

# Profile of Jeffrey Ravetch

Jeffrey Ravetch's career path began with a focus on the smallest scale—individual molecules—then ramped up to studies in microbes, mice, and finally humans. For his work in immunological research, including contributions to unraveling the key mechanisms by which receptors for the invariant stem (Fc) region of antibodies operate, Ravetch was elected to the National Academy of Sciences in 2006.

In his inaugural article, Ravetch and colleagues identified a receptor for sialylated Fc that stimulates anti-inflammatory pathways (1). The receptor could potentially be a useful therapeutic for many autoimmune diseases, according to the study.

Ravetch, 57, is currently the Theresa and Eugene M. Lang professor and head of the Leonard Wagner Laboratory of Molecular Genetics and Immunology at the Rockefeller University (New York, NY). He grew up in nearby Brooklyn, excited by scientific breakthroughs like the launch of Sputnik in the late 1950s and the subsequent space race. Books such as Paul de Kruif's *Microbe Hunters* (2) and biographies of Louis Pasteur and Albert Einstein fueled his imagination. "My heroes were scientists, not sports figures," he says.

## Clouds of Chlorine

Ravetch's parents were teachers in New York City public schools, and although neither taught science, they were able to provide their son with books, enrichment programs, and leftover lab equipment. "They let me do what I chose to in the basement. I had a little makeshift laboratory where I would dabble," he says. "You'd get books at the library that would tell you about doing certain experiments and I'd make quite a mess, as you might imagine. I recall clouds of chlorine gas very distinctly when I discovered the power of laundry bleach."

This self-directed learning foreshadowed Ravetch's academic career. From his initial basement work through high school, which offered little in terms of science education, Ravetch conducted his own experiments and pursued his own projects.

"[My high school] was a parochial school and didn't have any [science] facilities or teachers, so my education was basically things I could do on my own," he says. He would go on to spend summer camps at Carnegie Mellon University (Pittsburgh, PA), work in a research lab on Long Island, and spend time in a marine research lab in Brooklyn in lieu of formal classwork during his youth.



Jeffrey Ravetch

After high school, Ravetch was admitted to Yale University (New Haven, CT) in the late 1960s. "When I went to Yale I was finally exposed to true science," he says. "I was fortunate in being able to work in Don Crothers' lab as an undergraduate and that was how I became a scientist. I really owe Don for having the patience to let a complete neophyte into the lab and break things." The Crothers group studied the physical biochemistry of nucleic acids, in particular, synthetic RNA duplexes.

"I got there in my freshman year and I just stayed. Nights, weekends, summers, it was really my first scientific home. I published my first paper when I was an undergraduate with Don" (3).

## The Great Names

Sure that research was his destiny, Ravetch enrolled in Rockefeller's new M.D./Ph.D. program administered in tandem with Weill Cornell Medical College (New York, NY). As a molecular biophysics and biochemistry and English major, he thought the combined program was a good way to get grounded in biology, and its novelty attracted him.

"In those days Rockefeller had a curriculum with no courses, no exams—it reminded me of my early years being self-educated. You chose a laboratory, you chose a mentor, you decided what it was you wanted to study and designed a curriculum for yourself. The qualifier was, you had to find 3 faculty members who signed off to say you fulfilled their sense of requirements in their discipline," he recalls. "I thought it was a great idea. I loved the idea that to qual-

ify in genetics you sat in Norton Zinder's office for an hour and talked genetics. If he thought you knew enough, you were qualified. It was more of the same with Günter Blobel in cell biology. You had the opportunity—and you were required—to spend time with some of the great names in the field."

Ravetch worked in Zinder and Peter Model's joint lab at Rockefeller, focusing on bacterial and phage genetics. DNA sequencing was a brand-new technique. "Through the rumor mill we heard it was a technique Wally Gilbert had developed," he says. "I was sent up to Wally's lab to learn DNA sequencing—there was no other way to do it. I remember sitting in Allan Maxam's little cubicle and he showed me all of the reagents and gave me the protocols on hand-written pages that I Xeroxed. Then I brought the gels and DNA sequencing to Rockefeller and started teaching people how to do it here."

One problem in the early days of sequencing was getting hold of restriction enzymes to manipulate DNA. "There were no companies selling these back then, and you had to make each enzyme yourself, so there was a black market in restriction enzymes," he says. "You would make a few and then swap a few with a laboratory that had other ones," Ravetch says.

After finishing his Ph.D. (in 1978) and M.D. (in 1979), Ravetch joined Phil Leder's lab at the National Institutes of Health (Bethesda, MD). Leder had just finished a remarkable series of studies on the genes that encode the light chain of Ig proteins and the rearrangements that generate antibody diversity. Ravetch arrived in time to study the heavy chains of immunoglobulins.

"There was a whole new world to figure out and we knew nothing about how the constant region could undergo this class switch recombination," he says. "There were various postdoctoral researchers in all these labs around the world competing with each other. Each week we'd read each other's work in papers and Phil would go to a meeting and call us back and say, 'Well, there's a lot of new information,' which was the bad news, but we were still in the game and I think we did some interesting work from 1979 to 1982. It was an intense period of investigating this marvelously complex system of genes" (4, 5).

This is a Profile of a recently elected member of the National Academy of Sciences to accompany the member's Inaugural Article on page 19571 in issue 50 of volume 105.



C. Howley, Sr. Award and the William B. Coley Award from the Cancer Research Institute. He is a member of the Institute of Medicine, and is a Fellow of the American Academy of Arts and Sciences and the American Association for the Advancement of Science.

But Ravetch's life isn't totally consumed by science. Besides his love of

poetry, which began when he was an undergraduate at Yale, he has devoted one corner of his lab to orchids, which he, his staff, and students grow for fun, relaxation, and competition. "The orchidarium is one of the places where people can sit and chat and have coffee," he says. "It provides a welcome distraction. It's part of my philosophy—

you should want to spend all your time in the lab, it should be the best place you know. It's all about having an environment where you look forward to coming to work and just enjoy sticking around."

Philip Downey, *Freelance Science Writer*

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