Mentee to Colleague: Paths to a Research Career
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Approximately 40 years ago, I rested comfortably in the arms of a nurturing Alma Mater. For 4 years I was immersed in an environment that beaconed for the nation the politics of the civil rights and voting rights struggles. I participated in the civil rights marches in Washington, sit-ins North Carolina and various places in the South. We met and listened to presentations by Malcolm X, Martin Luther King, the Kennedys, the Ossie Devises and Harry Belafontes of the time. Excitement filled the air–Alma Mater afforded me a wonderful cultural experience.

I did well academically and believed that Alma Mater provided me with the basics to excel at any other university in the world. Two University of Wisconsin professors served as my mentors–pushing and guiding me towards a career in the biomedical sciences. They knew, better than I did, that it was in my best interest to go away for graduate study.

I received many warnings that my new academic world in New England was not a welcoming world–and indeed I found the administration cold and formal–but in retrospect, I believe the administration treated all incoming students with the same indifference. I was delighted to be accepted into an Ivy graduate program; after all, I received tuition remission and $200 per month–but above all being in a graduate program kept me from being drafted for the Vietnam war.

Looking around in my new environment at that time, I saw no Asians, Hispanics or Latinos. I was one of two blacks–and for the first year my best friend was Angelo, the singing Italian janitor with whom I had coffee at 7 every morning.

Suddenly, I was thrown into a new mix of academia and I soon realized that I had been living for 4 years in a fantasy world rather than the real world of scholarship.

I lost my safety net. I was culturally isolated alone and challenged.

How intimidating it was to be surrounded by the brightest fellow graduate students who spent much of their time testifying about themselves. To make matters worse, Paul Weiss had just published his general biology textbook and I was assigned to assist in his course–that meant staying one chapter ahead of some of the most inquisitive undergraduates I had ever met.

I had three options: retreat back to the safety net–Alma Mater, go to Vietnam, and the third was to tough it out.

That year there were eleven incoming graduate students. All eleven students met every morning for 9 months and were introduced to six different academic fields during that period. At least four faculty in each field and sometimes their postdocs were always present–lecturing on cutting-edge activities in their fields, but mostly challenging the graduate students who had to discuss current journal articles. Imagine for 6 weeks sitting with a classical geneticist like Herman Chase, a Drosophila geneticist like Stanly Zimmering, a molecular geneticist like Lederberg, and a population geneticist like Quevedo. Or for an additional 6 weeks with developmental biologists Paul Gross, Richard Goss, Mac V. Edds, and John Coleman. The air was electric, exciting, sometimes confrontational, sometimes amusing—

However, the experience meant being introduced and immersed in the real world of scholarship at its best. So we had similar experiences with biochemistry, cell & molecular biology, evolution/environmental biology, and the new biomathematics.

Underpinning the program were two compulsory courses–a not-for-credit course in ethics that dealt with scientific integrity and responsible conduct of research, and a for-credit course in Foundations where students discussed relevance of scientific inquiry, how to write manuscripts and grants, how to read a paper actively rather than passively, career counseling etc. At the end of a 9-month period the professors essentially said "here is your laboratory and in a couple years we expect an excellent thesis." We were then immersed fully in research.

- The program introduced us to cutting-edge activities in each field.
- It brought us close to the faculty and the faculty close to the students.
- We were able to decide what our areas of interest were, which professor or professors we wanted to work with and which students professors would want to work with.
- We had the power of intelligent choice–we had the privilege of opportunity.
- The faculty also, had the privilege of choice. Intelligent unions and alliances could be formulated.

Here then was the importance of a strong formalized program that served the best interest of student and faculty. The gulf between faculty and student was breached. The faculty were illuminating examples, and students were impressed by their teaching, by their personalities, by their eccentricities, and by their competence.

In time mentors became co-workers and colleagues and nothing could rend such a powerful union.

We must also understand the circumstances that prevailed in the 60s. These were the days of discovery in areas of cell and developmental biology. Scientists were organized into three basic camps. Electron microscopy was the most current imaging tool–and the strict anatomists like Don Fawcett, George Palade and Keith Porter preserved the cell structure and suggested a function. They published in the then 2-year-old *Journal of Cell Biology*. Palade, representing this group, received the Nobel Prize in Medicine.

