## *Becoming a Scientist*

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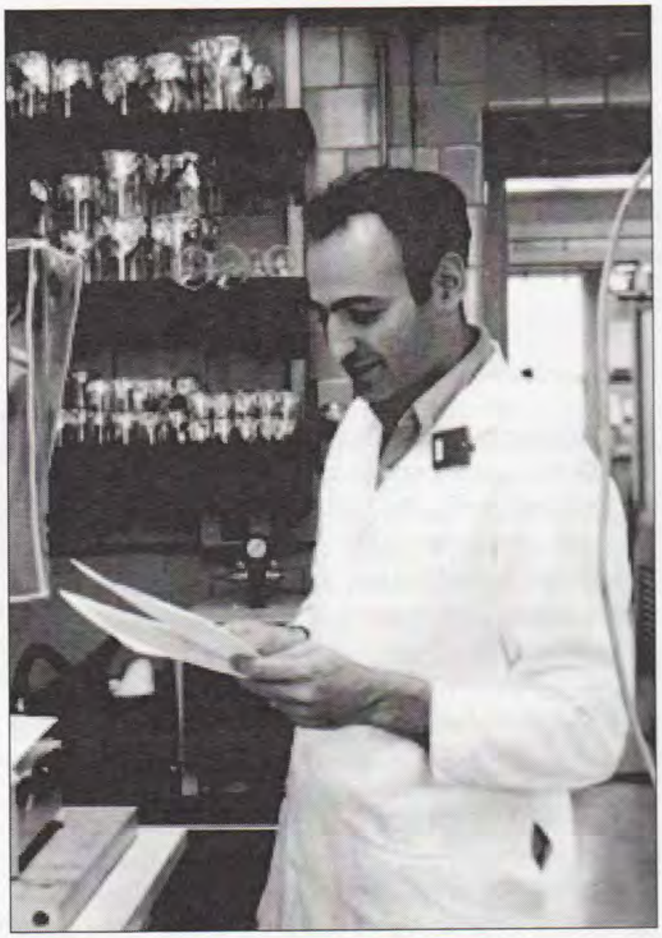

*The author in his lab, about 1970.*
*Photos: author's collection.*

My first bitter taste of the hardcore profession of science came unexpectedly when I attended the annual meeting of the American Society of Cell Biology shortly after I had established my laboratory at the National Institutes of Health (NIH). Scientists scooted from one room to another to hear the scheduled talks, small groups huddled discussing the latest news filtering through the grapevine, and individuals sat at small tables in the hallways sipping coffee or making last-minute changes for their presentations.

Postdoctoral fellows and young scientists like myself mixed with university professors and esteemed winners of coveted research prizes. My dreams of success collided with the daunting challenge of negotiating the vast sea of a science career with seemingly no bottom and an unreachable horizon. I felt like a kid at the beach, my toe in the chilly water, and anxious to swim but afraid of the surf and undertow. I remember well that lonely, apprehensive feeling more than forty years ago.

I was going to present my discovery that insulin caused cultured lens cells to elongate by promoting the assembly of structural elements called microtubules, a type of cellular skeleton. The findings were consistent with numerous studies of others associating microtubules with cell shape. I felt confident that my research would be well received and viewed as promises for bolder, more incisive investigations in the future on how embryonic lens cells specialize, or, in science terminology, differentiate.

There was standing room only for the presentation before mine, a very good sign. Spectators were taking notes copiously. Dr. Beth Burnside, an eloquent scientist at the University of California at Berkeley, showed dazzling electron micrographs of microtubules in the fish retina. However, moments before my presentation my hands felt shaky and my heartbeat increased. My data lacked the quality of Burnside's, my scientific story was not as rigorous as hers, and my specific plans for future research were still a blur. A well-deserved round of applause followed her presentation. She answered numerous questions artfully. Nervously excited about the large audience, I anticipated following in her footsteps. But when she stepped down – oh my god! – most of the audience filed out, leaving the few remaining scientists under a blanket of silence.

I bit my lip in resignation and delivered my talk listlessly, boring myself as much as I must have the few stragglers in the room. Even worse, I felt that my science was not up to par, not innovative, nothing special: mundane. I stood behind the podium berating myself, ignoring whatever qualities my talk might have had. In my hotel room that evening I felt defeated. What had even propelled me to become a scientist? It seemed so hopeless.

That I never doubted that I would be a scientist made little sense, yet I never considered a different career, strange as that seems now fifty years later. I had no exposure to science as I grew-up and had no idea of what a scientist actually did. I never played with chemistry sets, tinkered with the mechanisms of watches, assembled short wave radios, or read about science. My one connection with science as a youth was fresh water tropical fish. Many aquaria lined the walls of my bedroom. I bred the livebearers (guppies, platys) and marveled at the diverse and colorful species (hatchet fish, neon tetras, angelfish and many more). If this was science, it was an aesthetic experience. During my teenage years, if I wasn't attending school I was playing tennis or nibbling on candy bars as I watched movies on our black and white television set. Science didn't occupy any space in my mind. The only science course offered in my high school was chemistry, and my laboratory experiments seldom worked out correctly. As for math: I had no particular talent for it and, frankly, it scared me. Two-dimensional geometry was bad enough, but solid geometry was a catastrophe. I dreaded trying to apply mathematical formulas to three-dimensional shapes, which I struggled to visualize. I think conceptually in terms of ideas and stories, not structurally in terms of images and physical models.

