

Becoming a scientist: what I learned from Gunny

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It was the spring of 1968, I was 19 years old and a sophomore at University of Illinois in Urbana, and I very much needed a job. A chemistry classmate had mentioned that he was working some afternoons in the research lab of an organic chemist, washing glassware and preparing solutions. I went to see my friend at work and meet his boss, who told me that he didn't have another job available but suggested that I go down the hall into the East Chem building and talk to a Professor Gunsalus, who he said often hired part-time people. My first memory of I.C. Gunsalus (Gunny to everyone who knows him) was hearing his unforgettable, mellifluous baritone voice as he welcomed me into his office. Gunny looked over my resume, which listed my previous work experience on a farm, as a caddy, a busboy, a factory worker, and dorm dining hall worker, plus my grades and courses in the chemistry curriculum, as I nervously awaited his verdict. When I left his office that day, I was walking on air about my good fortune in landing a laboratory job paying, what was to me at the time, the luxurious rate of \$1.50 per hour. But I hadn't an inkling that the course of my life was changed at that moment because I had taken the first step on the path toward becoming a research scientist.

I started in Gunny's lab at what must be the lowest rung on the research career ladder: part-time assistant to a part-time lab assistant. I first was given the responsibility of keeping the lab's coffee pot filled and then was taught how to isolate mutants of a strain of the bacterium *Pseudomonas putida* that was able to degrade camphor [1]—a subject of investigation that seemed very odd to me in the beginning. I learned that Gunny was interested in this organism because it provided the opportunity to use the new tools of microbial genetics to understand the structure and function of oxidative enzymes, including P450 cytochromes, which

had homologues in mitochondria. Soon the biochemical genetics of camphor catabolic enzymes became my world, too. Within several months, I had successfully isolated several dozen interesting camphor degradative mutants and done some initial bacteriophage transductions to obtain preliminary linkage information. Having become very interested in what I was doing, I made another appointment to see Gunny to ask him if I could have this as my own project for an undergraduate thesis. He first gave me some very basic microbiology experiments to do: generating graphs of turbidity vs. colony forming cell concentration vs. dry weight measurements of broth cultures. I remember his walking around his desk to sit in a chair next to me in his office to look at my data and hand-drawn graphs. Gunny surprised me by taking all this basic stuff extremely seriously, but he apparently approved of the careful way I had done those experiments and recorded the results in my lab notebook, so he gave me the go-ahead. I began spending all my free time in the lab, working on my project and doing many other lab assistant duties, including raising phage-neutralizing antibodies in rabbits for use in transductions and maintaining agar slant and lyophilized stocks of all the bacterial strains and mutants under investigation in the lab. The senior people there, Al Chakrabarty, Carol Gunsalus, Mark Wheelis, George Chou, Randy Tsai, and Steve and Sherry Queener, were always willing to teach me basic concepts, gene mapping methods, and enzyme assays, and so my thesis project progressed. I was always impatient until it was my turn again to present my results at the weekly lab meeting.

In the spring of 1969, a serendipitous intersection of classroom learning with the subject of my research changed my project from sound but unremarkable to something that so excited me that I decided to pursue a career as research scientist. A year into the project, I had found that the five specialized oxidative enzymes responsible for converting camphor to isobutyrate

