

Behind the paper: saved from the drain

In June 2005, radio engineer John Mountz was working 18-hour days, building a new studio in Houston, when his feet started to feel numb. By the next day, he had lost feeling below the knees, and a day later he had no sensation from the waist down.

After the numbness crept up to his belly button, Mountz went to a local hospital and was diagnosed with multiple sclerosis. The doctors immediately administered steroids and, a few months later, put him on a regimen of Rebif, a recombinant form of interferon- β (IFN- β) that works by modulating T cell activation in people with multiple sclerosis.

Rebif, made by Geneva-based Merck-Serono, normally comes in preloaded 0.5-milliliter syringes—containing 44 micrograms of IFN- β —that cost around \$120 per dose and are self-injected three times each week. At the full dosage, Mountz's symptoms subsided and feeling returned to his body, but the enzymes in his liver shot up dangerously high. He tinkered with the quantity of drug and found that the perfect dose for him was only 0.25 milliliters.

The doctors told him to squirt the excess medicine down the sink, but that felt wasteful. "It didn't seem right to me that something that darned expensive is getting dumped down the drain," Mountz says. He called his father, John Mountz Sr., a rheumatologist at the University of Alabama at Birmingham (UAB), who sent him a batch of 50 autoclaved Eppendorf tubes, latex gloves and a bottle of lab-grade alcohol.

Mountz Jr. started saving the leftover drugs, but the needles full of fresh Rebif kept coming in the mail. To clear out the growing surplus of small tubes filling his fridge, he gave the excess stock to his father.

Then, in early 2006, Robert Axtell, at the time a UAB immunology graduate student, mentioned to Mountz Sr. that he wanted to find a way to boost IFN- β levels in mice to better understand the pathology of multiple sclerosis. Grant money was tight, and lab-grade mouse

IFN- β costs far more than the human drug.

After their brief chat, Mountz Sr. "sort of walks away and it's almost like this light bulb went off in his head," recalls Axtell. "He turned around and said, 'Hey, I've got a bunch of IFN- β in my refrigerator if you want to use it.'"

Axtell took the opportunity and ran with it. He first showed that the human IFN- β performed almost identically to the mouse version of the drug at treating a mouse model model of multiple sclerosis. Then, in 2007, he took the drug with him for a postdoc position with Lawrence Steinman at the Stanford School of Medicine in California. There, he showed in mice that IFN- β effectively combats disease mediated by only one type of T cell—T helper type 1 (T_H1) cells—but not disease mediated by T_H17 cells. The findings may now help identify subtypes of the disease, says Steinman. "MS [multiple sclerosis] can be parsed along very rational axes, and it's not a homogenous disease."

The researchers submitted the findings to *Nature Medicine* in April 2009, but the reviewers and editors called for corroborating results from humans. Fortunately, Chris Polman, a neurologist at the VU University Medical Center in Amsterdam, had just the right samples—26 blood collections stored in his freezer taken from individuals with multiple sclerosis before they started IFN- β treatment, as well as detailed records of who responded well to the drugs. The researchers found that those who benefited from the medicine had low levels of a T_H17 cytokine, interleukin-17, before treatment began. The findings jibed with the researchers' animal data and now provide a path to the development of molecular screens for determining which patients will respond best to IFN- β therapy.

"This is the first hint that there might be a biomarker that will give you a prediction of what will happen if you do the therapy," says John Russell, a neuroimmunologist at Washington



Waste not, want not. John Mountz saved his expensive drugs for mice.

University School of Medicine in St. Louis, Missouri.

Five years after his initial diagnosis, Mountz Jr., now 32 and a radio program director and engineer in Nashville, says he's back to near-perfect—"I'm almost completely fixed"—and he continues to inject his reduced dose of Rebif three times a week. But he no longer keeps the excess meds, as he ran out of Eppendorf tubes a few years back. "I probably should ask [my father] for more tubes, because recently I've just been squirting them in the sink," he says.

Mountz Sr., meanwhile, still keeps a sample of his son's spinal fluid and blood samples in case the symptoms flare up again and he wants to run some diagnostic tests. Unfortunately, however, he didn't collect blood before the IFN- β treatment began, so he'll never be able to measure interleukin-17 levels to know whether his son would have been predicted to respond to Rebif. "Now, in retrospect, that would be nice, but I don't have that [sample]," he says. —*Elie Dolgin*