

Updates



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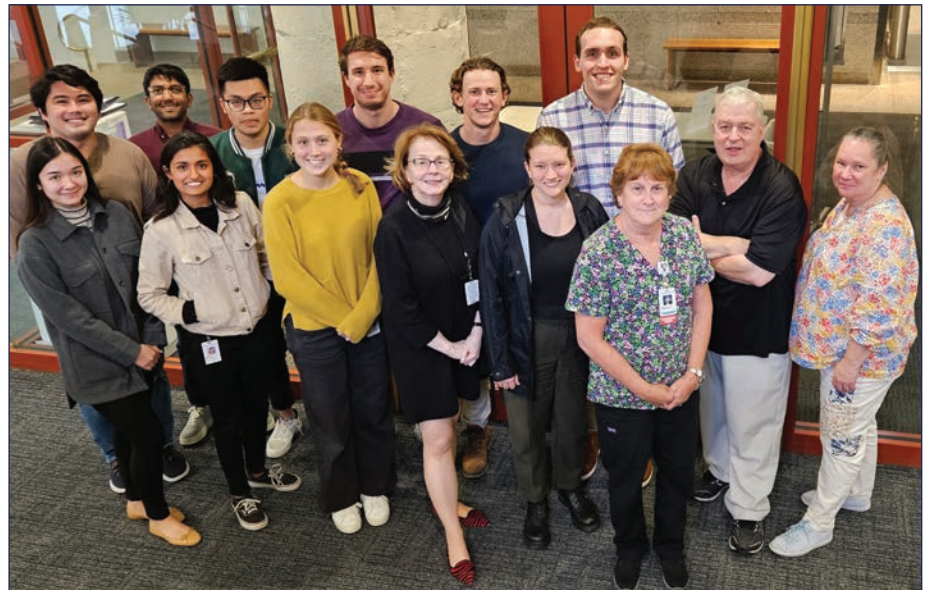
from the Faustman Laboratory at Massachusetts General Hospital

Fall 2023

A Note from Dr. Faustman

The Phase II BCG clinical trial in adults with longstanding type 1 diabetes is nearing completion. There is still a lot of work to be done analyzing the data and preparing for publication. This Phase II BCG trial is the first large, placebo-controlled trial of BCG as a treatment for established type 1 diabetes, and the read-out is a major milestone for our lab and everyone impacted by type 1 diabetes. Stay tuned!

We have not, however, forgotten the children. We currently have two new BCG pediatric trials that are open and actively recruiting, including the most recent trial in “new-onset” children. Please encourage anyone



who might be eligible to contact the lab.

BCG is a safe and affordable vaccine, but these FDA-regulated trials are expensive to run. We have come this far through the support of patients and families impacted by type 1 diabetes. We hope you

will help us move this important work forward. Please contact us if you have any questions, diabetestrial@partners.org.

Sincerely,

Denise L. Faustman, MD, PhD

BCG Clinical Trials to Reverse Type 1 Diabetes

More than 500 individuals with type 1 diabetes have been enrolled or are scheduled to enroll in ongoing BCG clinical trials at MGH. This includes almost 300 type 1 diabetic subjects who have been treated with BCG.

Adult Clinical Trials

The adult Phase II BCG trial is almost complete. All 150 patients have been followed for at least five years. The trial has two groups: BCG (100 patients) vs placebo (50 patients). The primary outcome of the trial is HbA1c, which is the clinical measurement of blood sugar control and the most impactful biomarker of type 1 diabetes. Several important secondary outcomes being followed include insulin use and c-peptide, the measurement of endogenous insulin production.

When all of the patients in the trial have reached their five-year follow up, the next steps will be data analysis and ultimately peer review publication. This process can take a year. Plans for a Phase III trial are already underway.