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(a compound metabolizable by enzymes common to many bacteria) were tightly linked to one another but were unlinked to any other known genes on the *P. putida* chromosome. Paul Sypher, then in the U of I Microbiology Department, taught an excellent course on microbial genetics, which I was taking that spring. At the end of his lecture on F-factors and the transfer of genetic material by conjugation in *E. coli*, my mind was spinning. I could hardly sleep that night as I planned the experiments I would do over the next few days to test my hypothesis that the CAM genes resided on a transmissible plasmid. The experiment consisted of mixing an amino acid auxotroph of Cam⁺ *P. putida* with a Cam-negative *P. putida* mutant or the camphor non-metabolizing bacterium *P. aeruginosa*, then plating the mixture on minimal medium agar having camphor as sole source of carbon and energy to look for survivors. The experiment showed that the genes encoding this set of enzymes were transferable en bloc from one bacterium to another and represented the heart of my thesis, which I finished in 1970. The manuscript I left with Gunny when I went off to graduate school was published several years later as the first report of a transmissible plasmid bearing functionally related genes in bacteria [2]. This was followed soon thereafter by the discovery of plasmids bearing clusters of genes encoding enzymes that degrade octane [3] and naphthalene [4]. My extraordinarily good fortune in discovering the CAM plasmid and earning Gunny's interest and respect for this work gave me the youthful sense of certainty that I could go on and be successful as a research scientist.

Gunny's wise advice, never proffered unless asked and always articulated gently and mindful of what I was able to take in and make use of at the time, helped me make excellent choices for my graduate education. After leaving his lab, I went on to doctoral and postdoctoral training in classical genetics and then mammalian cell biology. The subjects of my subsequent research moved far from catabolic pathways and oxidative enzymes in bacteria. Yet, the patterns of thinking about how to approach scientific problems that I formed in Gunny's lab during my 2 years there have stayed with me. I sought out scientists for my graduate training, first briefly with Bob Demars at Wisconsin and then for my doctorate with Howard Green at MIT, who were interested in finding ways to study mammalian cells as microorganisms in culture. Most of my research into mechanisms of human epithelial cell growth, differentiation, and malignant transformation during the past 25 years has used experimental strategies very similar to those I learned and applied to my microbial genetics project in Gunny's lab (for example, see reference [5]).

Gunny positively influenced my life in many ways during those 2 years in his lab long ago and afterward, far beyond what I ever could have expected from an undergraduate thesis advisor. His kindness and gener-

osity while I was working in his lab meant everything to me. As the result of some serious family difficulties, midway through my sophomore year I had to become responsible for all of my support, including finding a way to cover my college expenses. I hadn't told Gunny any of these details, but his wife, Carol, whose desk and lab bench were next to mine, learned of my situation and I found out that Gunny would pay me for as many hours as I was willing to come into the lab. This let me finish college on schedule as a regular full-time student, freeing my mind to devote to learning and planning for a brighter future. My experiences leading up to college had been rather limited, having grown up on a farm near a very small town in Illinois. Having come from a humble, Dakota country background himself, Gunny showed me that it was reasonable to strive for a life unlike any that I had previously witnessed. I learned that one's work could be so interesting, rewarding, and fun that one can completely forget its connection to the paycheck that comes each week or month. Most importantly, Gunny taught me to hold with the highest regard the privilege of being able to call oneself a "scientist."

I remember some of the special things that Gunny did for me and for others who worked for him that helped us find our direction in life and, for those of us who would make a career of research, gave us such a good start toward our goal. The first was that he gave me a project of my own, even when it would have been much easier to put me under the supervision of a graduate student or postdoc. The nature of my project, on microbial genetics and enzymology, was a perfect introduction to research. I could do a new experiment almost every day, put my agar plates in the incubator and broth cultures in the shaker, see the results the next day, and set up my next experiment. I was left alone enough to make mistakes, figure out what I had done, and have the lesson imprinted in my mind. One of Gunny's favorite little stories on this subject was about a postdoc going to the head of the lab to advise him that a student appeared to be setting up an experiment the wrong way, so that he was certain to get no useful data. The lab head whispered in reply, "Shh—he's learning!"

