Profiles and Legacies

Serendipity, Fate, Science and Leadership

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This invited editorial merely reflects the opinions and perceptions of the author. This is dedicated to the memory of Dr. Ed Garber (1919-2004), lifelong mentor extraordinaire. I would like to acknowledge my other mentors, Drs. David Ginsburg, Bob Mayer and Fred Ruddat, for all their sound and timely advice and for their support, and to gratefully thank my longtime collaborators, colleagues and friends especially Drs. Andrea Frilling, George Mutter, Hartmut Neumann, Monica Peacocke, Christoph Plass and Wolfgang Sadée, and Ms. Kathy Schneider. I cannot thank enough my lab members, past and present, for helping me achieve what I have achieved and for their staunch support. Drs. Kristin Waite and Frank Weber, and Mr. Ross Waite, as well as a few anonymous reviewers critically reviewed drafts of this editorial.

“And then serendipity struck and I found the mechanism for that observation” was an indelible saying of my late longtime mentor, Edward D. Garber, Ph.D., who also wisely said, “An experiment without a control is an act of faith.” As scientists, we would immediately agree with his second adage. But what of the first? We are scientists, after all: objective, logical, rational and who pride ourselves in being masters of our own fates. Yet, in looking back over my academic career, it strikes me that where I am today could be a direct result of a series of (what would appear to be) coincidental events…. or …. fate.

I was born and raised in Singapore except for a year in Bristol, UK when I was three years old. My maternal uncles could be considered very prominent academics in Singapore. My number one uncle was Professor of Medicine and our then Prime Minister's personal physician, an impressive diagnostician trained in London and Edinburgh. My second uncle was Professor and Chairman of Geography at the National University of Singapore. My third uncle would eventually run the whole public utilities in the country. Inspired by my uncle, I have always wanted to be a physician, and as things were, I should have trained in medicine in Singapore and stayed there forever.

But it was not to be. When I was 13 years old, my father was sent on a scholarship by his employer, the Institute of Education, to the University of Chicago (U of C) to study the economics and sociology of education. I was an only child, so my mother and I accompanied him. Culture shock: I was transported from an all-girls school in Singapore to a co-educational private school in Hyde Park, the University of Chicago Laboratory Schools. Because of the currency exchange rate at that time, my father's salary did not amount to much. Our neighbor, a graduate student, felt sorry for us and lent us his old TV and radio. As for paying for private education, fortunately, I won a scholarship to Lab School. Once I got used to this school, I really enjoyed myself. I found I could progress at my own rate, taking 12th grade honors classes in 9th and 10th grades. Having taken Mandarin as my second language in Singapore (which I never enjoyed, having been shoved down our throats), I took French instead. While only in 9th grade, I at first felt I was already too old to learn a new language, but thanks to the excellent didactic skills of the teacher, Mr. Randy Fowler (he spoke nothing but French in class!), I actually picked up French and began to love the language and culture of France. I am sure Mr. Fowler would be surprised if he knew that I am now able to act as Rapporteur to the doctoral theses in France and reviewer of various grants written in French from Quebec and France. The Lab School teachers were simply amazing—not only were they truly expert in their own subject(s), but they were decent human beings who really cared about their students. Lab School rigorously prepared me for the academic life to come, but between the caring Lab School teachers and my father, the great mentor, I was given the impression (clearly false) that all teachers, professors and authority figures would be equally mentorly. Lab School even prepared me for the non-academic things that one never thought would be useful: I took a typing class and have never looked back since. Now, I do nothing but type email and directly type out my manuscripts, grants, grant and manuscript reviews, and letters without an intermediate hand-writing phase.

After three blissful years at Lab School, my father completed his Ph.D. (this is a social sciences Ph.D. at the U of C, normally taking up to 10 years) and had to go home. He was “bonded” by the Singapore government and thus forced to return to his previous employer. I adamantly wanted to stay in Chicago. This was indeed uncharacteristic of me: I was a homely Singapore Chinese girl who liked living with parents. The principal of Lab School at that time said that as a minor, I could not stay without parents and go to school. However, after some thought, he suggested that I matriculate in the College of the University of Chicago as a solution to this dilemma.

So, at the age of 16, I entered the University of Chicago. Despite being in the accelerated program at Lab School, I found that the standards of the College at that time were extremely high. My former teachers, Mrs. Matchett and Mrs. Hindman, were more than
willing to give me “private tuition” for my Honors Calculus classes. Such was the commitment and dedication of our Lab School teachers. This paid off as I received straight As for Honors Calculus. The Chair of Mathematics thought I should be a math major and signed me up for Honors Analysis in Rn for my second year. He was disappointed when I declared that my dream in life was to go to medical school and be a physician scientist. Our Advanced Biology teacher at the Lab School, Mr. Murray Hozinsky, was an inspiration. He was very interested in genetics, and thus, infected us with the genetics “bug.” In his off hours, he studied cancer education. These were the seeds which sparked my own quest to put genetics and cancer together, well before it was fashionable to do so.