My mother always assumed I would be a scientist. Perhaps she thought that it would avoid comparison with my famous cellist father, or perhaps she had wanted to become a scientist herself. She never mentioned that but it was clear to me that my mother admired scientists. Her sister, my aunt Bethsabée, had taken a temporary stab at scientific research in reaction to her son dying a few days after birth, and later she established the Batsheva (the Israeli equivalent of Bethsabée) de Rothschild Science Foundation in Israel, but she never continued as a practicing scientist. Instead she sponsored modern dance in Israel after befriending and supporting the famous dancer Martha Graham and then Jeanette Ordman.

My father had talked romantically about oceanography and jungles and snakes and fantasized about experiences in nature, but these were castles in the air for him and synonymous with science, with no appreciation that nature occupies at most a corner of a science career; science is a human endeavor, an interpretation of nature that comes from disciplined labor. My father had poetically embraced the idea of nature and spoke about the importance of submerging oneself in a world larger than oneself, which was music for him. Both he and my mother discouraged music for me; it was obvious that I had little talent or predisposition to be a musician. Moreover, my father loved music but said that he detested the music profession with all its traveling, politics and tensions. My mother had studied piano for years in France in her youth with the famed pianist, Alfred Cortot, but remained frustrated, convinced that she lacked that magical gene for music. Later she recognized that I did too. Thus, both my parents nudged me into the grandiose world of science, each in their own way.

I must have unwittingly projected the image of a scientist to my classmates in high school since my senior yearbook foreshadowed me as a big-shot oceanographer living on a yacht on the Mediterranean. How romantic! But childhood predictions are hardly reliable. My experiences followed a bumpier road to becoming a scientist.

If scientists are supposed to be "brainy" (a term requiring a liberal definition!), an IQ test I took in the eighth or ninth grade didn't bode well for my future in science. "Were you feeling all right?" my teacher asked the following week. "Ahaa!" he said as soon as I mentioned that I had a cold that day. There had to be an explanation of why I scored so low. "Please retake the exam," he said. I did the following day in the Principal's office, where I was told there would be no distractions. I guess no one considered the fear factor of sitting alone in the Principal's office retaking an exam I had presumably flunked (whatever that means for IQ) the first time around to judge my intelligence. Neither my first or second IQ test results were divulged despite inquiries by my mother and me. "We don't want Joram to develop an inferiority complex," is my memory of their reasoning. Considerate. On the positive side, not knowing my IQ allowed me to flap my wings and hope I would fly. To this day my IQ remains fluttering invisibly in the blue sky.

The mandatory college entrance exams – those nasty Scholastic Aptitude Tests (SATs) – were another nightmare. Practice SATs made it clear that I needed improvement to be accepted in a college of my choice. To boost my score in English I tried to increase my vocabulary. I guess I spent too much time on a tennis court and not enough time in the library. The words in the practice booklets were listed alphabetically and I dutifully memorized their definitions in alphabetical order. I ran out of steam with the words starting with the letter *m*. Nonetheless, my efforts were sufficient to raise my SAT score a few hundred points. What a ridiculous measure of ability to do well in college! Today some colleges are doing away with SATs, finding that they do not correlate well with academic success. Miraculously I got into Harvard, but probably my

SAT results had little to do with that. The more likely reasons for being accepted were that I was a highly ranked junior tennis player in Southern California (I had an especially mean left-handed serve), that my father was who he was, a famous cellist, and that I was academically first in my class in Black-Foxe Military Institute (however of only seventeen students). I am certainly not a military type, but military schools were popular after the war. It's also likely that being from Los Angeles I added "geographic diversity" to their student body, a euphemism I was told that is attributed to a Jewish quota at the time.

Soon after I arrived at Harvard I took extensive aptitude tests given to freshmen for guidance towards a major field of study. A few weeks later I received a concise letter stating that I had no aptitude for any of the natural sciences. I was advised to major in social relations, called SocRel, where I might be able to achieve Dean's list. They kindly wished me luck in my future studies. The student grapevine considered SocRel a watered-down mixture of psychology and sociology. What was I to do? Give up my ephemeral dreams of being a biologist? My thoughts turned to the advice that my father had received as a student in Russia from a professional cellist, Mr. Kinkulkin, recounted in my father's autobiography, *Cellist* (Doubleday, 1965):

*"While I played, Mr. Kinkulkin tapped his tiny fingers on a table and cleaned his nails with a toothpick. He remained silent until I had put my cello away. 'Listen carefully, my boy. Tell your father that I strongly advise you to choose a profession that will suit you. Keep away from the cello. You have no talent whatsoever.'"*

My poor father didn't even have the benefit of being directed to another career, a SocRel equivalent. He quit the cello for a short stint, but not for long, and his subsequent rise to becoming a famed cellist is history. In a leap of faith based on the cliché that the apple doesn't fall far from the tree – like father, like son – I interpreted the unfavorable evaluation of my science aptitude as destiny to future success in science. With this blend of foolishness and arrogance, I majored in biology.

My disregarding the results of the aptitude tests initiated a lifelong pattern of questioning authorities and, especially, considering alternative views. My father was a champion at such mental gymnastics. For example, I remember being home on semester break from college and telling him that nothing can travel faster than the speed of light, a fact I had learned in my physics class.

