



## Background

- Under the direction of Dr. Denise Faustman, the Massachusetts General Hospital (MGH) Immunobiology Lab is conducting research to develop a curative therapy for human type 1 diabetes.
- This research is based on the lab's findings that a brief, non-toxic treatment in mice with advanced type 1 diabetes eliminated their defective white blood cells (the "bad" T cells that destroy the insulin-producing cells of the pancreas).<sup>1,2</sup> This approach permanently reversed long-term type 1 diabetes in the mice.
- The lab has also shown that humans with type 1 diabetes have bad T cells that are like those found in diabetic mice<sup>3</sup>; therefore, a similar therapeutic approach might be effective in humans.
- Based on these findings, the BCG Human Clinical Trial Program was initiated in 2008. Data from the first human study shows that BCG is a promising treatment for advanced type 1 diabetes.

## The BCG Human Clinical Trial Program

- This program is investigating whether bacillus Calmette-Guérin (BCG) vaccination will eliminate the pancreas-destroying T cells in humans with advanced type 1 diabetes.
- BCG is a generic drug that has been used for over 80 years in different capacities, including vaccination against tuberculosis. We are testing BCG at different doses and schedules than those currently used.
- In humans, BCG temporarily elevates levels of a substance called tumor necrosis factor, or TNF. We have shown in lab experiments<sup>3</sup> and in a Phase I human clinical trial<sup>4</sup> that elevating TNF can eliminate the bad T cells in the blood of individuals with type 1 diabetes, which may have clinical benefits.
- Our goal is to bring forward a new, inexpensive, non-toxic treatment for advanced type 1 diabetes.

## Our Type 1 Diabetes Research Program Is Unique

- Our goal is to *reverse* advanced diabetes, not just temporarily halt new-onset disease or treat symptoms.
- The trials do not require lifelong immunosuppressive drugs or cell transplants.
- The trials are designed to kill only the disease-causing cells, sparing healthy cells.
- The trials employ BCG, a safe and inexpensive generic drug. If BCG is shown to be a successful diabetes treatment, it could become available to people with type 1 diabetes much more quickly than a new drug.

### **Phase I Trial**

- This FDA-approved, double-blind, placebo-controlled Phase I human clinical trial investigated BCG vaccination in advanced type 1 diabetes.
- This trial showed that BCG is safe for people with type 1 diabetes. There were no severe reactions to the vaccine. Mild inflammation was observed at the injection site, as expected. All safety data were submitted to and reviewed by the U.S. Food and Drug Administration (FDA) and the MGH data safety monitoring board.
- The trial also showed that BCG can eliminate the disease-causing T cells and restore insulin production, at least briefly, in people who have had type 1 diabetes for many years. (The people in the trial had diabetes for an average of 15 years.)

### **Phase II Trial**

- Funds are now being raised for a Phase II trial, which will look at what doses of BCG are needed to make this a functional and sustained type 1 diabetes therapy, and how frequently it would need to be given.
- This study will cost a total of \$25.2 million.
- For an update on our progress, please visit: [www.faustmanlab.org](http://www.faustmanlab.org).

### **References**

1. Ryu S, Kodama S, Ryu K, Schoenfeld DA, Faustman DL. Reversal of established autoimmune diabetes by restoration of endogenous beta cell function. *J Clin Invest*. 2001; 108 (1): 63-72.
2. Kodama S, Kuhlreiber W, Fujimura S, Dale EA, Faustman DL. Islet regeneration during the reversal of autoimmune diabetes in NOD mice. *Science*. 2003; 302 (5648): 1223-7.
3. Ban L, Zhang J, Wang L, Kuhlreiber W, Burger D, Faustman DL. Selective death of autoreactive T cells in human diabetes by TNF or TNF receptor 2 agonism. *Proc Natl Acad Sci USA*. 2008; 105 (36): 13644-9.
4. Faustman et al. ADA Scientific Sessions, 2011.



Philanthropy is a vital part of our program to reverse advanced type 1 diabetes and develop inexpensive, safe drugs for autoimmune diseases. Please help us move these human studies forward.

#### **To Learn More or Make a Donation:**

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