EpiVax Press Release
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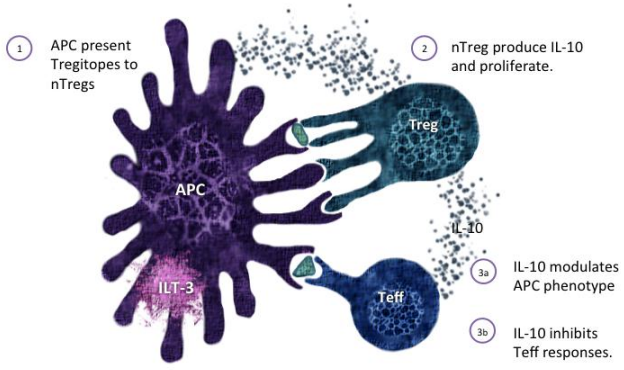
EpiVax Grant for treatment of Pompe Disease brings SBIR infusion to $3.4M for Proof of Principle Studies

Providence, RI - Providence-based biotech EpiVax, Inc. was awarded a new NIH SBIR Phase II grant totaling **$300,000 in funding** from the National Institutes of Health (NIH) NIAID for the first year of a two year program to **application of Tregitope to Pompe disease** through the NIH Small Business Innovation Research (SBIR) program. EpiVax recently received an additional SBIR award of $775,000 for application of Tregitope to Hemophilia, bringing the total to more than $3 million dollars in research funding. The surge in funding will result in new hires at the Providence-based biotech company, which is considering spinning off the Tregitope technology should angel or venture funding be made available.

The new SBIR, just announced this week, will be devoted to developing **a treatment for babies** who are born with Pompe disease, who lack the enzyme GAA and require treatment with replacement enzyme (Enzyme Replacement therapy, or ERT). Because the enzyme is a foreign protein, some of the babies develop antibodies to the drug. Currently, GAA-ADA sero-positive babies are treated with a combination of immunosuppressive drugs to induce immunological tolerance to ERT, but the long-term effect of these regimens is unknown. Alternative approaches that might redirect the immune response toward antigen-specific tolerance without immunosuppressive agents are needed. With funding from the NIH SBIR program, Tregitopes (T regulatory cell epitopes) will be tested (in animal models) for the future treatment of CRIM-negative Pompe disease.



Tregitopes were discovered in 2008 by the team of De Groot and Martin at EpiVax and the program is currently managed by Scientific Director, Leslie Cousens, Ph.D. The original discovery was published in the journal Blood in 2008[1], more recent papers include a comparision to IVIG that

[1] De Groot A.S., L. Moise, J.A. McMurry, Erik Wambre, Laurence Van Overvelt, Philippe Moingeon, W. Scott, W. Martin, Activation of Natural Regulatory T cells by IgG Fc-derived Peptide "Tregitopes". Blood, 2008,112: 3303. http://tinyurl.com/ASDeGroot-Blood-2008

was recently published online at Autoimmunity Reviews. Tregitopes are linear sequences contained within the framework of monoclonal antibodies and immunoglobulin G (also known as gamma globulin). **The Tregitopes act as a natural 'off switch" and have been shown in standard preclinical models, and by collaborating laboratories, to suppress and treat autoimmune disease, allergy, and to effectively suppress the immunogenicity of co-administered proteins**. According to **Dr. Srini Kaveri a well-known expert on IVIG (INSERM**) in Paris, "*It is most likely that some of the well established and successfully practiced therapeutic strategies such as intravenous immunoglobulins to treat several serious autoimmune and inflammatory diseases in order to induce tolerance, may actually be harnessing the potential of Tregitopes".*

Anticipated uses of Tregitope include induction of **tolerance to co-administered protein drugs**, a market worth more than **$100B globally**. Also known as **biotherapeutics**, drugs such as Campath, Rituximab, enzyme replacement therapies such as Myozyme, and blood factors such as FVIII often induce antibodies, rendering the drugs less effective or ineffective. In addition, Tregitopes may have broad applications in **Transplant** according **Nader Najafian, M.D.**, who is using Tregitopes in research being performed at Harvard Brigham and Women's Hospital, and therapy for **autoimmune diseases** such as **Multiple Sclerosis**. Researcher **Samia Khoury M.D.,** an internationally recognized MS researcher also based at Harvard Brigham and Women's hospital, says that pre-clinical studies of Tregitope being carried out in her laboratory by researcher **Wassim Elyaman, Ph.D.,** are "promising". The Tregitope technology won awards from the **American Transplant Association (ATA)** and from the **American Association of Pharmacologists (AAPS)** in 2010 and 2011.