"Nothing?" he said.

"Nothing," I answered, proud of my new knowledge.

Refusing to accept such dogma, my father asked, "What about the speed of dark?"

Ridiculous? Yes, scientifically, but illustrative of an inquisitive, alternative mind that insisted on originality.

And then there was the confusing ambiguity of formal education in my family. Of course my parents valued a first-rate education. However, neither had college degrees. My mother, the daughter of Baron Edouard de Rothschild, was tutored at home in France. I never probed for the details of my mother's early education. I doubt that her home schooling was rigorous; girls were considered second-rate citizens at that epoch, waiting for marriage. My mother's school credentials amounted to a certificate of equivalence to a high school diploma obtained after she, at twenty-eight, immigrated to the United States at the beginning of World War II. I believe that she also took a few correspondence courses at Temple University in Philadelphia during the war years. Yet, she accomplished more in each of her diverse interests (chess, sculpture, writing, tennis, music) than most in a single area. The absence of conventional schooling certainly did not limit her accomplishments. It would not surprise me if it freed her to follow her instincts.

My father had a different trajectory, although clearly it is not possible to be guided by his youth in Czarist Russia and his remarkable talent in music. He never went beyond the third or fourth grade, yet he emerged a world-famous cellist, authored an autobiography published in English and translated into Japanese, Hungarian and German; he was typically the center of attention in social gatherings, including professors, writers, artists and other highly educated people. His intelligence and charisma (he was a renowned story-teller) shined more brightly than any diploma could have. In short, there were no templates for success in my family, just a high bar to clear.

"A doctorate degree diminishes the man," my father said in jest.

"How so?" I asked, thinking of my future plans.

"Well," he responded, "who is more significant, Beethoven or *Dr.* Beethoven?"

Clever! But, then again, genius follows its own rules.

On more than one occasion my father asked me when I was going "to enter the school of life." I took that to mean book learning was worthwhile but not sufficient. He had his point; however, he was not training to be a scientist.

Thus, my becoming a scientist had no semblance to the uplifting refugee story common in America of children professionally surpassing their less educated immigrant parents. Quite the contrary: I was raised with the sense that conventional schooling, although beneficial, could also hinder excelling and originality. My challenge was to match the success of my atypical and gifted European parents *despite* being a native-born, formally educated, American blessed with a surplus of advantages. "Privileged boy makes good" hardly makes a headline, and positive headlines were plentiful in my family.

I had two summer jobs during my college days on my way to becoming a scientist. The summer following my sophomore year I worked in the Department of Zoology at the University of California at Los Angeles (UCLA). My first task consisted of topping off partly filled bottles containing fish fixed in formaldehyde and stored in a dark room on dusty shelves. The secluded room reeked of insignificance. While that might sound mundane, the diversity of fish species impressed me and recalled my tropical fish hobby from the past. I remember being told that new species of fish were discovered each time the research vessel went on a collecting trip, and this kindled my desire to go on one of those collecting trips. I began to see science as a huge collection of what's not known. There was so much to discover! If this was science, I figured that the aptitude tests must have been flawed: I had the ability to remove lids from bottles, add liquid and then replace the lids. I also knew how to appreciate ignorance.

After a few weeks when I was woozy from the smell of alcohol mixed with formaldehyde, Arthur Myrberg (if I remember his name correctly), a PhD graduate student working for Professor Boyd Walker, took pity on me topping off jars containing dead fish and asked if I would assist him in his research on fish behavior. Would I? Yes! He was studying imprinting in tropical reef, cichlid fish. Cichlid fish were among those in my youth ("Kissing" Gouramis and Angelfish). I felt back on familiar terrain. During the rest of the summer at UCLA I sat in the middle of the darkened laboratory so as not to disturb the behavior of the fish in the tanks – heaven forbid! – and documented in a tape recorder how often and for how long fish fanned a batch of developing eggs with their fins to generate a gentle current that oxygenated the embryos. When the eggs hatched, the parent fish protected their babies from predators until they could fend for themselves. A tiny hatchling that wandered astray was sucked into the mouth of one of its parents and spit out to join its siblings. In nature, the fish fanned and cared for their own young in a secluded corner of a coral reef. Experimentally, however, a developing batch of eggs could be switched for those of another species of cichlid fish. A parent fish became "imprinted" on the first species of hatchlings it cared for, whether that was its own species, as would occur in the wild, or another species in an experimental situation when species were switched. A fish imprinted on a foreign species would still fan its own eggs if it bred again, but it would eat their babies when they hatched. My exposure to imprinting in cichlid fish in the summer of 1960 was my first true exposure to scientific research.

The neurological basis of imprinting intrigued me. I considered a career studying the brain and took several psychology courses in addition to the many science courses at Harvard, including one on the neurophysiological basis of behavior, and another from the famed B.F. Skinner. I visited Nikolaas Tinbergen at Oxford University to explore the possibility of doing graduate work in animal behavior; Tinbergen won the Nobel Prize for behavioral research later in 1973. My naïve idea was to determine what happens in the brain at the moment that a thought or an epiphany or a forgotten name at the tip of one's tongue suddenly flashes in mind – the "ahaa" moment that makes one exclaim, "Oh yes, I remember," or, "I get it." Ultimately I did not travel that route. I believed that understanding the biochemistry or biophysics of abstract thought was not possible yet, that it was a research topic for my children or grandchildren, should I be lucky enough to have them in the future. But how fascinating the idea was at the time – the biology of a thought or an epiphany – and still is. If only I had more than one life to live.