The second camp was populated by persons like Christian De Duve, Siekevitz, Alberts and others who roamed through the cell with the help of a centrifuge rather than a microscope, isolated organelles, determined their biochemistry and alluded to function. DeDuve and Alberts representing this group received the Nobel Prize in Medicine.

The third camp included scientists like Alex Novikof, Russ Barnett, Arnold Seligman, Paul Nakane, Morris Karnovsky, Pearse and others who used cytochemical and immunochemical tools to show reactions and cell functions yet still maintaining the integrity of the cell. These scientists all had one overarching theme–to correlate cell structure with function.

Some of us fell comfortably in all three camps.

Discoveries amazed us as we attempted to determine fact from artifact. Everything was a surprise. We were explorers amazed by the magnitude of terra incognita–we were Cytonauts investigating the splendor of cells and organelles. We competed to show the most beautiful pictures–and I remember the scientific world was amazed when Jean Andre first showed the best images of the lowly centriole, while others discerned the subunit structure of neurotubules.

Lajos Piko, Ris, Andre and others demonstrated photographs of DNA in typical mitochondria–and as a graduate student we hit the jackpot by best demonstrating the largest extranuclear mitochondrial DNA repository in trypanosomes, and in the same organism we described subplasmalemmal system of microtubules. As a graduate student I published my first citation classic–but it could not have been done without the guidance, mentoring and inclusion of my mentors. Using this platform as a basis of future research we worked with scientists like Jean Andre who first localized mitoribosomes in mitochondria of Tetrahymena and yeast, and we further localized DNA profiles in mitochondria of the corpus luteum and, using techniques of Hans Ris and Barbara Stevens, the circular profiles of DNA. My graduate experience was indeed in a land of scholarship and fantasy, creativity, and romance. I went on to publish 10 papers as a graduate student–again only through collaboration with my mentors who might now be classified as colleagues. Those were the best of times. I had privilege and opportunity–I was included and therefore had the ability to be competitive.

My debt goes out, therefore, to my early mentors in science. These faculty mentors recognized the value and challenges of mentoring, of sponsoring new graduate students–these mentors who showed their interest first by example, second through inclusion in laboratories, and third through exposure/opportunity. The faculty took every opportunity to propel students into mainstream research–they provided the means, the encouragement and guidance. In Elizabeth Leduc’s absence I presented lectures in cell biology–in Richard Ellis’ absence he knew that his electron microscopy course was covered. The mentor provided the opportunity for the student to develop skills as a teacher, as well as a researcher. All six ingredients of good mentoring were therefore displayed: advising, opportunity, support, guidance, confidence, and example. I believe that the mentor should have a vision of seeing his/her students as future leaders–believing in their abilities and helping them to realize their potential. The good advisor reminds the students of their strengths and permits the students to learn from their failures.

It must be recognized that creating future scientists takes relentless guidance, undivided supervision, endless optimism, inexhaustible patience and constant encouragement. We should be careful about shaping young scholars in our own image–which may be dated. Instead, we should encourage new and unexpected images–not what best fits a fashion or market prospects. Above all, mentors should not be appointed–rather they are chosen by the student for reasons of scholarship/intelligence and inspiration.

I recognized one other very important fact, which is that my mentors did not have to look like me to be effective and inspiring. I list among my most valued and contributing mentors Hewson Swift, Morris Karnovsky, Don Fawcett, Elizabeth Leduc–just to name a few.

Talk about opportunity–towards the end of my graduate career, one of my mentors Elizabeth Leduc said, “how would you like to study in France?” Of course, I couldn’t resist the opportunity and the rest is history–I spent two years at the University of Paris as an American Cancer Society postdoctoral fellow. Andre’s lab was a hot bed of science–a virtually rotating door of the best-known scientists at the time. We were exposed to the Faure Fremiets, Jean Brachet, Sjostrand, Bjorn Afzelius, Alberto Monroy, Baccettis, and others. Led by Baccetti, Andre, Fawcet, Afzelius and others in Europe, we organized ourselves into the International Society of