About Pompe Disease

Babies born with Pompe disease require life-long treatment with enzyme-replacement therapy (ERT). Despite the human origin of the therapy, recombinant human lysosomal acid α glucosidase (GAA, rhGAA), ERT unfortunately leads to the development of high titers of anti-rhGAA antibody, decreased effectiveness of ERT, and a fatal outcome for a significant number of children who have Pompe disease. **De Groot and her fellow researchers have been pursuing the idea that Tregitopes could be applied to "CRIM-positive" Pompe disease** for some time, and that the treatment would induce tolerance to the life-saving enzyme "GAA" that these babies require. The severity of disease, anti-drug antibody (ADA) development, and the consequences thereof are directly related to the degree of the enzyme deficiency. Babies born with a complete deficiency GAA are said to have cross-reactive immunologic material (CRIM)–negative Pompe disease and are highly likely to develop GAA ADA. Less frequently, GAA ADA develop in CRIM-positive individuals. Teaching the immune system to tolerate GAA by co-delivering GAA with Tregitope peptides might dramatically improve the lives of CRIM-negative babies and could be applied to other enzyme replacement therapies to which ADA have been induced. Funding from the NIH will support proof of principle studies in GAA-deficient mice, in collaboration with Dwight Koeberl of Duke University. See also **http://www.ninds.nih.gov/disorders/pompe/pompe.htm**

"The endorsement, and more so the continued funding, by the National Institutes of Health of EpiVax's Tregitope program, is further validation of the promising research pioneered by Dr. De Groot and her colleagues and collaborators," stated **Richard G. Horan, managing director at the Slater Technology Fund**. *"Rhode Islanders have been well-served by the support provided EpiVax from the Slater Fund in the company's early years. In addition to generating a return on the fund's investment, the company has generated over a decade of high value, high wage jobs funded by steadily-increasing grants and contracts with pharmaceutical and biotech companies. It's a great example of academic innovation translating into robust economic development in biotechnology."*

About Tregitopes

In recognition of the importance of the discovery for biologics, the American Association of Pharmacologists awarded Tregitope an "Innovation Award" in 2010: **http://tinyurl.com/EpiVax-AAPS-Award.** NIH and Foundation funding for Tregitope research at EpiVax amounts to more than $6 M over the past 4 years.

The SBIR Program

The **Small Business Innovation Research (SBIR) program** enables small businesses to explore their technological potential and provides the incentive to profit from its commercialization. The mission of the SBIR program is to support scientific excellence and technological innovation through the investment of Federal research funds in critical American priorities to build a strong national economy. The program's goals are to stimulate technological innovation, meet Federal research and development needs, foster and encourage participation in innovation and entrepreneurship by socially and economically disadvantaged persons, and to increase private-sector commercialization of innovations derived from Federal research and development funding. By including small businesses in federally funded R&D, the program fosters entrepreneurial spirit while bolstering specific research and development needs.

The **SBIR program was established under the Small Business Innovation Development Act of 1982**, and through 2009, over 112,500 awards have been made totaling more than $26.9 billion. Congress has continued to support the program with numerous extensions, the most recent of which extends the SBIR program through 2017.

About EpiVax

EpiVax, Inc. is a Providence, Rhode Island biotechnology company focused on the development of vaccines and immunotherapeutics. EpiVax is one of the world's leading innovators in the field of "Immunogenicity Screening". The company uses immunoinformatics tools to screen protein therapeutics and to deimmunize these drugs so as to reduce adverse effects in the clinic. The Tregitope technology adds to the EpiVax Immunogenicity Toolbox, as it is expected to improve tolerance of protein drugs such as replacement enzymes, blood factors, and monoclonal antibodies.

The company was spun out of Brown University in 1998 with start-up funding from Slater Biotechnology (a state-backed investment fund). Led by Dr. Anne S. De Groot, M.D., Immunoinformatics and vaccine design thought leader, EpiVax has enjoyed success in the fields of immunology and bioinformatics, and has developed proprietary immunoinformatics tools for the development and improvement of biotherapeutic drug candidates. Through the application and utilization of these computational tools, EpiVax is helping to engineer safe, more effective therapeutic proteins and to rapidly design protective and efficacious new vaccines. EpiVax. *Science Without Fear.*

http://www.epivax.com/

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