

# Newsweek

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## Diabetes: Of Mice and Men

By Sharon Begley

Biomedical researchers who challenge the conventional wisdom on health and disease are quick to claim that the establishment is trying to shut them down, and that if only they were given a chance to apply their theories and animal studies to people, patients would be cured.

[Denise Faustman](#) can make a good case for the first point. More on that below. Now we'll see about the second: whether her iconoclastic approach to juvenile diabetes will lead to a true cure for this cruel disease. After years of setbacks, a clinical trial of a therapy that cures diabetes in mice is finally getting underway in people.

It has been seven years since Faustman, a scientist at Massachusetts General Hospital and Harvard Medical School, reported that [a novel approach she developed](#) had cured mice of type-1 diabetes. She proposed the next logical step, trying the same therapy in patients with type-1 diabetes. But the [Juvenile Diabetes Research Foundation](#) declined to fund a clinical trial (which can cost millions), and no drug company wanted to turn her idea into a commercial therapy.

Not that Faustman had any illusions about what the diabetes establishment thought of her. Still, even she was surprised, after she [cured yet more diabetic mice in a 2003 study](#), by a letter two Harvard colleagues sent to the New York Times. In it, they slammed her claims and apologized to people with diabetes “on behalf of Dr. Faustman” for “having their expectations cruelly raised.” JDRF circulated the (unpublished) letter.

Declining Faustman's requests for funding, JDRF did fund three competitors (including a team led by one of the scientists who wrote the scathing letter to the Times) who wanted to test her theory—or, as sportswriters suspected, bury it once and for all.

It didn't work out that way. In March 2006, all three teams reported in the journal *Science* that they had [confirmed](#) the key aspect of Faustman's work: that it was possible to bring the cells that produce insulin back from the dead, curing the diabetes in about one-third of the mice.

Some quick background. In juvenile (type-1) diabetes, the pancreas does not produce insulin, usually because cells of the immune system mistakenly attack and destroy the organ's insulin-making “beta cells.” Insulin breaks down a hormone that turns the sugar (glucose) that you get in food and drink into a form cells can use for energy. Without insulin, sugar builds up in the blood, which is why diabetics require at least three daily insulin shots (or an insulin pump) and finger-\*\*\* blood glucose monitoring to avoid hypoglycaemia (low blood sugar) or hyperglycaemia (high blood sugar). Because keeping glucose in balance is so difficult, diabetes can lead to kidney failure, blindness, cardiovascular disease including stroke and heart attacks, and nerve damage that can lead to limb amputation. Type-1 diabetes is different from the more common type-2, also

known as adult-onset diabetes, in which you make insulin just fine but your cells lose sensitivity to it. Faustman's work does not address type-2.

To bring beta cells back from the dead, Faustman—and then the three teams of rivals—did two things. She gave diabetic mice a compound called BCG. Bacillus Calmette-Guerin has been used for 80 years as a vaccine against tuberculosis, but it also destroys cells of the immune system called killer T-cells. Destroying killer-T cells is supposed to stop the immune system from chomping up beta cells. In mice, it did.

The real shock, however, was that with the killer T-cells eliminated, beta cells apparently regenerated enough to pump out sufficient insulin to cure the mice's diabetes. No one had any idea before this that a diabetes-ravaged pancreas might still harbor enough beta cells, or be able to resurrect them, to reverse diabetes, at least in lab animals.

Now for people. With the usual sources unwilling to fund a clinical trial of what worked in mice, the Iacocca Foundation stepped in with \$11.5 million. (Former Chrysler executive Lee Iacocca established the foundation in 1984 after his wife, Mary, died of type 1 diabetes.) In the clinical trial now enrolling volunteers at Mass General under the direction of David Nathan (and answering questions at [DiabetesTrial@partners.org](mailto:DiabetesTrial@partners.org)), volunteers will get BCG injections. They will be monitored for adverse reactions—phase-1 trials are designed primarily to assess the safety of a new treatment—as well as for signs that BCG is getting rid of the killer-T cells that destroy insulin-making beta cells.

“This is the very first step in what is likely to be a long process in achieving a cure,” Nathan said in a statement. “We first need to determine whether the abnormal autoimmune cells that underlie type 1 diabetes can be knocked out with BCG vaccination, as occurred in the mouse studies.”

Now the diabetes establishment, not to mention patients desperate for a cure, will learn whether Faustman has been tilting at windmills and “cruelly” raising patients' hopes—or whether she has truly discovered a cure for diabetes.