



## Profile

### David Hafler: a ceaseless drive to solve multiple sclerosis



Published Online

March 4, 2019

[http://dx.doi.org/10.1016/S1474-4422\(19\)30073-0](http://dx.doi.org/10.1016/S1474-4422(19)30073-0)

As a young man, David Hafler had something to prove. He had poor expectations to shatter and the weights of history and hardship to shrug. Now, it is safe to say that, as the Chairman of the department of neurology at Yale School of Medicine, one of the world's leading authorities on multiple sclerosis, and a recently elected member of the National Academy of Medicine, he has achieved that objective and then some.

Hafler grew up in Teaneck, New Jersey, just outside New York City (USA), with his two younger brothers, his mother, and father—a holocaust survivor. His father had arrived in New York by boat soon after World War II. "He was 17, didn't speak a word of English, didn't have a penny in his pocket," says Hafler. But his father's strong work ethic enabled him to progress from being a carpet layer to the owner of a small linoleum shop as Hafler and his brothers grew up.

Money was tight in the Hafler household. "I remember my father saying [to my mother], 'I don't have enough money for you to buy food,'" says Hafler. But while Hafler's dreams of learning a musical instrument were quickly quashed on the basis that it would not provide an income, his dreams of science were harder to suppress, despite the presumptions of those around him. "When I was in elementary school and would say, 'I'm going to be a doctor' or 'I'm going to be a scientist,' people would pat me on the head and say, 'sure you will. Your father is laying carpet. Of course.'" recalls Hafler. "I said, 'no, I'm really going to do this.'"

Poor expectations were not the only challenge for him to overcome. "I was the youngest in the class," he says, which made school that much more challenging. And, he adds, "we weren't an academic family. My parents weren't reading to me." Nevertheless, Hafler was clearly bright and, perhaps most importantly, he had an internal motivation that was akin to a rapidly spinning flywheel—once engaged, it would drive his whole career. "I think it was one of the valuable things of being a child of a holocaust survivor," says Hafler, "it [instills] a certain drive in terms of who you are and what you're going to do."

At the age of 6 years, when Hafler was given a toy microscope, a passion for science and biology started that has never since waned. "I would stick myself with a needle and make blood smears and stain it," he recalls. "How I had the guts to stick myself with a pin, I don't know." But, so fascinated by blood was Hafler that a few years later he made an appointment with a haematologist. "I biked over to the office, walked in... and I said 'I want to be a hematologist and I want to talk to the doctor about it.'" The accommodating doctor talked at length to young Hafler

and gave him a textbook to take home. From this book and other readings, Hafler soon became hooked on white blood cells. "How could you not want to study them, they're so interesting," he says.

After spending his high school years in Florida, where his family had moved to escape the declining economy of the North East, Hafler headed to Emory University. There, his passion for immunology became paired with an equally riveting interest—neuroscience—when he began working under the mentorship of multiple sclerosis expert Dale McFarlin.

Hafler carried this interest with him through medical school, internship, and residency. And, he says, he had the surety of purpose that multiple sclerosis was not only a problem he wanted to solve, but also one he believed he potentially could. At the time, it was known that multiple sclerosis, which weakens muscles, impairs eyesight, and causes fatigue and other symptoms, was associated with activation of the immune system. But whether it was an infectious agent or something else that caused the disease was not clear.

As a researcher at Harvard, Hafler made the critical discoveries that immune activation in multiple sclerosis was systemic, not localised to the brain, and that patients' T cells recognised and reacted to the coating of neurons—myelin—thus establishing that the disease was autoimmune in nature. He was subsequently instrumental in the discovery of regulatory T cells and showed that, in patients with multiple sclerosis, these cells are dysfunctional. Hafler's work, which includes the first genome-wide association studies for multiple sclerosis, has stretched from the basic biology of the disease right through to identifying clinical targets that have led to drug development. "It's incredible to be able to help [patients] and have treatments that work now for relapsing remitting [multiple sclerosis]," he says.

Hafler is rightfully proud of his career and achievements, including his rise from humble beginnings, but his election to the National Academy is the cherry on top. "Outside acknowledgement from peers of what one has achieved is immensely gratifying," he says. It was "probably the most rewarding moment of my career."

While Hafler certainly has nothing left to prove, there is still a lot of science to be done, he says. He is currently interested in how the transcriptomes of T cells differ between healthy people and those with multiple sclerosis, for example. So what is it that keeps him going? The same as it has always been, says Hafler: a potent mixture of "curiosity" and "fire in the belly".

Ruth Williams