After my junior year in college I asked my distant cousin, Lord Victor Rothschild, a British biologist at Cambridge University, if he could arrange a summer job in science for me in England. He put me in touch with Dr. Harold Barnes investigating barnacles at the Marine Station at Millport on the tiny Scottish Isle of Cumbrae located between Scotland and Ireland. This aroused my sense of adventure: science on a remote island! Barnes wanted a summer helper who knew about spectroscopy. "That's a special interest of mine," I said, and then I bought a book to find out what spectroscopy was. I barely knew how to spell it. It turned out that all Harold Barnes wanted was a student willing to spend hours determining the optical density of colorimetric reactions using a UV spectrophotometer, a rote process requiring more patience than skill. For six weeks that summer I performed experiments directed by Barnes to determine how long a species of barnacle living in the intertidal zone – a region covered by the sea only at high tide – could survive without water-dissolved oxygen. I measured the accumulation of lactic acid, a product of oxygen-free metabolism, by keeping the barnacles for an increasing amount of time in a nitrogen-saturated atmosphere. In science jargon, I determined how much of an oxygen debt the intertidal barnacles could accumulate, which was what they did when exposed to air at low tide. In some experiments I needed to take samples periodically for twenty-four continuous hours. I was grateful for thick Scottish sweaters since I was asked politely to not use the portable electric heater in the chilly nights in order to conserve money. Apparently the Scotts earned their reputation for thrift.

The janitor came to the laboratory shortly after five in the mornings to tidy up before the scientists arrived, and when I had worked through the night we greeted the sunrise together with a biscuit or two and a cup of tea with milk; he insisted that hot tea with milk was the key to a happy life. I never met a man who seemed more contented than that elderly janitor with a steady job in a beautiful environment. The seagulls started chattering at the first light of dawn announcing and accepting their place in the world. We looked at the brightening sky over the quiet sea and sipped our tea together, remarkable moments in the corners of time.

"What a great life," the janitor would say, and I felt the same way. I never had a deeper sense of being where I belonged than in that remote marine laboratory, engaged with barnacle metabolism, an esoteric subject to some, but a crucial aspect of life to me, a topic so important that the time and money expended needed no justification.

Dr. Barnes included me as an author in the publication of our experiments, and this was my first scientific publication: a beginning that meant a lot to me, and still does.

One experiment I performed in Millport stands out in my memory. It ended in disaster, but taught me a lesson I never forgot. I had dried barnacles, each in a separate pre-weighed bottle, in a warm oven overnight. I placed the bottles sequentially next to one another, left to right, as if reading a book, saving the trouble for me to label each one. What I hadn't considered was the almost imperceptible vibration of the oven. The next morning I found, to my horror, that all the unlabeled bottles had shifted position slightly. I looked for a pattern of movement attempting to recreate the path of each bottle in order to identify the sample, but it was hopeless. I never again failed to label every sample of every experiment. Science had its poetic aspects, but it also required meticulous discipline. There were no shortcuts.

I learned another lesson of a very different sort that summer. Our findings showed that barnacles were able to create an oxygen debt far greater than expected in their natural environment. I concluded that to be successful, which in barnacle language meant to survive hundreds of millions of years, it was imperative to have a greater depth of resources than are typically needed at the moment. If the barnacles were cruising along on minimum supplies of whatever was essential for surviving the normal conditions in which they evolved, it is likely that they would perish – become extinct – if there were suddenly a significant change, even a transient change, in environmental conditions. Barnacles, like all successful species, operated on a surplus. One unexpected surge would wipe them out. I generalized that success in anything – evolution, competition, career, sports – required a deep reserve under the visible surface, a buried foundation to survive and succeed.

To fully appreciate my sense of satisfaction doing research at Millport requires a few words about the preceding month. I was at Eze-sur-Mer in the south of France visiting my mother's family. We stayed in the Heinz estate (I believe) that was rented by my uncle, Guy de Rothschild. The house overlooked the Mediterranean Sea, a visual paradise. Most people would crave to spend a few weeks at such an idyllic place. There was a full house of guests at the estate, including Guy's wife Marie-Hélène (Guy joined us later), my cousin David, a more distant cousin, Eli, various guests, including the future President of France, Georges Pompidou, and a few others that came and went. The lengthy meals were, by my standards, formal; a foulard (a neck scarf) and a long-sleeved shirt were required attire even for luncheons on the patio in the balmy weather. Political issues were among the more interesting topics of conversation, but I struggled to comprehend the rapid French idioms. Mealtime banter also included gossip and various forms of character assassinations. I remember a catty discussion about who had the most and the least sexy skin in Parisian society. On occasion we went to fancy restaurants in the evenings. Also, there was gambling at Monte Carlo, although I never went there; gambling never held any interest for me.

In the midst of my stay I came down with what a local doctor suggested was typhoid; later tests confirmed the diagnosis. I had a high fever, diarrhea, and was confined to bed. To keep my sanity, I read a layman's book about Einstein and relativity. Marie-Hélène wandered into my room from time to time to find out what strange things were occupying my mind. Since I was too sick to go to my job with Barnes in Millport on the appointed date, I went to Paris with Guy and Marie-Helene instead. Once the fever receded (not completely) after a few days in Paris I decided to go to Scotland against the advice I received, but I couldn't miss my golden opportunity for a job in science.

