

## Richard Scheller/Autobiography

I may have been the only child in my elementary school not to go through a phase of wanting to be a fireman, a police officer, or an astronaut. From my earliest memories, I always wanted to be a scientist. My classmates had posters of rock bands or cars on the walls in their bedrooms; I had the periodic table of the elements.

My fascination with living things and what makes them tick took root in the basement of my childhood home. There my first lab consisted of a couple of chemistry sets, a microscope, and any utensils I could swipe from the kitchen. Fortunately for me, my mom and dad took kindly to my early forays into biochemistry, which basically consisted of dragging pond water, bugs, and most anything else slimy and transportable through the house and down the stairs. The suburbs of Milwaukee, Wisconsin provided the backdrop for my quintessential 1950's American upbringing. My father was a social worker who later became a hospital administrator. My mother was a homemaker. She kind of surprised all of us when, after I went to college, she did too! Today she is an accomplished artist whose work I proudly display in my home. I couldn't have asked for better or more supportive parents.

I enrolled at the University of Wisconsin at Madison, a beautiful place to go to college that has an outstanding biochemistry department. My freshman year in Madison coincided with the publication of James D. Watson's Molecular Biology of the Gene, and I recall devouring it cover to cover in a week. The reading of that classic textbook, which covered pretty much everything you needed to know about biology at the time, was a major event in my life. Prior to reading the book, I knew I wanted to be a biochemist. After reading it, I knew why.

Few people achieve any measure of success without a coterie of dedicated teachers and mentors. My freshman chemistry professor at Madison, Bassam Shakhshiri, was the first in the long line of talented scientists with whom I've had the great opportunity to study and work. Perhaps best known for his Science is Fun series of books and presentations, Bassam is an amazing teacher whose enthusiasm is infectious. Reading Watson's book and meeting Bassam were the one-two punch that validated my longtime dream of making science my life's work.

While at Madison I became interested in x-ray crystallography and structural biology, specifically the work being done by Richard Dickerson at Caltech. I was thrilled to accept his invitation to pursue my Ph.D. in his lab. Richard Dickerson had just brought Keiichi Itakura to Caltech. Itakura invented a faster way to chemically synthesize DNA and a team was formed between the Caltech group and Arthur Riggs at City of Hope. It was at Caltech, while working on the structural problem of crystallizing the *lac* repressor protein, that I circuitously began my enduring relationship with Genentech. UCSF Biochemistry Professor

Herb Boyer had just co-founded Genentech and the company was seeking to synthesize the human protein somatostatin in bacteria. Itakura's new DNA synthesis method was a way to synthesize a Somatostatin gene so Boyer thought it best we all combine forces, which I believe officially made me Genentech's employee #5. At that point no one could have predicted that Genentech would become a huge corporation and spawn an entire industry. I left part of the way through the project to finish my dissertation, which was more basic science than engineering oriented. I was involved in the early days of recombinant DNA technology, chemically synthesizing restriction enzyme sites useful for cloning and investigated the organization of genes and repetitive DNA sequences in the laboratory of Eric Davidson. Eric also taught me to critically analyze data and papers, a skill that serves me well today.

I left Caltech to begin my postdoctoral studies at Columbia, where I had the privilege of studying with Richard Axel and Eric R. Kandel, amazing men who had a profound influence on my work. Indeed, one of the great experiences of my life was spending time with Eric. Many hours were whiled away in his office where we tutored each other. It was an unspoken compact: I'll teach you molecular biology if you teach me neurobiology. I spent an equally large number of hours in Richard Axel's office learning about science, how to be creative, and sharing a good joke.

The early 1980's, when I was at Columbia, were a particularly interesting time to be studying neurobiology, with the debate raging over whether studying model systems was relevant to the study of human behavior. It was an especially fascinating debate for someone coming from molecular biology like myself, where the relevance of model systems was taken as a given. Axel and Kandel had the courage of their convictions and believed in simple model systems for studies of the brain. I had the opportunity to participate in one of the first "molecular neurobiology" studies working on the egg-laying behavior of *Aplysia*. Work in *Aplysia* led to the understanding of fundamental principles nerve cells in all animals. Both Axel and Kandel would go on to win independent Nobel Prizes for olfaction and learning and memory mechanisms respectively.

