

## KILLING THE KILLER CELLS

## Denise Faustman

DIRECTOR, MASS GENERAL  
IMMUNOBIOLOGY LAB

**H**er name draws sparks. Critical scientists question her methods and challenge her findings. But Denise Faustman's supporters see her as a "tough tester of scientific hypotheses," which is how the 51-year-old Massachusetts General Hospital lab director describes herself. Feelings run high in part because the stakes are huge: reversing type 1 diabetes, projected to double in children by 2020. Faustman has done it in mice. Now she and colleague David Nathan are running a clinical trial to see if they can do it in people.

Faustman previously reported that she had cured mice with "end stage" type 1 diabetes, meaning they had lost all ability to produce insulin. A drug called CFA was a vital key to her multistep treatment. It provoked an inflammatory response that killed the



JONATHAN WIGGS—BOSTON GLOBE / LANDOV

immune system's rogue cells, which had destroyed the pancreatic cells that make insulin. Mice that should have been dead scampered in the sawdust, normal blood sugar restored. When they were autopsied, clusters of insulin-making cells were found in their pancreases. Stopping the autoimmune attack had let the pancreas heal, an ability previously unknown, she says.

In the current clinical trial, Faustman is analyzing blood from a small

group of people with "end stage" type 1 diabetes and from healthy controls. All are receiving either a placebo or BCG, an inexpensive drug long used as a tuberculosis vaccine. Faustman believes the old drug can knock out rogue cells in people the way CFA—which is not manufactured for human use—did in her mice by triggering the same immune response. It is only a toxicity study, but Faustman will be alert for signs of pancreatic regeneration.

It's a "fishing expedition," says Jay Skyler, chairman of TrialNet, an international network of type 1 diabetes trials. He says that regenerative potential is likeliest in diabetics who retain some pancreatic function, and that in past trials, BCG didn't help and even worsened type 1 diabetes. Faustman says the drug flopped because of dosing problems and a poor grasp of how BCG works in people. She agrees there could be setbacks ahead. But not trying, she says, "is 100 percent failure." —L.L.

## FAT THAT FIGHTS FAT

## C. Ronald Kahn

DIRECTOR, JOSLIN DIABETES  
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**F**at you want to pack on, not lose, because it burns up calories instead of storing them as unwanted blubber? C. Ronald Kahn, head of the Joslin Diabetes Center's section on obesity and hormone action, has tracked down this miraculous stuff. Now he's trying to figure out how to direct the body to produce more and make it work harder.

Kahn and his research team did not discover brown fat, as it is called because of its color. It was well known that infants are born with deposits between the shoulders that generate heat until the baby's body can regulate its thermostat on its own. Then the fat usually disappears. But Kahn suspected that the fat hangs around in many adults. Radiologists had



JEFFREY MACMILLAN FOR USNEWS

complained for years that in some patients, stray globs of dark-toned fat got in the way during scans for head and neck cancers. "We wondered if maybe they were right," says Kahn.

A large-scale study published by Kahn's team in the spring in the *New England Journal of Medicine* confirmed that they were. Scans of nearly 2,000 people showed brown fat around the neck and behind the collarbone of about 1 in 13 women and 1 in 30 men. The fat was more likely to be switched from passive into

calorie-burning mode in people who were younger or thinner than in those who were older or heavier.

In one of those research coincidences, two other groups had also found brown fat in adults. Their much smaller studies were published along with Kahn's, with an editorial calling the findings of the three studies "a powerful proof of concept" that brown fat might be harnessed as an anti-obesity weapon. It might be possible to figure out how to tell the body to make more or how to rev it up.

How either would be accomplished remains to be seen, but the goal is irresistible. "You don't have to have very much active brown fat to burn up a lot of calories," Kahn says. Less than 2 ounces of active brown fat can gobble up as much as 20 percent of calories taken in, he says. For a man who consumes a typical 2,500 calories a day, that's 500 calories—as much energy as expended by jogging about 4 miles. —Susan Brink