Standing on the deck of the ferry from Wemyss Bay, Scotland, to Millport, out of touch with the rest of the world for those few hours gave me a blended sense of freedom and purpose I'll never forget. The cool sea breeze sucked away any disease that still lingered in me. The contrast between the luxurious lifestyle at Eze-sur-Mer and my research experience at the sparse marine laboratory made the latter seem as genuine as the former contrived. I was completely happy.

A few years ago (January 6, 2010, to be exact) I heard President Obama give a short speech in a televised ceremony recognizing outstanding science and math teachers. He said that he believed every prizewinning teacher at the ceremony had a mentor, or had attended an event, no matter how brief, that changed his or her life in a pivotal and positive way. As I listened to Obama, Professors Leigh Hoadley from Harvard and Albert Tyler from Caltech came to mind as mentors who influenced me when I was a student.

Professor Hoadley was not a distinguished scientist, did not have a strong reputation as a teacher or scholar, and tended to ramble. A short obituary in the Harvard Crimson (Nov. 10, 1975) implied that Hoadley's devotion to students and his role as Master of Leverett House "cut in to his scientific work in terms of fulfilling potential." James Watson, a Nobel Laureate and Harvard professor famed for determining the double helical structure of DNA, wrote in his memoir, *Avoid Boring People*, that "conversation followed the lead of Master Hoadley, incapable of either levity or deep thought." I remember Hoadley more kindly than that. An important moment for me was when he challenged the class by asking what would happen if an early frog embryo were cut in half. I raised my hand and answered, "It would die." That seemed logical then (and still does today!).

"Not necessarily," said Dr. Hoadley. "The two parts of the cut embryo can adjust so that each half develops as a normal embryo, resulting in twins."

"How does that happen?" I asked, suddenly feeling as if I was having a private conversation with the professor.

"I don't know," Hoadley confessed, and then mentioned "morphochoresis," a term he coined to mean the dance of developing form. I liked the term. It had a self-explanatory artistic ring, although it explained nothing. I never heard anyone else use that expression. He went on to discuss variations on the effect of splitting an amphibian embryo that depended on the cleavage plane, and then talked about embryos of other species that didn't self-regulate to produce twins, the so-called mosaic-type embryos. Embryos were more than machines, even more complex than memories; they were diverse, resilient and mysterious, and they danced as they developed. I think that Hoadley's poetic sense, his admission of ignorance and his appreciation of mystery made biology more accessible for me. He gave science more depth than formulas and graphs. In a blurred kind of way, I could see myself as a biologist, perhaps a dancing biologist, or maybe a spectator biologist in the audience of a dance performance. I didn't quite fit any mold, but that was all right, maybe even preferable. It was who I was.

Following the introductory course, I wanted to take Hoadley's advanced, graduate workshop in development. However, he told me that he wouldn't teach it unless he had at least eight (if my memory serves me correctly) students enrolled and very few had signed up. I recruited several more, but failed to obtain the required number. I pleaded with Hoadley to give the course anyway, and he finally consented. Our small group met informally in his office and discussed various topics of embryonic development that were reviewed in a classic book, *Analysis of Development*. To me these discussions seemed as much art as science, with nature as the medium. The free-association discussions also resonated to some extent with my father's ramblings on science, giving my sessions in Hoadley's office a personal flavor. While I understood that science was based on hypotheses, experiments and observations, I started thinking about science as playing with imaginative ideas, reinforcing my intuitive notion that scientists and artists shared qualities.

Meeting in the intimacy of Hoadley's office and pondering the immensity of biology rather than listening to formal lectures in a classroom had a refreshing impact on me. I wrote a term paper for the course, reasoning as follows. If half an amphibian egg can form a whole embryo, and if a lizard can regenerate a tail, as some can, a person should be able to regrow an arm or a leg if one knew how to make that happen, or in today's language, if one knew how to turn on the right cascade of genes in the stump remaining after amputation. I predicted that in the future an amputee would be a stark reminder of the medical dark ages that existed at the time I was taking the course. I was beginning to think about science more practically, although I never evolved from a basic scientist with artistic inclinations into a goal-oriented scientist with a destination. I still believe as I write that the day will come when humans will be able to regenerate amputated appendages. Hoadley portrayed science for me as beautiful mysteries that could be whittled into ambitious dreams.

My senior year at Harvard was decision time for my future career. Some of my classmates applied to medical school, and Hoadley advised me to do the same. He said that being a physician would give me license to practice medicine as well as to mix academic medicine with research, while a PhD degree would limit me to research. "You never know," he said, "when you might want or need to practice medicine." Sage advice, for certain. I listed the pros and cons for being a physician or a basic scientist, and I concocted the following argument that influenced me to go for the PhD. I imagined that if I was a physician peering into a microscope I might ask myself, "What's *wrong* with those cells?" If I were a PhD staring at the same sample I might wonder, "What's *right* with those cells?" Perhaps these questions were just two sides of the same coin, and that posing the question the way I did was no more than sophistry. Certainly there are examples of major basic discoveries made by physicians as well as medical advances made by basic scientists. I preferred the idea of spending my life immersed in health than in disease and decided to apply to graduate school for the PhD. I still believe after a fifty-year career in research that there are fundamental differences between a basic scientist and a medically oriented scientist – the context of the research, the scientific literature read, the conferences attended – although I submit that the lines can blur.