Having decided that I should be a human cancer geneticist in high school, I looked around for an honors thesis advisor in college. I was immediately attracted to Dr. Janet Rowley’s work with the Philadelphia chromosome and chronic myeloid leukemia. Unfortunately, she had no openings for an undergraduate. I remain, to this day, a big fan of hers. Nonetheless, another undergraduate recommended that I visit Dr. Ed Garber. But he was not a human cancer geneticist but a plant fungal geneticist. After much thought and discussion with my parents, I decided that it really didn’t matter in what field I started undergraduate research but I believed that it was the advisor who would be vital. Thus begun a lifelong relationship with one of the greatest mentors in my life.

The College of the University of Chicago prepares its graduates extremely well for any academic (and non-academic) career and for life in general. Having come from the British Commonwealth academic background, I was surprised that I could not merely take science classes to prepare for the rigors of medical school. I cannot say how glad I am to have been trained in the liberal arts as well, which stands me in good stead: public speaking, grant writing and manuscript writing, and just an enjoyment and appreciation for many things in life, from the fine arts to the sciences.

Apart from the fact that I was terrified that I could not get into any medical school, I enjoyed the College, and thoroughly enjoyed undergraduate genetics research with Dr. Garber. I have been feeling somewhat guilty ever since I begun to mentor undergraduates myself as Dr. Garber was always around (he rarely was away for meetings—what an envious existence!) and personally supervised his undergraduate researchers. From him, I not only learned the fundamentals of good science and how to have fun doing good science, but also decency and the true meaning of mentorship.

I matriculated in the M.D.-Ph.D. program at the University of Chicago as an Early Decision Program student. Medical school, I thought, was everything that I had imagined it would be. Soon it was time to begin my Ph.D. research training, and to select an advisor. After Ed Garber, it seemed impossible to find an advisor who would be as vital. Thus begun a lifelong relationship with one of the greatest mentors in my life.

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recommendations of a professor whom I trusted, I selected a thesis advisor. While he seemed to have fun, it seemed to those of us in his lab (and perhaps his fellow faculty as well) that he had too much fun, and just did not supervise or advise us closely enough (we were graduate student and junior technicians in his lab). This turned out to be a painful, yet useful, lesson in how not to behave as a thesis advisor or principal investigator. It was indeed a relief to return to medical school and the clinical years. But that Ph.D. experience required reaffirmation that I could make a good scientist and still enjoy science so I took a research elective with Dr. Garber and his equally decent mentorly colleague Dr. Fred Ruddat. My faith was reaffirmed, but I would put my scientific dreams aside for four years.

I matched in internal medicine at the Beth Israel Hospital, Boston (The BI). I must say that our extremely (too?) rigorous training as medical students made internship and residency seem relatively easy. Clearly, the program directors seem to somehow know that graduates of certain programs are clinically rigorous already and could look after patients well. We were started in the ICU’s, CCU’s and inpatient wards; I continue to be surprised that Harvard Medical School graduates were started in outpatient electives! What impressed me with the BI is their treating us as family, and collegiality was abound. Housestaff at the BI rotated through the Dana-Farber Cancer Institute. There was no greater dream than to be a Fellow in medical oncology at the Farber. What training from such clinical geniuses as Drs. Bob Mayer, our fellowship director, George Canellos, Art Skarin and Steve Cannistra: I really felt that after one year of clinical training, I could handle any situation in medical oncology. Beyond that, these attendings were decent human beings as well. Bob, I thought, could join the ranks of being a great mentor.

Ever since Lab School, I had always wanted to “do” cancer genetics. In my untrained mind, that meant both clinical practice and bench-based research. I freely spoke about my aspirations. One day, Dr. David Livingston called on me and said that the Farber believed that clinical cancer genetics would one day be rather important, and the senior professors have selected me to formally train at the bench and the bedside. He asked whether I would like to go to Hopkins, Utah or the University of Cambridge. I knew that the former two had strengths at the bench, but not at the bedside. So I immediately chose Cambridge. He asked whether I needed time to think. “No,” I said, “I do not.” This was after all, the dream of a lifetime.

The three years at Cambridge were the three most enjoyable years of my life. Sure, it was difficult to come back to the bench after having been away for over four years, but the perspective brought to science from a firm clinical background, I found, enlightening. Except for rare individuals, those trained clinically as well seem to think differently scientifically. However, after a week, everything seemed to come back to me. The first year was difficult in that one person in the team did not wish to share vital information. But after a week, everything felt differently. The second year was equally challenging, but this time the mentor was a bit less hands-on. The third year was the most enjoyable, with an advisor who truly believed in my work and was always willing to help. The experience was truly enriching.

In retrospect, I believe that I would have benefited from a more structured approach to my training. I had too much freedom and not enough guidance, which led to a lot of wasted time and energy. However, I also learned that I need to be proactive in setting my own goals and priorities, and that I cannot rely solely on others to make decisions for me. This experience taught me to be more independent and self-motivated, skills that I have found invaluable in my subsequent career.

