

Legends and Legacies Book Chapters

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Varsha V. Gandhi, Ph.D.



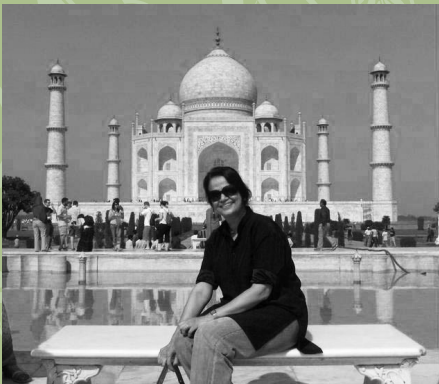
**Professor of Experimental Therapeutics
Ashbel Smith Professor**



While growing up in India, Varsha was photographed holding two wooden sticks (Dandiya) in her left hand as she prepared to lead the group dance Dandiya Ras.



Varsha frequently visits New York City to spend time with daughter Meghana, who always has a new restaurant for them to try.



One of Varsha's favorite sites is the beautiful Taj Mahal, where she often takes M. D. Anderson colleagues when they attend conferences in India.

Had I been asked long ago whether I someday planned to become a faculty member at one of the world's premier cancer centers and, in addition, whether I planned to write a vignette of my life experiences, my answer would have been a screaming no! During my high school and early college years, I knew a little bit about research and cancer but nothing about M. D. Anderson Cancer Center. Today, I find myself in a profession that I savor every day, and this is the direct result of a combination of circumstances, opportunities and developing new interests.

Just before my birth, my parents moved from the Indian state of *Gujarat* to Delhi, the capital of India. Born at home with the help of a midwife, I was the second child and daughter of my parents. A few years later, my brother was born, and my parents were very happy that they now had a son who would carry on the work of their *Ayurvedic* medicine store as well as the family name. In the Indian culture, boys are considered more important than girls are. I am very proud of my parents for rejecting the age-old tradition of keeping girls uneducated and unchallenged and instead providing their two daughters with access to a great education.

Before I could start school, my parents moved from Delhi to Kanpur, a city in India's northeastern state of *Uttar Pradesh* (UP), the state that includes the world-famous Taj Mahal. So that I would not forget my mother tongue, my parents enrolled me in a school in which courses were taught in *Gujarati*. As there were no age requirements for admission into this small school, I started first grade at age four. My parents soon realized, however, that in order to assimilate with the people of the region, I needed to be fluent in the *Hindi* language, so they transferred me to an all-girls school where everyone spoke and learned in *Hindi*. I tried to make new friends, but the language barrier prevented many girls from asking me to join their already-established groups. Resolute, I forced myself to rapidly learn the language. In this way, my early school years taught me to overcome obstacles with determination and to assimilate and enjoy a new culture. Many years later, I found these lessons useful when settling in America.

After high school, I wanted to go straight to medical school, but I was too young to enroll. After earning a bachelor of science degree in two years, I again considered this. Disappointingly, though, I discovered that in addition to the money needed for tuition, books and supplies, my parents had to first donate a huge sum of money to the medical college before I could be accepted. Student loan programs did not exist in India, and I was aware of my parents' financial situation, so I dropped the idea of becoming a physician. Instead, I enrolled in a two-year program leading to a master of science degree at Christ Church College, one of the top-ranked colleges affiliated with Kanpur University. Inspired by the teachers in the

undergraduate classes, I chose a concentration in botany. At one point, I considered teaching that subject for the rest of my life after completing my graduate degree.

The results of my master of science degree examinations were fantastic. Not only had I earned first division (top-tier) honors in my degree program, but also I was ranked first among all botany master's students at Kanpur University. My friends and family were proud of my accomplishments, and I was relieved, as I had disappointed both myself and others by not receiving first division honors previously, including in my undergraduate work. Celebrations of my achievements were short-lived, though, as I applied for but did not receive a teaching job in the botany department of a local college. Many of my classmates had also applied for this position, but as it turned out, the successful applicant knew a city leader and had him push her application. This was my rude awakening to the fact that having outstanding credentials, though necessary, is not always sufficient to land a job.

Since I was without work, I decided to continue my graduate studies. Delhi University, one of the best universities in India, accepted me into its botany doctoral program with a scholarship. I was assigned a supervisor as well as a Ph.D. project on which to work. Life in Delhi brought excitement in the form of new experiences, both educational and social. My recently constructed hostel (dormitory) housed an amalgam of individuals from all over the world; now, English — not *Hindi* — was the main language of communication on campus. The botany department took up an entire building, not just a single floor, and my research project involved the challenging and interesting work of both histo- and biochemistry. Though great in these respects, Delhi University had no air-conditioned buildings, and there was no running water in my third-floor lab. On scorching summer afternoons, temperatures in the upstairs laboratories were sometimes higher than temperatures outside, reaching up to 46°C (115°F). Moreover, some of my histochemistry procedures required washing glass slides in running water five to six times; each time, I had to walk downstairs to the ground floor and then climb all the way back up. Such adverse conditions implanted “work-hard” genes in me; such traits are a must for success in any career and particularly for research, which demands a high level of energy, as it is constantly changing.

