

EpiVax Press Release

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New \$2.25M infusion of NIH funds for EpiVax' Tregitope, proposed "Paradigm-Shifting" Treatment

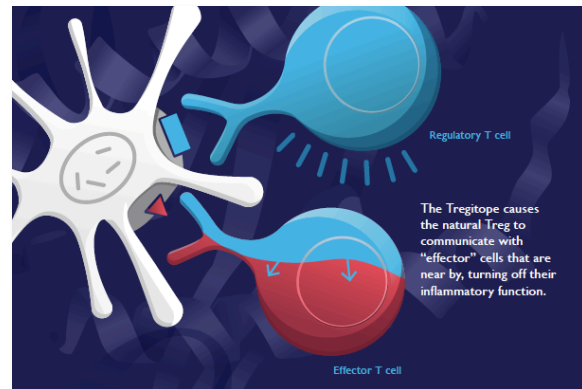
Providence, RI - Providence-based biotech EpiVax, Inc. was awarded a new NIH SBIR Phase II grant totaling **\$1.5M in funding** from the National Institutes of Health (NIH) NIDDK to **explore formulation, dose, route and delivery vehicle for Tregitope through the NIH Small Business Innovation Research (SBIR) program**. EpiVax anticipates receiving an additional SBIR award of approximately \$775,000 within the next few months, bringing the total to over \$2.25 million dollars for the first half of 2012.

The new funding from NIH will allow EpiVax to move this **important treatment for autoimmune diseases forward in preclinical studies**. 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 2008¹. These 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. Sridhar Kaveri of the Centre de Recherche des Cordeliers (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



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>

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.

The receipt of the original **Phase I SBIR grant awarded in 2008 allowed EpiVax to generate substantial evidence that Tregitopes may explain the effectiveness of IVIG**, a current leader in auto-immune treatment. In animal models, Tregitope appears to “reset” the immune response away from autoimmunity and towards tolerance, normalizing blood sugar levels. *“This is another great example of the important role the SBIR program has played in helping Rhode Island small businesses,”* said **Senator Sheldon Whitehouse**, who worked to re-authorize the program in the Senate last year. *“I commend EpiVax for its hard work and dedication over the years, and congratulate it on its SBIR grant. This funding will support Rhode Island’s knowledge economy by helping EpiVax continue its important research on the prevention and treatment of harmful diseases.”*

The initial target for Tregitope therapy will be Type 1 diabetes (T1D). Each year more than 13,000 young people are diagnosed with T1D. Islet replacement therapy is still in the experimental stage for individuals with advanced disease, but EpiVax believes that T1D-Tregitope therapy will facilitate this novel treatment for individuals in the later stages of T1D. Furthermore, preliminary studies carried out by EpiVax and collaborators indicate that Tregitope may be useful for inducing tolerance to transplants, protein drugs, and blood replacement therapies, suggesting that Tregitope may be useful for patients with other auto-immune diseases. EpiVax will use this new round of funding to develop a dosing and delivery procedure for Tregitope therapy in preparation for an IND. Preliminary “Safety and Toxicity” studies are also supported by the NIH Phase II.

“Developing more specific therapies to promote tolerance to the beta cell antigens that trigger the autoimmune response is a critical component of a comprehensive therapeutic approach to type 1 diabetes,” said **Julia Greenstein, Ph.D.**, assistant vice president of cure therapies for **JDRF**, whose previous funding for EpiVax helped the company derive preliminary data to support the new NIH funding. *“It’s great to see the NIH support EpiVax’s approach as this therapy may have the potential to reduce the harmful immune responses to the insulin-producing beta cells, thereby preserving the body’s ability to make its own insulin.”*

“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

Tregitopes are a set of peptides (small amino-acid sequences) that activate natural regulatory T cells. Tregitopes are promiscuous MHC Class II T cell epitopes located in the Fc and framework regions of Fab from IgG. Tregitope technology, an in-house discovery by Dr. De Groot, could be the foundation for a cure for (T1D) through induction of a T1D-specific immune system ‘off-switch’. This type of immune system off-switch is a natural mechanism for suppressing tissue-destroying immune cells that are the root cause of ‘organ-specific autoimmune diseases’, and in addition, modify immune responses to biotherapeutics (such as FVIII and other biologics). 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 \$3.5M 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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