Spermatology. We were the Spermatologists, searching the animal and plant kingdom for the most unique and mesmerizing images of sperm. Again–correlating structure with function and development of sperm cells. Using techniques developed primarily by Hanker, Seligman and us, we were able to study the metamorphosis of several spermatids, but we specialized on the snail–Helix–sperm that was known to have helices filled with intramitochondrial glycogen. Marking the spermatid mitochondria with cytochrome oxidases and glycogen with silver proteinate, Paul Personne and I observed mitochondrial fusion around a glycogen compartment that was positive for phoshorylase activity, formation of a complex paracrystalline and membranous sperm middle piece surrounding a centrally located axoneme. The paracrystalline compartment labeled positively for the cytochromes, the matrix compartment was labeled for Krebs cycle enzymes, and ATPase was present in the axoneme. The following scheme for middle piece functioning is illustrated.

My papers with Personne on mitochondrial differentiation and metabolism remain classics in the field of spermatology. I published 15 papers from this laboratory and all this time in Paris I never visited the Louvre—that was a pity. My papers with Don Fawcett at Harvard helped elucidate the role of the manchette in the metamorphosis of germinal cells. Collaborating with Arnold Seligman, Jacob Hanker, and Lisa Perotti in Milan, we exploited further the diaminobenzidine reaction to vizualize cytochrome c oxidase activity in mitochondria and to establish respiratory quotients for muscle and pancreas. A publication on this subject appeared in *Science* and another was a citation classic. Subsequently, significant findings were made using the diaminobenzidine protocol to develop myoglobin and cytochrome c as molecular tracers for vascular permeability, and markers to track and visualize fusion of sperm and oocyte mitochndria after fertilization in sea urchins.

Through contacts with scientists, access to research labs in France, Naples, Siena, Banyuls, Rostock and even Stockholm was made easy, and collaboration flourished. The postdoctoral allowed opportunity to explore numerous avenues of intellect and to make firm alliances that would be important in future careers. Again, mentoring, collegiality, exposure and opportunity were the critical benefits of being in the right academic environment.

Too often postdoctoral students have scant supervision, ill-defined goals, poor access to peers, have a sense of stagnation and isolation, have poor benefits, and lack institutional connections. They too need mentors in designing good research, developing competitive resumes, rehersals for interviews, seminars, prepare manuscripts, raise grant funds, and learn about the current job market. Postdoctorals need mentors to help them develop into mature and productive colleagues, bring them to a stage where they can demonstrate independent thinking, undertake independent research and feel their own originality developing.

A great department like Fawcet's spawned many of today's experts in reproductive, cell and molecular biology. Harvard was filled with a plethora of talented and gifted scientists. Morris Karnovky, a pathologist from South Africa, Torsten Wiesel, Dave Potter and Ed Furshpan neurobiologists became my heroes–first because of their science and then because they expressed empathy and were largely responsible for recruiting blacks and Hispanics into Harvard medical school. I also had another hero, Harold Amos, who was the only prominent African American professor that I ever met along the educational pipeline.

Arnold Seligman, Alex and Phyllis Novikoff, and Stanley Bennet were also my heroes, not just because of their scientific accomplishments, but because they were willing to share their expertise and were, in addition, real humans. We were able to utilize the protocols of these scientists to study vascular and ovarian permeability in insects and mammals. Studies indicated that the perifollicular basement lamina served as a very coarse filter and in the insect there was a clear pathway for molecules as large as 110A between follicular cells to the oocyte.

The oocyte was a voracious phagocyte engulfing cytochromes, peroxidases and ferritin indiscriminately into yolk. In contrast, in mammals, large molecules like ferritin (110A, 500 kDa) met a barrier at the basement lamina, while peroxidases at 35 kDa percolated through the reticulum that composed the antral spaces and the meshwork of the zona–but were not phagocytized by the mammalian oocyte. Using the phosphotungstate protocols, the antral reticulum and zonal network can be clearly visualized.

