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Guru

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The title comes from a comment made by K.T. Madhusudhan, who had worked in my laboratory for several years and who played a major role in planning for a symposium to mark my retirement from the University of Oklahoma Health Sciences Center. He asked how to reach my *guru*, i.e., Gunny, so he could be invited. My dictionary lists several definitions for *guru*, one of which is "**somebody influential**, *somebody who is prominent and influential in a specific field.*" On reflection, that seemed like an appropriate title for this reminiscence.

I was raised in Joliet, Illinois, and until I graduated from high school, had never traveled any farther than Chicago, 35 miles away. My first out-of-state experience was as a deck hand one summer on the Great Lakes ore boat the *Myron C. Taylor*. It was a big event for me to attend the University of Michigan as an undergraduate and ride the train from Chicago to Ann Arbor. After graduation in 1950, with a B.S. in psychology, I was at a loss for a future career. Psychology was interesting and there was actually a very good program in experimental psychology at the U of M, but this didn't appeal to me as a career. I had one course in bacteriology while at the U of M taught by Malcom Soule, who was on the side of the germs against humans. Antibiotics were just being introduced to the general public and Soule regretted the taming of bacterial pneumonia, which he referred to as the "friend of the aged."

The Department of Bacteriology at the University of Illinois

Since I was a resident of the state of Illinois, I decided to attend the University of Illinois to begin work on a Master's degree which would prepare me to be a science teacher. Courses in biochemistry and bacteriology were part of this curriculum. My first course in biochemistry was taught by William C. Rose, who was a dynamic teacher even though he was in the twilight of his career. I didn't know at the time that he was also a famous biochemist.

Alfred E. Borg was the advisor for my Master's degree program. Al taught me a lot about unusual microbes and how to grow bacteria strictly anaerobically using catalytically deoxygenated hydrogen—and I lived to tell about it. No thesis was required, but there was a tough written examination, which one of the senior graduate students called a "mini-Ph.D." examination.

However, the attention-grabber was the introductory course in bacteriology. The Department of Bacteriology at the University of Illinois had just undergone a major transfusion of new talent. The new chairman was Harlyn O. Halvorson, a distinguished food/industrial microbiologist, who hired Salvador Luria, Sol Spieglman, and I.C. Gunsalus, three of the most prominent names not only in bacteriology but in all of biological science. They organized a superb course in basic bacteriology with bright, new material and thoughtful discussions. It was stimulating to be intellectually challenged rather than to have to memorize sugar fermentations. The lectures by Luria were elegant and clear, even with his Italian accent and volatile temperament. Spiegelman's lectures were beautifully organized and presented. Gunny's lectures projected tremendous energy although, at times, he seemed to speak in parables.

After leaving Illinois, Luria shared the Nobel Prize in 1969 with Hershey and Delbrück; Luria for his work on the "jackpot effect," work actually done while at Indiana. Luria, Spiegelman, and Gunsalus all became members of the National Academy of Sciences. Quite a

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coup for "Doc" Halvorson. Later important additions to the faculty were Elliot Juni and Ralph Wolfe.

Life in Gunny's lab

The buzz around the Bacteriology Department was that Gunny was the star. While working on my Master's degree, I hung out with some of Gunny's graduate students and liked what I heard from them. I wanted to stay on to work for the Ph.D. with Gunny; but would he have me? I screwed up my courage, approached Gunny about the possibility of working in his lab, and to my amazement was accepted.

This was an exciting time in biological science, perhaps the most exciting time ever. The Watson and Crick structure of DNA would be published shortly and this provided the groundwork for the later explosion in molecular genetics. However, the hot research topic at that time was intermediary metabolism; biochemists were learning how to work with cell-free extracts and partially purified enzymes to isolate biochemical reactions. Fritz Lipmann's concept of high-energy phosphate earned him the Nobel Prize in Physiology and Medicine in 1953 which he shared with Sir Hans Krebs.

Gunny's lab was room 367-A of the Noyes Chemistry Building. The students I remember from that time were Roberts Angus Smith, John Stamer, Douglas Gillespie, Lowell Hager, and William E. Razzell. Lowell Hager was working on pyruvate oxidation by extracts of *Escherichia coli* and on the roles of lipoic acid and thiamine in that reaction. Bob Smith continued his work on isocitrate lyase, the enzyme that cleaves isocitrate to glyoxylate and succinate. Bob discovered this enzyme while working on his Master's degree in Jack Campbell's laboratory at the University of British Columbia. Bill Razzell was working on pyruvate oxidation in *Proteus*. I was studying *Streptococcus faecalis* 10C1 to see if it would ferment gluconate by a non-Embden–Meyerhof pathway. It did [1].

