has never been reported. By contrast, RALDH2 exploits a well-known retinoic acid pathway to evoke mucosal immunity.

About Profectus BioSciences

Profectus BioSciences is a clinical-stage vaccine development company developing preventive and therapeutic vaccines for infectious diseases and oncolytic vaccines for cancer immunotherapy. Profectus vaccines are based on the company's proprietary VesiculoVax™ and DNA vaccine delivery platforms. Used alone, first-in-class VesiculoVax™-vectored vaccines lead to rapid expansion of B cells to provide protection against emerging infectious diseases of public health and biodefense importance such as Ebola, Marburg, Chikungunya, and the Equine Encephalitis viruses. When used as a boost after priming the immune system with best-in-class pDNA vaccines, VesiculoVax™-vectored vaccines lead to the expansion of primed T cells into effector cells that are uniquely suited to killing virally infected cells and cancers.

Current programs using the Prime/Boost System of Vaccines (PBS Vax™) strategy include hepatitis B virus (HBV), human papilloma virus (HPV), herpes simplex virus type 2 (HSV-2), and human immunodeficiency virus (HIV). Partners and collaborators include Vyriad, the Galveston National Laboratory at UTMB, Yale University, the Institute of Human Virology, the Center for HIV/AIDS Vaccine Immunology, the National Cancer Institute, the NIH Division of AIDS, the Bill and Melinda Gates Foundation, the International AIDS Vaccine Initiative, the HIV Vaccines Trials Network, and the AIDS Clinical Trials Group. Profectus has been funded by Cross Atlantic Capital Partners ("XACP") of Radnor, Pennsylvania. XACP's primary investor is the Pennsylvania Public School Employees' Retirement System (PSERS). For more information, please visit www.profectusbiosciences.com.

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