My career in vision research spanned a golden age of basic research in biology (1960-2009). The astounding discoveries in genetics, development and evolution, all direct interests of mine, were due in large part to the intellectual freedom and generous funding for research without needing to claim immediate medical relevance. My own basic research led me to study gene expression in the eye lens and cornea of chickens and mice and squid and scallops and even jellyfish: in short, a selected zoo of creatures with eyes! It even included the blind mole rat that lacked visible eyes (although they do have degenerate eyes buried beneath the surface). I doubt that if I had been a physician I would have followed a similar trajectory or made similar discoveries. Choices matter.

I set my sights on the California Institute of Technology (Caltech) for my graduate studies. Apart from being a scientific powerhouse, Caltech would force me to confront my difficulties in the physical sciences and math; I wanted to overcome these glaring weaknesses. Also, my primary interest was developmental biology, the specialty of the Caltech professor, Dr. Albert Tyler. Not very professionally, I dropped in on Tyler, whom I'd never met, without an appointment before applying to Caltech when I was in Los Angeles visiting my parents. By chance, I found him in his office. Despite my uninvited intrusion, he was gracious and talked with me. I told him that I was a senior at Harvard, interested in developmental biology and wanted him as my PhD mentor (what chutzpah!). Rather than dismiss me, he was encouraging and advised me to apply through the regular channels. In retrospect, I believe that he might even have been flattered because, like Hoadley, he was not an especially popular mentor. I didn't know this, of course, at the time; I knew nothing about Tyler's professional standing or quirks. All I knew was that his specialty was fertilization of sea urchin eggs and that he had published more articles than I had read. Mountains look so high from their base.

Tyler introduced me to Dr. Ray Owen, the Chairman of the Biology Department before I left. After a brief discussion about my interest in biology, I asked Owen, "Would I have to take the graduate record examinations (GREs) if I applied to Caltech?"

"Not take the GREs?" Owen looked confused.

"Yes," I pursued.

"No one has ever asked me that before," he said.

In fact, I had never thought of asking that before. It was an impulsive thought, and a foolish one at that.

Nonetheless, I persisted.

"But would you still consider my application if I didn't take the GREs?"

I remember thinking that that it would be better to let them imagine that my GRE results would be commensurate with my academic record at Harvard (*cum laude* in biology), Dean's list (but no sparkles) despite the aptitude test's prediction, rather than to have a poor GRE result tacked on to my record, which I feared a likely outcome considering my pattern of low performances on standardized tests.

"There's no written requirement to take them that I know of," he said, scratching his head. "But every applicant takes them."

In parting, I asked him about my chances for acceptance in general.

"Well, we turned down Jim Watson." It was a cold, hard statement of fact.

Ouch!

When my peers at Harvard went to take the GREs, I went to a Humphrey Bogart movie at the famous Brattle Theater next to Harvard Square. What was I thinking? It's still hard for me to believe that I was so brash. However, despite the absurd risk-taking, I was admitted to Caltech. My guess is that Tyler must have supported me within the admission committee. I'll never know.

Immediately after being accepted, Tyler arranged for me to spend the summer at the Woods Hole Biological Laboratories on Cape Cod, a vibrant scientific center, before starting my graduate work. He enrolled me in the Fertilization and Gamete Physiology Training Program organized by his former student, Dr. Charles Metz, a professor at the University of Miami, Florida. Before ever starting my graduate studies it was apparent that science operated by selective networks, and I was fortunate to be incorporated into Tyler's network at such an early phase of my career. My mentor in the research-training program was C.R. Austin (nicknamed "Bunny"), who was the Charles Darwin Professor at Oxford University and an authority on mammalian fertilization. My research that summer showed that a dissolved solution of the jelly-coat (called fertilizin) surrounding sea urchin eggs was capable of eliciting the acrosome reaction – a structural change in sperm that occurs during fertilization. I presented my findings to the scientific community at Woods Hole and published two abstracts. I was starting to feel like a scientist.

While I loved the research and immersion in biology, small human exchanges – "little things" – also meant a lot to me. Once on a sunny day, I sneaked away from my peers in the training program and went for a swim at the beach. I waded into the cool salt water, my body warmed from the sun, feeling at peace with the world. Suddenly Alberto Monroy, an instructor in the training program and professor at the University of Palermo, surprised me from behind.

"Skipping work, eh?" he said, knee deep in the water.

"Err, what? Just for a quick swim. It's so beautiful out here," I stammered, embarrassed to be caught playing hooky.

"Your experiments in good shape?" he asked.

"I know I'm supposed to be in the lab," I said, falling short of answering his question.

He hesitated and then said, "Only technicians would stay in the laboratory on a day like today. The scientists, the *real* scientists, would be out here!"

Such an innocuous statement, more social than meaningful, and yet . . .