Carol Gunsalus was one of the postdoctoral workers in the lab during the time I was a student. Another was Mort Dolin, who was working on electron transport in bacteria, including *Streptococcus*, considered by most to be a strictly fermentative organism. Mort was a postdoc who apparently did not need his stipend because he stashed his paychecks in his desk until he got around to depositing them. Willi Gruber was an excellent German organic chemist, working on lipoic acid chemistry. Willi had been in the Wehrmacht in WWII and even though he had a Ph.D. in chemistry, he was used as an enlisted soldier. No wonder they lost the war.

There were semi-regular evening meetings at the Gunsalus house with beer and chips where we would discuss our results or review current literature. The denizens of Noyes laboratory even had a hangout—Farwells, directly across the street from Noyes lab. The food was pretty bad, but the company was good—even the nerdy chemists.

Gunny knows everybody

Gunny seemed to know everybody and many of them came to Urbana, which was not exactly on the main track. Fritz Lipmann was one such visitor, and I was privileged to run the slide projector for his seminar. Marianne Grunberg-Manago spent a few months in our lab before leaving to work with Severo Ochoa doing the research on polynucleotide phosphorylase that helped him share the Nobel Prize in 1959 with Arthur Kornberg—Ochoa for synthesis of RNA and Kornberg for synthesis of DNA. Roger Stanier spent a summer in the laboratory working on *Pseudomonas*, an organism foreign to most of us at that time. Carol Gunsalus collaborated with Stanier on the enzymology of the mandelate pathway in *Pseudomonas*. Roger Stanier was the consummate gentleman, and I was flattered that he recognized me at national meetings. One of the most interesting visitors was Mike Doudoroff, a colleague of Stanier's. Gunny delighted in telling us that Doudoroff's father was an admiral in the Russian Navy. Others that we met were Thressa and Earl Stadtman, the "Cornell mafia"—which included Jack Campbell, a former graduate student, Paul Van Demark, and Marty Gibbs.

Graduate education

Graduate training in bacteriology involved learning lots of chemistry—things as foreign to me as physical and organic chemistry. This was Gunny's way of inserting exact science into biological science. We also learned how to maintain the equipment—at that time nothing more complicated than the Beckman DU spectrophotometer and Warburg respirometer. However, calibrating that latter was a once-in-a lifetime experience. I enjoyed organic chemistry, in part because the University of Illinois had a fine Chemistry Department, with many high profile name such as Roger Adams, Herb Carter, Reynold Fuson, "Speed" Marvel, and E.J. Corey. Gunny was also a very good chemist and we frequently consulted him about problems, particularly in the identification of organic compounds. Fuson was a dapper dresser and always seemed to be a bit detached, but this was deceiving because he was a top-notch organic chemist. He was on my general examination and thesis defense committees and during the oral general examination he sat staring out the window until it was his time to examine. He asked me to propose an organic synthesis, which I've long since forgotten. After I gave

him my answer, his reply was "You are correct, but it is wrong in all the textbooks" and then went back to looking out the window.

Gunny emphasized the quantitative approach to research which was somewhat new to biological sciences. I still remember an admonition from him at one of our evening lab meetings when we were trying to make sense of some curious data. He said that "Every experiment must have one control that goes and one that does not go." The data that we were analyzing lacked the zero control so there was no way to know where the bottom was. My thesis defense committee included Luria, Ralph Wolfe, and Reynold Fuson in addition to Gunny. Not a bad hand!

Get a job

After graduation, I did a 2-year postdoc with Carl Stevens at Washington State University, got married, and moved to the University of Oklahoma Health Sciences Center at Oklahoma City, where I spent the next 41 years, as a professor of microbiology and immunology, associate dean of the Graduate School, and then as chairman of Biochemistry and Molecular Biology in that order. However, after moving to Oklahoma, Gunny and I stayed in touch and he influenced my career until the day I retired and then some.

Enter Academic Press

One of the milestones in Gunny's career was the launching of *Biochemical and Biophysical Research Communications*, which provided a venue for accelerated publications, a common practice today with many journals. This began a long association with Academic Press (now Elsevier) which lasts till this day. Volume 1, Number 1, was published in July 1959, and the editors of that volume were Paul Berg, David Bonner, I.C. Gunsalus, B.L. Horecker, and Howard K. Schachman. Gunny is still an editor as of this writing.