While still finishing my thesis, I received a job offer to be a lecturer (assistant professor) at *Daulat Ram College*, an all-girls college. Even though it was an *ad hoc* position, I took the job because I knew that once my thesis and viva examination were finished, I would be considered a prime candidate for a full-time position. (A viva is a final oral examination conducted by a faculty member from outside the candidate's university.) Although I enjoyed things

like being around students (to whom I became a role model and mentor), teaching my favorite subject, and wearing beautiful *saris* and matching jewelry, I knew that someday I would tire of all this, since there was no creativity in what I was doing. I soon decided to abandon the monotony in favor of something that would never get old: research.

Toward the end of my doctoral studies, my uncle, who lived in Delhi, introduced me to his friend's son, who was visiting from America after completing his studies there and who subsequently became my husband. Ours was an arranged marriage, although not in the way often envisioned by Westerners. A couple of generations ago, it was true that parents arranged their children's marriages without the children's knowledge or consent. However, times have changed; in our case, we met several times, met each other's families, and independently decided to get married. The marriage brought me to America.

To a woman in her mid-20s arriving from a developing nation, the United States seemed the embodiment of luxury, opportunities and progress. I thought that there would be no barriers or boundaries to achieving success, but as I started to apply for jobs, I quickly realized that I had been idealistic. When I moved to Houston, I still did not have my Ph.D., as I needed to take a viva examination. Therefore, I was mostly applying for research intern or research assistant positions. Human resources staff at various universities told me that I was overqualified, did not have enough relevant experience, and/or lacked the necessary communication skills. Changing my tack, I decided to reach out directly to faculty members. While I felt certain that they would notice the aforementioned deficiencies in my credentials, they would also see a researcher who was passionate about science, driven and determined to succeed, and prepared to start working immediately. This strategy worked, as I made several contacts with plant science faculty members and received a paid research internship that involved plant tissue cultures for biomass production at the University of Houston. While working, I audited biochemistry, molecular biology and other courses to gain a better understanding of the developments in these subjects in the United States. I realized that there were limited options for plant scientists in Houston, so I began to search for a postdoctoral position in molecular biology, once again by contacting faculty. When the opportunity arose, I became a postdoctoral fellow in molecular biology at Rice University, where I used *Drosophila* as an experimental model system. During this period, I achieved two milestones: first, I took and passed the viva and final examination for my Ph.D., which took place at the University of South Carolina. Second, during my time at Rice, I used the open spaces of the campus to learn how to drive.

Although the work and training at the University of Houston and Rice were good, my science did not have any direct applicability to human life,

and I was not getting any quality mentorship. Moreover, being around the Texas Medical Center rekindled my desire to be in the medical field. I knew, however, that it would not be easy for a trained plant biochemist with some experience in *Drosophila* molecular biology to land a postdoctoral position in cancer research. Because my husband and I had a steady income from his job, he encouraged me to take a risk and look for work that I liked, even if it meant being unsalaried in the beginning. I landed a postdoctoral position as a volunteer in the laboratory of the late Dr. Grady Saunders, head of the Department of Biochemistry at M. D. Anderson Cancer Center. I worked on Wilms' tumor (a pediatric kidney tumor also known as nephroblastoma), and a few months later, Grady mentioned that he had included my name in a grant application. If it received funding, I would become a paid postdoctoral fellow in his lab. I felt confident that he would get the grant.

While waiting for Grady's grant to come through and before starting a family, my husband and I decided to visit Europe. We brought home more than 12 books from the public library and prepared for our journey. For five weeks, we traveled across Europe by Eurail, staying in unusual but inexpensive places and visiting many of the recommended sights. I knew that I loved new customs and cultures from when I was transitioning between Kanpur and Delhi and establishing myself in America, but until I visited Europe, I did not realize how much I enjoyed traveling and hopping from one country to another, admiring in turn each area's art, architecture and ambiance.