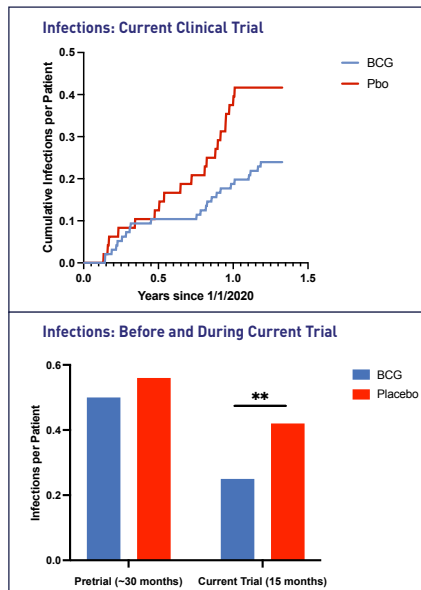
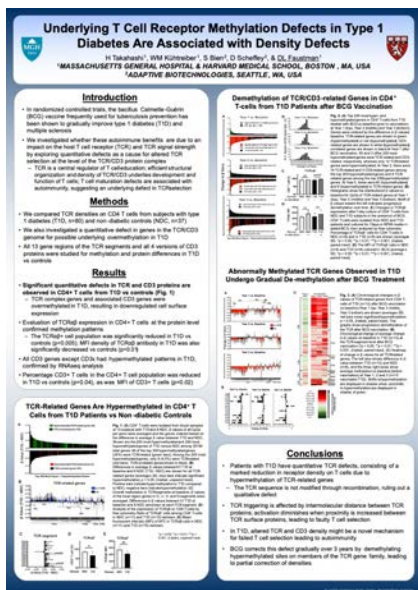
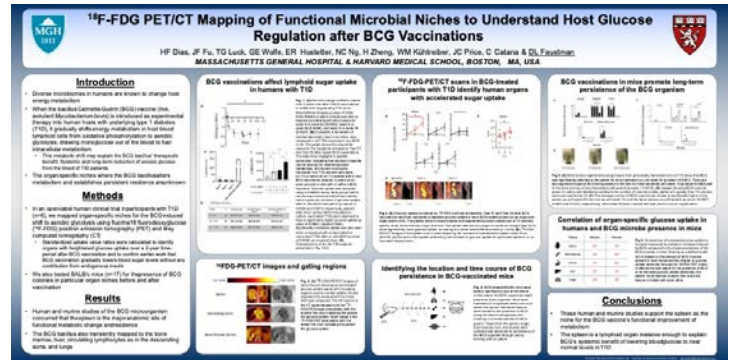
Pediatric Clinical Trials

Type 1 diabetes is often called juvenile-onset diabetes because the majority of people with type 1 diabetes are diagnosed as children. When the adult Phase II trial was fully enrolled, we applied to the FDA to start pediatric trials. In 2022, we launched the first trial in children ages 12 to 18 who have lived with type 1 diabetes for at least two years. This year, we launched a second pediatric trial in children ages 8 to 18 who have had type 1 diabetes for less than a year.

Please contact the lab if you or someone you know would like to learn more about participating!

Research Updates

While the clinical trials advanced, we continued our efforts to understand the underlying mechanisms of BCG and type 1 diabetes. This included new publications, as well as presentations at the Endocrine Society, Federation of Clinical Immunology Societies, and the Immunology of Diabetes Society. Topics ranged from prevention of type 1 diabetes to immune system changes in type 1 diabetes driven by BCG.



Not long after BCG was introduced 100 years ago, the evidence began to come in that BCG could protect against a range of infections beyond tuberculosis. Albert Calmette, BCG's co-inventor, noted a 4-fold decline in child mortality (unrelated to tuberculosis) in vaccinated children. During the COVID-19 pandemic, we looked at BCG and infectious disease. Our lab published data showing that BCG protects against a broad range of infectious disease symptoms from bacterial and viral infections.

BCG Working Group

Viviane Callier from *Scientific American* attended our October 2022 BCG Working Group conference. The result was a terrific summary of both the meeting and the explosion of global research on the “off target” effects of BCG. The article, published in March, is available on the *Scientific American* web site.



In 2024, we will be convening the 6th International BCG Working Group. Each year, the group grows bigger and the data gets more compelling. In 2022, we had researchers from around the globe join us, stretching from Stanford to the University of Melbourne in Australia.

BCG Beyond Type 1: Alzheimer's, Infectious Disease and More

In 2023, a neurology group we collaborate with at MGH published new data on Alzheimer's disease and BCG in *JAMA Open Network*. The BCG-treated patients had a lower rate of Alzheimer's disease and related dementias with an even lower rate among patients age 70 years or older at the time of treatment. Alzheimer's disease is also a complication of type 1 diabetes.

“Our team, consisting of several uro-oncologists as well as Alzheimer's disease researchers, was surprised and excited to see the striking association of BCG treatment with lower mortality in Alzheimer's disease,” said Marc S. Weinberg, MD, PhD, principal investigator and physician in the Alzheimer's clinical and translational research unit at Massachusetts General Hospital. “This was not the primary goal of the study but may suggest that BCG should be studied for potential benefits to mortality outside of the context of neurologic disease.”