In 1960, Gunny and Roger Stanier launched the series of volumes entitled *The Bacteria*, also published by Academic Press. These were timely works and enthusiastically received treatises. Stanier was widely acknowledged to be an excellent microbiologist, but not everybody knew that Gunny was as well; another lesson he hammered home was to know the organism you are studying. The first five volumes were *Structure* [2], *Metabolism* [3], *Biosynthesis* [4], *The Physiology of Growth* [5], and *Heredity* [6]. When Gunny and Roger Stanier decided to leave the series, they nominated Nick Ornston and me to continue the work. Nick was a protégé of Stanier's and had also spent time in Gunny's lab. I already had a relationship with Academic Press, because they published my first book, *Bacterial Physiology and Metabolism* [7], through the London office. The relationship with Academic Press continued throughout my academic career with publication of two volumes of *The Bacteria* [8,9], co-edited with Nick Ornston; a treatise on *Archaebacteria* [10], edited by Carl Woese and Ralph Wolfe; a treatise on *Antibiotic-producing Streptomyces* [11], edited by Stephen W. Queener and Lawrence Day; and *The Biology of Pseudomonas* [12], edited by me. All told, there were 12 volumes of *The Bacteria* with Gunny as the editor-in-chief or consulting editor [13,14]. My other publications with Academic Press were volumes 166 and 324 of *Methods in Enzymology*, both on branched-chain amino acids, edited by Robert Harris and me [15,16].

Life in Oklahoma

Even while working in Oklahoma, I continued to meet several more of Gunny's friends. Jud Coon, one of the editors of this issue, was a site visitor for my application for a Research Career Development award. Since the award was made, I remember the visit clearly. Steve Sligar, another editor of this issue, was a prominent attendee at several of the University of Illinois social hours at the FASEB meetings. Out of the clear blue sky, I got a letter from Sidney Elsden at the Sheffield University asking me if I would be interested in doing a sabbatical leave in his laboratory. I was fascinated with the idea since we had never been out of the country and jumped at the chance. Our family, Carol, my wife, our children, David, Barbara, and Karen, left for England on the Queen Mary courtesy of a Fulbright travel grant. After arriving in Sheffield, I learned that Gunny had put the idea of the sabbatical leave in Sidney Elsden's head.

Pseudomonas metabolism and genetics

In the 1960s I began work on pathways of branched-chain amino acid metabolism, initially using a strain of *Pseudomonas aeruginosa* isolated from soil, the old fashioned way—by using enrichment cultures with branched-chain amino acids as the sole source of carbon and energy. However, with the advent of microbial genetics, it was apparent that we would need to work with a better defined organism and with a genetic system. *E. coli* was out because its growth was actually inhibited by valine. One of my former graduate students, Vincent Marshall, was working in Gunny's lab as a postdoc and was doing very well. We paid a visit to Gunny's lab so that Vince could show one of my technicians how to do the assay for branched-chain keto acid dehydrogenase, which was a bit tricky. There I met Al Chakrabarty and learned about their work on camphor metabolism using

Pseudomonas putida PpG1 and PpG2. Al had constructed a conjugative plasmid, XYL-K, which worked with these strains so that genetics could be done. Al moved to General Electric Company in Schenectady, and I spent 2 weeks in his lab there learning how to use XYL-K, which worked like a charm with *P. putida.* PpG2. However, it did not work with the Australian strain *P. putida* PPN; conversely; the sex factors used by Bruce Holloway and his colleagues did not work with *P. putida* PpG2. I continued to work with *Pseudomonas putida* PpG2 for the rest of my career. In fact, a piece of mail addressed to *P. putida* at the Department of Microbiology, University of Oklahoma Health Sciences Center, made it straight into my mailbox.

The *Pseudomonas*. symposia

In the 1970s and 1980s *Pseudomonas* research was becoming fashionable because of the many ways these organisms and their cousins affect our lives. In 1986, the first *Pseudomonas* symposium was held in Geneva and was titled *Pseudomonas*: Biotransformations, Pathogenesis, and Evolving Biotechnology. Gunny gave introductory talks at many of these meetings because he was "Mr. *Pseudomonas*." There was an amusing event that happened after the opening banquet in Geneva when my wife Carol and I were walking back to our hotel and chatting. A voice behind us called "Excuse me. I can tell by your voices that you are Americans. I wonder if you know a friend of mine in the United States? His name is I.C. Gunsalus." It turns out that she had been a nanny to the twins.