In Gunny's lab I was first exposed to the global village of academic science, in which one seeks the company of quality people based on shared scientific interests, without regard for national origin, political philosophy, religion, ethnicity, gender, or age. When I first met him, Gunny seemed impossibly old to me to have such energy and enthusiasm for what he was doing, although as I write this I am the same age as he was back then! It seems clear now that teaching and working with young people in the arena of science have kept him forever young at heart. Gunny has always had real respect for the abilities and potential of young people as well as for their individuality, taking time to learn what

a person is able to do and then, for mutual benefit, setting a standard of expectations at the limit of the person's capabilities. He always conveyed his respect and regard for the scientists who came before him, and now he is among the old and venerable ones himself. In my most recent conversations with Gunny, I hear most clearly his genuine love for the community of scientists and his delight whenever he is able facilitate a connection between fine scientists of different generations, working to preserve the cumulative wisdom of centuries of scientific endeavor, much of which is intangible or not easily set down in writing.

The cohort of students in college from 1966 to 1970 remembers that period with nostalgia mixed with sadness. The protests, marches, and teach-ins about the civil rights struggles and the Vietnam War awakened us to think beyond our narrow self-interests, but campus life was terribly disrupted and the students and their professors were distracted from their tasks. Gunny's lab was a haven from all the craziness outside. Of course, there was much discussion among the young people in the lab about the war and the campus demonstrations, but we knew that, in the lab, science was our world and productivity was the coin of the realm. Gunny never discussed his political beliefs in the workplace, and it was only later that I learned of the depth of his convictions about human rights, global cooperation, and peace and justice. In retrospect, I recognize how special that was, during a difficult period of my own life amidst the turbulence and disarray of American society in the late 1960s, to have had the privilege of developing my

young mind by working in a stable environment with a straightforward focus on high standards and scientific discovery.

I am forever grateful that Gunny made my first experience in a lab such a positive one. Of course, part of this was the luck of timing and that certain aspects of our respective personalities and ways of thinking made a fruitful match. His curiosity, open-mindedness, joy in discovery and in formulating a clever experiment to test an hypothesis, and his seriousness about the quality and integrity of one's experimental results all resonated with me early on. It seems that I can remember every reflection and comment about life and science that he ever told me. My hope is that some of the people who pass through my lab will be positively affected in a significant way by their experience, so that I can at least partly repay my debt to Gunny as he would most appreciate and respect—by “paying it forward.”

I had sent Gunny a Christmas card every year since I left his lab, but during the past 20 years I had seen him only once. Last summer, I phoned his son, Rob, a professor of biochemistry at UCLA, to find out Gunny's e-mail address. I learned that a 90th birthday celebration banquet was being planned in his honor at an international conference on P450 cytochromes at UCLA at the end of August 2002, which I was welcome to attend. When I arrived for the banquet, I was very pleased to find Gunny still standing tall and strong, a glass of wine in his hand, surrounded by many friends and former students, discussing science and reminiscing with undiminished acuity and enthusiasm (Fig. 1). Thirty-five



Fig. 1. I.C. Gunsalus (right) with Jim Rheinwald (left) at the banquet in honor of Gunny's 90th birthday at the Sixth International Symposium on Cytochrome P450 Biodiversity, held at the University of California, Los Angeles, August 24, 2002.

years after he had inspired me to start a scientific career, he inspired me again to stay active, to never look at the calendar, and to find ways to contribute to this wonderful world of science for as long as I am able.

My final anecdote about Gunny, one that is especially meaningful to me, exemplifies his ability to see the possibilities around him, thereby energizing himself and encouraging others to make them come true. At his banquet, I told Gunny that our son had graduated from Tufts 2 years before and was now living in L.A., seeking to become a screenwriter of television dramas and movies. I told him that during his college years Nick had written many excellent short stories and had real talent, but was still working at a series of temporary office jobs to make ends meet while he wrote a portfolio of sample scripts with which he could approach an agent. After the banquet, Gunny came out and chatted with me and several others from the meeting, as I waited for my wife and son to pick me up. When they arrived, I was happy that he was able to see Krystal again and that Nick was able to meet this man, whom I have talked about so many times through the years. Another one of Gunny's friends approached and he introduced me and then said,

"This is Jim's son Nick; he's a Hollywood screenwriter." I interjected that he was still *trying* to become a writer. Gunny immediately corrected me by saying with absolute certainty, "He's on his way."

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