Why would I remember that so many years later? Perhaps for the same reason that informal discussions on science in Hoadley's office humanized dispassionate science for me, or perhaps being considered one of the *real* scientists by an accomplished scientist like Monroy, or perhaps I valued kindness over judgment. Unfortunately, tolerance and kindness are often mistaken for weakness. I tried not to make that mistake in my career. I always gravitated towards kind mentors and colleagues, and never subscribed to the cliché that "nice guys finish last." My example was Charles Darwin. Everything I ever read about Darwin indicated a kind and gentle, even vulnerable, soul immersed in his work. It is interesting that he too rejected medical school when he was pushed to be a physician by his father.

Albert Tyler was a kind mentor who taught me both what to do and, by example, what to avoid, but he was not free of his own frustrations that spilled over to me. Perhaps we shared a similar issue unrecognized by me at the time: high expectations due to our backgrounds. While my acclaimed cellist father and Rothschild mother set immensely high, visible standards for me to meet, Tyler received his PhD at Caltech and was mentored by Thomas Hunt Morgan, one of the legendary founding fathers of genetics and development. Morgan had moved from Columbia University to establish the Caltech Biology Department in 1928 and received the Nobel Prize in Medicine and Physiology in 1933 for his many contributions to the role of chromosomes in heredity. Tyler received the first PhD degree from new Department of Biology and remained at Caltech his entire career in the long shadow of Morgan, creating very high scientific standards to match. Interestingly, Tyler's history made Morgan my scientific grandfather, which elevated the already high bar I felt pressure to clear.

On rare occasion Tyler exposed vulnerable feelings. One personal anecdote is telling. Tyler and I were discussing his efforts to engineer sea urchin eggs by "feeding" them genetic messages (mRNA), a process called "euphenics" instead of the better-known "eugenics." Euphenics involved biological engineering beyond the level of the gene, while eugenics involved tampering with the genes *per se*, which became a lively field of genetic engineering later with the advent of DNA cloning. Tyler's experiments were visionary but subject to alternative interpretations that might have discouraged further explorations in that direction for someone with a more objective viewpoint. Although aware of this, he procrastinated performing critical control experiments that would challenge his interpretations. He seemed to be driven to make a sensational discovery that would attract attention. I didn't let it go.

"Why not just do the control experiments and settle the issue? You don't know what will work and what won't," I said, overstepping my bounds as a graduate student.

"Well, it's complicated," he said, without much conviction. He was correct about that, but aren't all experiments complicated to interpret?

"How?" I asked.

He paused. "I guess I'm scared of the results."

This rare admission of Tyler taught me an important lesson: one must not confuse ourselves with our hypotheses, or our egos with our ideas. A scientist is never the master of nature, only a messenger, if lucky.

Tyler and I co-authored six articles together while I was a graduate student and one posthumously after Tyler had died suddenly at 62 from a heart attack (as had one of his two sons earlier) after I had already received my PhD. I arranged with John Saunders, the editor-in-chief of the scientific journal, *Developmental Biology*, to dedicate an issue to Tyler and have his former students contribute the articles. Linus Pauling, Tyler's long-time friend at Caltech, accepted my invitation to write an Introduction to the special issue, which made me very happy and I'm certain would have also pleased Tyler. The publication by Tyler and


*A smiling Albert Tyler on the day of the author's graduation from Caltec.*

me was the leadoff article in the issue (volume 21, 1970). Thus, I was the last student to receive a PhD from Tyler, capping the lineage of Morgan's scientific grandchildren, and our article was the last one Tyler published.

I had a strange premonition about Tyler's unexpected death when I was working on this article on a plane flying to Israel. I was a postdoctoral fellow at the National Institutes of Health (see below) and corresponding with Tyler about the interpretation of our data. On route I became extremely anxious to finish the article and, as I remember, I worked without interruption to complete the draft on the long flight and sent it to him as soon as I landed in Tel-Aviv. He received my draft, made modifications, mailed it back to me and then had his heart attack. Strange coincidence. Although I have always been driven to finish what I start, this was different, more acute than before. I had a sense of urgency that I had to complete this task in case anything happened to me (not him). While this single focus might have increased my productivity at times, it also had its pitfalls. Reflection over time generally raises quality, and taking the time to explore unexpected trails can be surprisingly productive. Thus I have tried to remember, although not always successfully, a clever statement of Igor Stravinsky's that my father told me years ago: "I have so much to do, I have no time to rush!" What a wonderful thought applicable to all, young or old.

I sat by Tyler's side in his office for a week or two for each article we wrote together, discussing every sentence as it unfolded until the last period was in place. I doubt many students ever had the privilege of such a close tutorial with their mentor, and I am very grateful to Tyler for that. It was an extraordinary education on data analysis and the mechanics of writing a scientific article.

Once, however, a difficult situation arose. I had devised a theory that I called "the revolving door hypothesis." Briefly, I posited that an amino acid (cells use twenty different amino acids to make proteins) added to seawater entered a fertilized sea urchin egg through a conceptual "revolving door" that would spit out an amino acid of the same type trapped in the hypothetical "door" when it started to revolve. I predicted that there were three classes of such "doors" located on the surface of the egg: one for positively charged amino acids, one for negatively charged amino acids and one for uncharged (neutral) amino acids. It was known that there were several channels to transport different amino acids across cell membranes. My thought was that these are "revolving" channels. Tyler must have liked the idea since he agreed to have his technician test it over a couple of weeks when he went out of town. I was busy with other experiments and was happy to have the help. The experiments worked as I had hoped, and we decided to publish an article proposing these conceptual revolving doors. The trouble started when the final period was placed in the manuscript.