After completing my postdoc at Columbia I joined the faculty at Stanford where I would ultimately spend nineteen glorious years, made immensely more so by an acquaintance I struck up with a talented neuroscientist who set up a lab next to mine a few years after I arrived. I was secretly delighted that long hours in the laboratory kept my lab neighbor, Susan McConnell, close by. The eleventh (yes, eleventh) time I asked her to marry me proved the charm. We share a house on the Stanford campus with two dogs and an extensive African art collection. I can't imagine my life without her.

My work at Stanford centered on understanding the cellular and molecular basis of how synapses work. I believed this was of fundamental importance as their specific formation and modulation underlies our ability to perceive sensations and to think. Modulation of the activity of synapses had been shown by Kandel and

others to underlie the formation of memories.

In the mid 1980's I became interested in understanding the molecular mechanism of neurotransmitter release and hypothesized that the proteins associated with synaptic vesicles would be involved in the process. In my lab we cloned and characterized the genes that encode the proteins that control release of neurotransmitters. This work culminated in an understanding of the mechanism of intracellular membrane fusion. The mechanism we discovered is universally utilized by all cells and at all levels of the secretory pathway. The specificity associated with the mechanism is responsible for regulating the organization of membrane compartments in cells.

With the sequencing of the human genome and other scientific advancements, by the late 1990's our understanding of human biology had reached the level where we could consider tackling problems of disease the way we tackled basic biology problems. This increased level of sophistication in the field coincided with a juncture that apparently occurs in the career of many a life scientist: that time when they consider whether there is a way to make a broader contribution beyond their lab.

Like many academic researchers, I had been fortunate enough to be approached with numerous offers to join the pharmaceutical or biotechnology industries over the years, always dismissing them. In a fortuitous confluence of events, just when I began seriously pondering how I might make a broader contribution, I met Art Levinson, then the CEO of Genentech. The fact that Art was a molecular biologist himself made it possible for me to consider coming to industry.

I will be forever grateful that Art had the confidence in me to make the proverbial "offer I couldn't refuse." I can't thank Art enough for his leap of faith, for the free reign he gave me to run Genentech research, and for his generosity in taking the time to tutor me about business, industry, and drug development. Because of the vision of the company's founders, Bob Swanson and Herb Boyer, and the huge influence of Art, Genentech, now a member of the Roche Group, is a unique and special place.

In my current role as head of Genentech Research and Early Development and member of the Roche Extended Executive Committee, my goal is setting strategy to strike the optimal balance between basic biomedical research and translational research aimed at developing therapies for cancer, Alzheimer's, and other serious diseases. Our more than 1300 researchers, scientists and postdocs consistently publish important scientific papers in the most prestigious peer-reviewed journals. Our primary mission is to use rigorous and groundbreaking science to help patients in need with first-in-class and best-in-class medicines. It is a pleasure to work with such an amazing group of colleagues. I am constantly inspired by their drive, their commitment, and their passion to help patients.

My scientific career has been rewarding beyond my childhood dreams. I am proud to be both a Member of the National Academy of Sciences and a Fellow of the American Academy of Arts and Sciences. I have been the recipient of Predoctoral and Postdoctoral Fellowships from NIH, an Alfred P. Sloan Research Fellow, a Klingenstein Fellow in Neurosciences, a McKnight Foundation Scholar, and a Pew Scholar in Biomedical Sciences. In addition to the Kavli Prize in Neuroscience, I have received the March of Dimes Foundation Basil O'Connor Award, the Society for Neuroscience Young Investigator Award, the Presidential Young Investigator Award, the Camille and Henry Dreyfus Teacher-Scholar Grant, the NSF-Alan T. Waterman Award, a MERIT Award from the National Institute of Mental Health, the W. Alden Spencer Award of Columbia University, the National Academy of Sciences Award in Molecular Biology, and the University of Wisconsin-Madison College of Agricultural and Life Sciences Distinguished Alumni Award. I am most grateful for all of these recognitions.