



## Breaking News

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### **Rhode Island Biotechnology Company Receives \$ 368K Federal Grant to Reengineer Botulinum Toxin Using "Immunoinformatics"**

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Business Wire

EpiVax, Inc, a leader in genome-derived vaccines, announced today that it has received a grant to reengineer botulinum toxin, a protein that is used for cosmetic purposes (the most commonly used brand is known as "Botox") and which is also used as a revolutionary therapeutic for movement disorders categorized as "dystonias" such as Parkinson's Disease and Cerebral Palsy.

This project is funded by an Innovative Research Grant (R21) by the National Institute of Neurological Disorders and Stroke (NINDS), a division of the National Institutes of Health (NIH). The grant will provide \$368,157 to fund studies that will provide a first proof of principle for the redesign program. The studies are anticipated to show that a reengineered Botulinum toxin protein does not cause antibody responses in a special strain of humanized mice. Since research on botulinum toxin outside of special containment laboratories is regulated, a non-toxic version of the natural toxin will be used in these preliminary studies.

"Our unique approach to developing safe and effective protein therapeutics by modifying T cell epitopes is at the core of this research effort," said Anne De Groot, M.D., President and CEO of EpiVax. "This funding results from our demonstrated ability to use our immunoinformatics tools to screen and reengineer protein therapeutics. Using the same approach, we anticipate that we'll be able to create a whole range of effective and "second generation" biologics such as toxins and monoclonal antibodies at a highly accelerated pace."

Demmunization of Functional Therapeutics (DeFT(TM)), the approach used by EpiVax to redesign proteins, modifies the parts of the proteins that bind to human antigen presenting cells such as dendritic cells. EpiVax's cutting edge approach to deimmunization includes rigorous validation in mice with humanized immune systems. These mice were initially developed for predicting the efficacy of human vaccines because the responses of traditional (nonhumanized) mice were misleading. EpiVax is pioneering the use of immunoinformatics and humanized mice for making safer, more effective human therapeutics.

Botulinum toxin controls unwanted muscle movement by blocking acetylcholine release from motor neurons innervating striated skeletal muscle. As are many therapeutic proteins, botulinum toxin is immunogenic. This means that a significant number of patients treated with botulinum toxin develop neutralizing antibodies to the toxin, which reduce or eliminate its therapeutic efficacy. A de-immunized version of botulinum toxin would allow patients to experience the benefits of botulinum toxin injections without developing neutralizing antibodies.

The EpiVax research program will be carried out in collaboration with Dr. Tom Mather, of the University of Rhode Island and with Dr. Joseph Friedman, a Rhode Island-based dystonia expert.

For more information on botulinum toxin, please visit the American Academy of Dermatology at <http://www.aad.org/public/Publications/pamphlets/BotulinumToxin.htm>.

According to the Dystonia Medical Research Forum, dystonia is a movement disorder that causes the

muscles to contract and spasm involuntarily. The neurological mechanism that makes muscles relax when they are not in use does not function properly. Opposing muscles often contract simultaneously as if they are "competing" for control of a body part. The involuntary muscle contractions force the body into repetitive and often twisting movements as well as awkward, irregular postures. Botulinum toxin can be used to diminish and sometime stop these unwanted contractions.

For more information on Dystonia, please visit the Dystonia Medical Research Foundation at <http://www.dystonia-foundation.org/>.

#### About DeFT

DeFT (Demmunization of Functional Therapeutics) is a unique process of reengineering a protein to be less or non immunogenic while preserving its functionality developed by EpiVax. Single amino acid substitutions identified using proprietary immunoinformatics tools, modifications are made in several locations in the protein to reduce the immunogenicity and then the protein is expressed in mammalian cells. Deimmunization is validated with in vitro and in vivo assays (in HLA transgenic mice). This accelerated process takes no longer than 12 to 18 months. EpiVax screens and reengineers proteins and monoclonal antibodies for major commercial clients.

For more information about DeFT, please visit <http://epivax.com/matriarch/documents/DeFT.pdf>

#### About EpiVax

EpiVax, Inc. is dedicated to merging in vitro immunology research with bioinformatics to generate new vaccines for infectious diseases such as HIV, TB, and hepatitis, as well as new therapeutics for cancer and autoimmune diseases. T cell epitope mapping, the selection of target peptides from any protein sequence, is a powerful resource for the development of novel protein therapeutics. EpiVax research shows that peptides chosen by EpiMatrix(TM) software are highly likely to provoke an immune response when presented to T cells. EpiVax tools can also accurately deimmunize proteins. For more information about EpiVax, please visit [www.epivax.com](http://www.epivax.com).

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