The time came for me to take a real job at the University of Chicago. One slow afternoon I went to the greenhouse where I struck up a conversation with an old fellow tending corn. To my surprise he spoke in depth and at length about the genetics of corn and Neurospora. I was perplexed and I left that encounter thinking that the University of Chicago must be an awesome place because even the gardeners knew genetics. I was to later find out that that old Gardner was former university President George Beadle, co-recipient of the Nobel Prize with Edward Tatum for their work with on biological reproduction and the relationship between genes and enzymes in Neurospora. In spite of that humbling experience I was recruited into Elwood Jensen's group, only to be further humbled by working alongside Charlie Huggins, two-time Nobel Prize winner, with Eugene deSombre and Guy Williams Ashman.

My lab lay adjacent to developmental biologists Aaron Moscona and Don Fischman. I taught a cell biology course with Hewson Swift–teacher supreme. Having access to antibodies to the estrogen receptor, we were readily able to identify their localization to the nucleus. Using the diaminobenzidine protocol that was earlier used to localize cytochromes and other heme proteins as labels, we identified an endogenous estrogen-induced peroxidase as a consistent biochemical marker for estrogen stimulation in uterine and vaginal epithelium and in estrogen-dependent breast cancer tissues in rats after dimethylbenzantrhracene treatment or in transplanted breast cells as xenografts in athymic nude mice. I received the Langer Award for this work. The enzyme was also present in the human cervical mucus during the estrogen-dominant phase of the menstrual cycle and proved to be a consistent predictor for ovulation in humans. Based on these studies and more, we further demonstrated that there was "cross talk" between estrogen and growth factors that regulated the proliferation and differentiation phase of the uterus during the estrous cycle. These studies were possible only because of a research environment that allowed exposure to brilliant coworkers doing cutting-edge science.

I have been privileged–along with my coworkers, to contemplate many marvelous aspects of the structure and functional organization of living cells. Mentoring by example and inclusion, in an environment that encourages research productivity and cooperation, are the key ingredients for success of today's graduate students and postdoctorals. Over time, when mentors become genuine colleagues, we have the truest indicator that the mentoring relationship has been successful.

No matter how brilliant a worker you are without the right laboratory infrastructure and environment it will be difficult, almost impossible, to make–as a metaphor–a silk purse out of a sows ear. The real estate people have it right–location, location, location. Too often we have witnessed the demise of several brilliantly trained minority scientists who are struggling under conditions that are fraught with infrastructural challenges and have great difficulty succeeding in a competitive world. It is important to ask why so few of these minority scientists have been accepted to tenure track positions in the Ivy and research-intensive institutions in which they received their training. For those who have arrived in science and now occupy important positions of authority–how and in what way are you influencing your institutions to train underserved and disadvantaged students? These are important questions that you must ponder.

The statistics suggest that fewer than 40% of the PhDs today are in academe and only a third of these are on tenure track. Many have gone on to industry, administration and management positions. Since the 50s emphasis in academe is on research–and then on teaching. The young scientist gets a job primarily based on his/her research competitiveness. Consequently, we as scientists recruit, train, socialize and mentor students in our own image–that is to become researchers. In today's world it is becoming obvious that we need to know where science is going–and we need to train, advise, and mentor our students accordingly. As gatekeepers, our gates may be too narrow–the gates and perspectives must be widened–since science is so fundamental to society. Perhaps we need to realistically look at our philosophy of mentoring. Perhaps we need to move from the highly disciplinary orientation of graduate studies to a broader and more diverse experience for graduate students as part of their research, education, and training in order to prepare them for changing employment opportunities. We must consider new alternative paths, such as careers in management, patent lawyers. etc. Finally, we must be aware and careful, because today's highly specialized fields of science can be dead tomorrow—so it is important that the students be trained to be adaptable, that the new scientists learn as many basic skills as possible such that he/she can explore different fields and branch into new areas that blend science and the humanities, industrial and biomedical research, and teaching and services. Mentoring these days may not only be for the young–but for those junior and senior faculty with none or decreased funding, and those with problems of aging.

As I approach the twilight of my own career I am pleased to see that the mentoring cycle has repeated itself–my own protégés have become serious mentors to their students. So as a challenge to the young people in the audience, acquire the skills of good mentoring: by influencing students you will receive rewards that money can't buy.

Congratulations to the Minority Affairs Committee and thank you for listening.