Gunny stories

There are, of course, many Gunny stories, some of which are even true. The picture of Gunny in Fig. 1 came about after one of my visits to Urbana with Dorothy and Gunny. I asked if there might be a picture of him available but he pooh-poohed the idea. Dorothy said nothing. A few months later, the picture came in the mail. During one of his visits to Oklahoma City, he saw the picture in my office and allowed as how it might keep the mice away. His reputation as an enologist was well known and his cellar was always stocked with a collection of fine wines. During one of his visits to Oklahoma City, there was a dinner for Gunny at which I asked him if he could identify the region of France from which the wine came. He sniffed the cork a couple of times and came up with the answer. At least no one there could challenge it. At one of the *Pseudomonas* symposia, I jokingly introduced my wife, Carol, to Gunny as "my daughter." He thought this was hilarious and since then has always asked about "my daughter." Gunny's use of

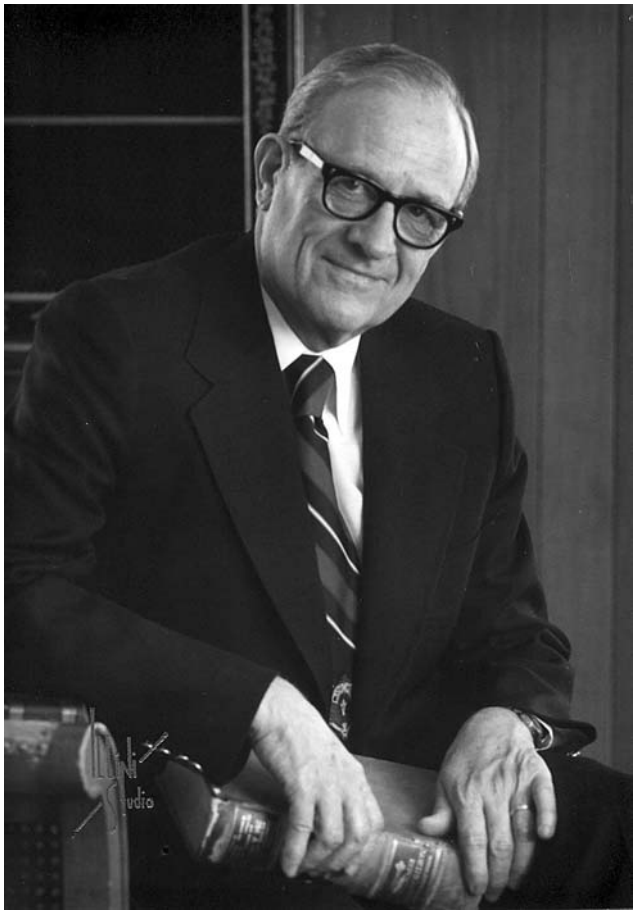

Fig. 1. I.C. Gunsalus, the guru.

the English language is legendary. We had contests in the lab trying to decipher the meaning of a paragraph. At the reception in Urbana celebrating the funding of the endowed chair in his name, there was quite a discussion on this point. The consensus was that the Gunsalus twins were the best.

The rest of the road

My scientific career covered many eras in microbial biochemistry; from intermediary metabolism [1], to enzyme purification [17], microbial genetics [18], cloning [19], regulation of gene expression [20], and structural biology [21], almost all with *P. putida*, PpG2. Gunny and I crossed paths in many ways not only until I retired but even after. There were also assemblies in Urbana for Gunny's 70th (1982) and 80th (1992) birthday symposia, held at the Beckman Institute. As pointed out in the Introduction, a retirement symposium was held in Oklahoma City for me sponsored by Paul Weigel, Chairman of the Department of Biochemistry and Molecular Biology, and by Joseph J. Ferretti, Senior Vice President and Provost of the University of Okla-

homa Health Sciences Center. Joe and I were colleagues in the Department of Microbiology and Immunology and later he became chairman and after that the CEO of the Health Sciences Center.

The Symposium was scheduled for May 4, 1999, and the invitees arrived on May 3, just about the same time as some of the worst tornadoes in Oklahoma history spanned the state from the southwest corner to the northeast corner, took 44 lives, and caused over a billion dollars in damage. The toll would have been worse if it weren't for extensive coverage by television and radio media. The invitees were certainly impressed but their relatives burned up the telephone lines into Oklahoma City checking on the safety of their loved ones. Not to worry; we had dinner that night in a restaurant in the basement of a large building. The next morning, Gunny led off the symposium with a talk about "Amazing Appetites: Pseudomonads find the Sea." The other invitees were Barbara Iglewski, Al Chakrabarty, and Paul Phibbs. Except for the tornadoes, not a bad way to go out.

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