(Source: *Helio*)

About BCG

BCG is a live, attenuated bacterial vaccine derived from *Mycobacterium bovis*. Discovered over 100 years ago at the Pasteur Institute in Paris, BCG has historically been given to protect against tuberculosis. In the history of medicine it is considered to be extremely safe, is on the World Health Organization's Model List of Essential Medicines for adults and children, and is given to roughly 100 million children per year globally. Over the last twenty years, a growing group of researchers and clinicians have begun to explore the “off target” effects of BCG for diseases including type 1 diabetes, multiple sclerosis, allergy, fibromyalgia, Alzheimer's disease and respiratory infections such as COVID-19.

Three Questions for Dr. Faustman

Is BCG immunosuppressive?

No. BCG works in long-term diabetic subjects by correcting an underlying defect in the white blood cells. The BCG vaccine gradually re-teaches the white bloods to correctly utilize sugar, not fats, for energy. This regulated blood sugar transport lowers HbA1c values long term. In the trials in children, we hope to additionally see if BCG will work to halt the white blood cells from attacking the insulin-producing cells.

Why is age of onset important in type 1 diabetes?

Age of onset refers to the age a person was when they were diagnosed with type 1 diabetes. It is important because it helps us characterize patients and may predict response. We know that those who were diagnosed as children are more responsive to BCG than patients diagnosed as adults, regardless of age at treatment, since the early age of onset means a very aggressive immune response to self.

Could BCG be used to prevent type 1 diabetes?

We are not conducting prevention trials, but there is evidence that multiple doses of BCG could prevent or delay the onset of type 1 diabetes. For example, researchers in Turkey and Greece have looked at records of BCG vaccination and found that the incidence of type 1 diabetes was significantly higher in children who did not have two or more BCG shots. It would certainly be interesting to conduct a large, placebo-controlled prevention trial at some point.

FUNDRAISING

Want to Host an Event?

If you are interested in hosting an event, please contact the lab directly. MGH has a terrific community fundraising tool called **BeCause**. For the last 20 years, community fundraisers like bike rides and dance parties have created a big impact on the awareness and funding of our research. Lee Iacocca used to say about the BCG trials, “These trials are for the people and by the people.” Get inspired and keep inspiring us. Please contact the lab for more information.

Donor Spotlight: Friends United for Juvenile Diabetes Research

In 1999, Susan Mandell founded Friends United for Juvenile Diabetes Research. We recently caught up with our “Friends” Susan and her co-president Carol Emer about their Chicago-based philanthropy.



What was the inspiration for Friends United?

We are both personally impacted by type 1 diabetes. I (Carol) have had type 1 for 43 years. Susan’s son Josh was diagnosed with type 1 at the age of 8. He is now 35. We had been fundraising for the JDRF, but we wanted to do something to move research forward directly without any middlemen. We wanted to know that 100% of what we raised was going to the research we were interested in.

How did you find out about BCG?

My (Carol’s) father read an article about Denise’s research and we reached out to her to learn more. From day one, she was so generous with her time. She even attended some of our Chicago events.

Tell us a little bit about the events you held?

We did big “gala” type events with food and entertainment. Those were great fun, but also a lot of work and expense. They took a big team, but the results were fantastic. Some of our smaller initiatives like game nights were very productive as well. We tried to make everything fun.

When you started, did you think you would end up raising as much as you did?

No, we certainly did not think we would be raising more than a million dollars over the run of our efforts, but it was a nice surprise. It is amazing to see some of that research, especially the BCG clinical trials, move from the “idea” stage into clinical trials.

Any advice to families looking to get involved?

Keep it simple. None of us ever took salaries, so everything we raised except for the event costs went right to research. Keep costs low and pick research projects you are excited about.

How You Can Help

Please consider making a tax-deductible donation to this type 1 diabetes research program. Every gift makes a difference.

1. To make a secure online donation, visit www.faustmanlab.org and click on “Donate.”
2. You may make a gift by check (payable to “**Massachusetts General Hospital**”) and mail it to:

*Diabetes Clinical Trial
c/o Dr. Denise Faustman
Immunobiology Laboratory
MGH - East
Building 149, 13th Street, CNY-3601
Charlestown, MA 02129*

On the memo line, please write: “Faustman T1D research.”

Thank you for joining us in the fight against diabetes!

For more information, visit www.faustmanlab.org or email DiabetesTrial@partners.org.

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