

Jeff Friedman

When Jeff Friedman began his career as a doctor, there was slim chance he would wind up a world-renowned researcher at Rockefeller University. But his discovery of leptin turned this 'accidental scientist' into a heavyweight among obesity researchers.

The year was 1980. Jeff Friedman, a resident at Albany Medical Center Hospital in New York, had tickets to the men's hockey semifinal at the Lake Placid Olympics. Friedman was a huge hockey fan, but he had been on call the night before and the US team was not expected to win. He decided to give the game a miss. In what has since been dubbed the "Miracle on Ice," the US stunned the Soviets. The game, which captured the tensions of the Cold War, was recently voted by the sports network ESPN.com as the greatest game of the twentieth century, and is the subject of a new movie.

The year was 1999. Friedman, now a full professor at Rockefeller University, had season tickets to a New York Rangers game. Too busy to attend, Friedman gave the tickets to Wolfgang Liedtke, an assistant professor in his laboratory. What Friedman didn't realize was that it was legendary player Wayne Gretzky's last game—scalpers were selling tickets at four figures—and another historic moment in hockey.

"I'm probably the only person to have tickets to the [Olympic] men's semifinal and the Gretzky game and have not seen them," Friedman says. "I have a history of missing important hockey games."

Fortunately, luck has favored Friedman in nearly every other walk of life. Although he began his career as a doctor, a series of coincidences brought him to obesity research. In 1994, after an eight-year quest, Friedman cloned the elusive *ob* gene and propelled the undeveloped field to new heights. "I wasn't sure this lab would ever find it," Friedman says. "I really tried to avoid even fantasizing what it would be like, but I had a lot invested in it at every level."

Genetically obese mice were first described decades ago, but until Friedman's team cloned the *ob* gene—quickly followed by the identification of leptin and the cloning of its receptor—progress in the field was slow. Simple as the task might now seem, in those days positional cloning was a tough job, notes Jim Darnell, Vincent Astor professor of molecular cell biology at Rockefeller, and Friedman's Ph.D. advisor. "The scientific impact of all this has made the study of weight control more a scientific matter than one that was in the dark ages before," Darnell says.

In his search for the *ob* gene, Friedman systematically mastered every emerging technique that might help him. Even after he had cloned the gene and its receptor, he continued to apply new techniques—he was among the first to use Affymetrix chips, for instance—to transform his genetics lab into one that could tackle the metabolic and neurobiological questions surrounding leptin and obesity.

"One of the things I most admire is that [Friedman] always has a big picture in mind—he never thinks small," says Markus Stoffel, Friedman's close friend at Rockefeller. "He tries to go where most people don't even think to go." Friedman pursued the *ob* gene to the exclusion of all else, Stoffel notes. If someone else had identified it first, Friedman's career would have looked very different, Stoffel adds. "Jeff took an enormous risk—he only did this one thing and nothing else. It was very, very brave."

Friedman, who describes himself as an "accidental scientist," grew up in Long Island, New York, where becoming a doctor was a foregone conclusion. After opening seven college rejection letters on the same day, he enrolled in a six-year program that allowed him to finish medical school at 22, but with little research experience. He recalls that when he tried to submit one early paper for publication, a reviewer wrote back saying,

"This paper should not be published in [this journal] or anywhere else."

"That was my experience with research," Friedman says. "For that period of time and a long time after, I thought you had to be a genius to write and publish a paper—that it was a monumental achievement that was highly likely to elude me for the rest of my career."

In his third year of residency, Friedman missed the deadline to apply for a fellowship. The department chair at the time, John Balint, suggested Friedman try research. Balint called his good friend Mary Jeanne Kreek, a researcher at Rockefeller University, who happened to have a postdoctoral position open. After just a few months in Kreek's lab, Friedman fell in love with research. He also realized he had no desire to be a doctor.

"I saw into my own future [as a doctor] and got nervous that as the learning curve flattened out more and more, I would get bored," Friedman says. "It's one thing to get bored and muddle by—it's another to get bored and muddle by in medicine, where people's lives are in the balance. I found that responsibility overwhelming."

Determined to pursue a career in research, he decided to enroll in Rockefeller's graduate program. He has stayed at the university ever since. On one wall of his spacious office hangs the northern blot that first identified leptin. He says he still remembers the feeling of elation when he developed the blot at 5 a.m. on a Sunday in 1994. There have been other great moments in his career since then, he says, "but never quite like that."

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Margherita Maffei, a postdoctoral fellow in his laboratory, had developed a film and found that one candidate, unequivocally called 2G7, was fat-specific. It was 10 a.m. on a Saturday, so the lab was nearly empty, but Friedman was there anxiously awaiting the results, Maffei recalls.

The next day, Maffei had to attend a wedding. After frantically trying to reach her, Friedman decided to hybridize the blot himself. In those days, there was a constant sense of urgency in the lab, says Maffei, who now heads a small lab at the University of Pisa. "One thing I recall very clearly is that everything had to be done right away—in the next 48 hours," she says. "There was a lot of anxiety, but now I realize how important it was—he really wanted everything done, and he was right."

Despite his single-minded focus in the lab, people describe Friedman as an extraordinarily enthusiastic, bright, funny, friendly and generous man. "You'll never meet anyone as generous as Jeff is," says Alex Soukas, a former graduate student. "Jeff will give you a glass of his best bottle of wine without having one himself."

Friedman's interests span books, music, history, politics, wine and food, friends say. But his biggest passion is sports, including basketball, tennis and skiing. As for hockey, Friedman says he is determined not to miss any more historic games. "The moral from all that is don't jump to conclusions," he says. "I won't make that mistake again."

Apoorva Mandavilli, New York