It was during my third year as Assistant Professor that I was selected to be North American Editor and Cancer Genetics Editor of Journal of Medical Genetics. I said yes rightaway and never looked back. Now, if a new investigator asked me whether they should accept an editor’s job, I would advise against it. Yet, I enjoyed my editor duties. The sense of being absolutely fair and objective was refreshing, and it made me realize the importance of clear and concise communication.
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decreasing turnaround time (from six months to 21 days) was very rewarding to me. As a bonus, I learned how to write abstracts that catches an editor's eye and good manuscripts. More importantly, I learned how not to write manuscripts. Then other editorships followed: first as Associate Editor of Cancer Research in 2002 and then as Senior Editor in 2004, and this year as Associate Editor of the Journal of Clinical Endocrinology and Metabolism. I continue to enjoy my editorial activities. I also learned that having a journal backed by a professional society is extremely important and who the editor-in-chief is is equally important.

I never wanted to be chief or director of anything, let alone a chair. And I suspect I would never have had any desire to do so if I worked for a boss like Ed Garber, David Ginsburg or Bob Mayer because they would have created such a wonderful environment to work in. In my second year as PI at the Farber, Fox Chase Cancer Center recruited me for an endowed chair in human genetics and The Ohio State University followed suit, to build and direct its clinical cancer genetics program. After much thought, I decided that yes I could be an effective leader and build the best programs in the world while creating an environment for my employees that would be conducive to outstanding work. After all, if I stayed where I was, I would always be put down. While I did not have the most charitable thoughts about the Farber when I left, in retrospect, all the issues most likely emanated from one person. Most of the other faculty and leaders were, in general, fine and very decent.

So I moved to Columbus, Ohio (where's that?) as a tenured Associate Professor and Director of the Clinical Cancer Genetics Program. I built the most comprehensive Clinical Cancer Genetics Program and created the curriculum for the first academic clinical cancer genetics training fellowship program in this country. In another unusual turn of events, I was invited to be a site visitor for NICHD. David Ginsburg chaired this site visit team. So in this stroke of serendipity, I met another mentor who would quietly advise me from afar over the years. I was promoted to Professor six and a half years after my first faculty appointment, was conferred the Klotz Endowed Chair and made Director of the Division of Human Genetics in the Department of Internal Medicine. I garnered the Doris Duke Distinguished Clinical Scientist Award. I truly thought that I could stay at OSU forever and grow old and retire from there.

My colleagues were collegial and the atmosphere supportive. I enjoyed mentoring many faculty, both junior and senior, and trainees, within OSU and at other institutions. But “it was the best of times, it was the worst of times.” (with apologies to Charles Dickens) Things changed in the last three years, imperceptibly at first, and then just little hints, many signs which I continued to deny for at least two years. Thinking over various recent events, I now ponder one of my mentors' visit last year to OSU. After repeated invitations over the course of five years, he finally took himself to Columbus to deliver a magnificent grand rounds. He stayed long enough to visit with only two people. When he visited me, after some pleasantries, he gave me one piece of advice and one warning. I was taken aback and thought I had learned all that from my good and bad experiences in life. How wrong I was. The mentor had emerged when his mentee required much needed advice. Fate or serendipity?

Yet, I was content enough at OSU; the chairman of medicine was extremely supportive. Then serendipity struck again. Dr. Wafik El-Deiry invited me to give a talk in his hematology/oncology seminar series (naturally, Wafik had insider information that I just love to visit Philadelphia). In visiting with Dr. Barb Weber, she triumphantly produced an email saying she was being solicited for names of candidates for a job that sounded just built for me. Naturally, she had already forwarded my name to the chair of the search committee. After seeing the email, I agreed it did sound like me but when I enquired where this job was, my heart sank because my perception, not based on any facts, of that city was unfavorable.

While I have been recruited to quite a few jobs (several a year) over the last six and a half years, I have not gone to visit except Ann Arbor in 2002. Nonetheless, keeping an open mind, perhaps with the subconscious sensation of the three-year long happenings at OSU and perhaps with my mentor's advice and warning in the subconscious, I decided to go on a fact-finding visit. On a wintry winter day, I was quietly whisked to the Cleveland Clinic to explore the possibility that I would lead its genomics efforts. I was extremely impressed by the seriousness of the Clinic's intent and the potential resources to build a strong program. After that visit, I noted that the job might be too research-only and enquired whether some recrafting of the job description could occur. The leadership was very flexible and I was invited to craft my platform, which would be a very translational bench-to-bedside one, including all aspects of clinical genetics next to bench-based translational genomics researchers. But I told them that they could not change their city (!). Perhaps they did as I did move to lead Cleveland Clinic’s Genomic Medicine Institute, and to be Vice Chairman of the Department of Genetics at Case Western Reserve University School of Medicine, after all.

Every major decision is always fraught with a bit of self-doubt. However, the events that followed my notification of my departure left me without a shadow of a doubt that I did absolutely the right thing at the right time. Let’s just say juxtaposed next to Cleveland Clinic’s formal press release of my appointment was apparently (so I was told by some of my decent colleagues) an internal OSU announcement of “She left to pursue other interests,” which caused one of my colleagues in my institute to quip, “Do they think you left to climb mountains? Maybe they should have also added a picture of you leading your team up Mount Everest.” And perhaps this is an apt analogy. Indeed, Everest awaits!

Dr. Garber always did say, “Serendipity strikes those who work hard.”