"So, who will be the first author?" Tyler asked.

I was taken aback. It was entirely my idea; he had agreed to let his technician do the experiments to save time while he was traveling. I was unsure what to say, afraid to be too assertive, yet thinking, "Me, of course. I should be first author." But I said something like, "I don't know. What do you think?"

"Well, my technician did all the experiments," he countered.

I was tongue-tied, my heart racing. "It's my baby!" my mind screamed silently. If Tyler placed himself first it would appear as if he generously tacked me on to help his student.

"Let's flip a coin," he said.

Flip a coin! What if I lost?

"Okay," I said, suppressing my growing rage."

He removed a coin from his pocket. "Heads or tails?"

"Heads," I said.

He caught the coin on its descent and flipped it onto his arm. "Heads," he announced.

I'll never know whether Tyler would have put his name first on that article if he'd won the coin toss. In fact, as I remember the event now, I never saw the coin after he flipped it. Perhaps it was tails, but he called it heads. Why do we always assume we know so much? Whatever details actually occurred, I have often thought back on this episode trying to not let ambition cloud my science or professional decisions, which is not always an easy path to follow. Thus, I learned as a graduate student that science is not a selfless rendezvous with Nature, which is an overly idealistic interpretation of my father's advice to immerse oneself in a world "bigger than oneself." Tyler showed me unwittingly that science is subject to the pitfalls of ambition with all its triumphs and disappointments, like any other profession.

Tyler also had a kind side. Again, an anecdote is illustrative. One Saturday Tyler and I went to collect a peculiar worm, *Urechis caupo*, which lives in a U-shaped tube in the estuarine mudflats. *Urechis* irrigates the tube by peristaltic body contractions. Suspended food particles are captured in porous mucus nets deposited by the worm at the entrances of the tube. While we were driving to the beach, our conversation drifted to what makes a successful scientist. At first Tyler said that mathematical and analytical skills were critical, but then, as if sensing my weaknesses, he quickly changed his mind.

"No," he said. "The successful scientist will be the one who has patience and is willing to work steadily to complete the often-boring work that is needed."

I had recently spent many boring hours making routine, mind-numbing measurements for my research experiments. What I heard, then, was that Tyler believed in me. Being a graduate student with a package of insecurities common to students (and often mature scientists as well), I never forgot this brief, if cryptic encouragement. It was on a par with Alberto Monroy telling me that a "true scientist" would be out for a swim on a sunny day at the beach when we were at Woods Hole. Funny how one remembers isolated, trivial experiences of no consequence as important life events, and how often those treasured memories are the experiences that touch one's vulnerabilities.

To be conferred with a PhD degree from Caltech I needed to pass a final oral examination. The examiners

*The author in a characteristic stance with Gregor Piatigorsky on graduation day.*

*The author's proud mother on graduation day at Caltech.*

(my thesis committee) included Albert Tyler (of course), James Bonner, Norman Horowitz (who had been Tyler's graduate student years earlier) and Sterling Emerson, all eminent scientists. Confident but nervous, I came to the examination dressed in a coat and tie. I doubt that any other graduate student ever dressed so formally at Caltech. When I walked into the conference room to be questioned, James Bonner took one look at me and said, "Piatigorsky, you're a square; you always were a square and always will be a square." I think it's self-evident what Bonner meant by "a square." It wasn't complimentary and made me feel uncomfortable and self-conscious. To some extent, I believe that my being overdressed was a remnant of my formal European background. However, this final doctoral examination was a major event in my becoming a scientist, a kind of performance that would change my status for the rest of my life. My father's image flashed through my mind. He always dressed in a coat and tie when performing or even in rehearsals or playing chamber music among friends. I saw him rehearsing in the heat of Puerto Rico at the Casal's Music Festival in a coat and tie when others were in sport shirts. "I don't play the concert informally," he said, "and this is a rehearsal – preparation – for what's to come." He didn't compromise his self-discipline. He also considered it an outward sign of respect to his audience, whomever they may be, to be well dressed. So, I thought, Bonner be damned. I'll set my own standards from a different example – my father – and I have adhered to that discipline throughout my career, a last minute lesson I learned as a graduate student.

Norman Horowitz asked me the final question of my oral exam. He was one of the scientists seeking life on other planets at the time, and was pessimistic that extraterrestrial life existed. "It's possible,' I said. "Really?" he responded, perking up. I had recently read that silicon was extremely reactive and had an atomic structure that could conceivably substitute for carbon, an essential element for life. "What if there was life based on silicon instead of carbon?" I ventured. He remained silent, so I continued. "It would be reverse to the life we know," I said, starting to feel worried. He looked curious, but still did not say anything. "Well, life as we know it," I said, "is based on carbon and works by having enzymes catalyze (speed up) the biochemical reactions that are needed at the time; stable life on earth is based on the low reactivity of carbon that requires special enzymatic catalysts to make the organic compounds required for life. But if silicon was used rather than carbon, life could depend on suppressing the reactions of the overactive compounds. Whenever a particular biochemical reaction was needed, the suppressor would 'lift its lid' so to speak, and let the reaction take place." It sounded pretty ingenious to me! Horowitz didn't holler with delight. "Wouldn't work," he said. "It's not thermodynamically stable."

And that ended my student days. I was now Dr. Piatigorsky, in a coat and tie.