Upon returning to the United States, I discovered that Grady's grant had not been funded — yet another circumstance that affected the unfolding of my career. When Grady's wife, Dr. Priscilla Saunders, told him that her officemate, Dr. William (Bill) Plunkett, was seeking a postdoctoral fellow to work on cancer therapeutics, Grady mentioned that if I were interested in chemotherapy research, I should talk to Bill. The chance to work in the medical field excited me, and, without thinking or making an appointment, I walked into Bill's office, the fingers of my left hand crossed while those of my right held my résumé. I have never met a faculty member more enthusiastic about his or her research than Bill. In addition, as a third-year associate professor at that time, Bill was senior enough to mentor a new postdoctoral fellow and junior enough to have the time to do so. The field of research was patient oriented — fulfilling a passion I had always had — and I was thrilled to become a postdoctoral fellow in his group.

After a lag period spent learning about this new area of research, I entered a long phase of productivity in the field of experimental therapeutics. We worked on nucleoside analogues such as cytarabine, fludarabine, gemcitabine and cladribine; it sounds like "bine"-counting, but, in reality, I was counting my blessings. Our overall goal was to understand the metabolic and mechanistic aspects of each analogue in order to use the analogues

optimally and effectively in the clinic as single agents or in combination with other chemotherapeutic agents. For example, based on the metabolic properties of cytarabine, I hypothesized that fludarabine would modulate the accumulation of cytarabine triphosphate. The fludarabine-cytarabine combination was tested in cell lines and then in primary leukemia cells; finally, we worked with our colleagues in the Leukemia department to design a protocol to move the combination regimen into the clinic. This clinical pharmacokinetics and pharmacodynamics work was published in the *Journal of Clinical Oncology*, and I celebrated the paper as my triumph, not because it was published in a journal with a high impact factor but rather because it was published in a journal that would have a great impact on clinical researchers and on patients. The combination was used as front-line therapy, further improved at M. D. Anderson, and tested in many cancer centers around the world. For the first time in my life, my research directly affected patients, which I found to be an extremely rewarding experience. The proverbial term for such investigations is translational research, and since then, this type of research has been the nucleus of my scientific endeavors.

In the midst of writing grants, designing protocols, writing manuscripts and traveling to present my work, a very precious thing happened in my life: I became the mother of a daughter, Meghana. It was difficult to balance family *and* work, although I loved both. At home, my husband helped me raise our daughter and do the chores. I wanted to spend as much time as possible with her before she grew up, so I sometimes took her with me on my trips, both domestic and international. While I worked during these trips, she either spent time with a babysitter, sat in the last rows of auditoriums to listen to my seminars, or — when she became old enough — visited places on her own. My colleagues, internal and external collaborators, and professional friends know her. I have many memorable pictures of her: with the late Nobel Laureate Dr. Trudy Elion (whose drug we were testing); with Dr. Emil J Freireich, dancing at an ASCO reception; with Dr. Michael Keating, rowing on a lake in Hamburg; with Dr. Steve Rosen — with whom I have been collaborating for a decade — on Hawaii's Big Island; with Dr. Bill Beck, who once arranged a stretch limo for us (mostly for her) to go to O'Hare Airport after my seminar at the University of Illinois in Chicago; and with everyone in Dr. Plunkett's and my labs. Today, she is a young woman, and we are the best of friends.

As my career progressed, I received valuable help from leading faculty in obtaining tenure and in acquiring an independent laboratory space. I held an assistant professor appointment for six years, an NTRA (non-tenured research appointment) for three years, followed by a tenure-track appointment for the next three years. At the end of the sixth year, Dr.

Robert Bast, who was then head of the Division of Medicine and ad interim department chairman, recommended that I be promoted to tenure-track associate professor. As required, he also appointed three faculty members to evaluate my credentials, and they unanimously recommended that I be promoted to associate professor with tenure. A tenured position at any university puts an individual within an elite group of faculty members, but at M. D. Anderson, tenure also meant that the institution would pay the salary of this faculty member.

Hence, a state educational and general (E&G) slot was mandatory for a tenured position; however, Dr. Bast informed me that he did not have a slot for me. This meant that I would have to pay 100 percent of my salary from grants, as I had been doing for the past six years as an assistant professor. I spent the next eight months educating myself about the mystery of E&G slots, writing numerous memos to Dr. Andy von Eschenbach (Executive Vice President and Chief Academic Officer), Dr. Margaret Kripke (Vice President for Academic Programs) and Dr. Fred Becker (Vice President for Research), and meeting with Drs. von Eschenbach and Bast. I learned that among 128 tenure-track assistant professors, I was one of only three who were paying their entire salaries from grant funds. Frustrated to see such disparities, I sent my curriculum vitae to senior faculty members such as Drs. Walter Hittelman, Waun Ki Hong, Marvin Meistrich, Ray Meyn, Raphael Pollock and Grady Saunders to get their opinions. The more I received confirmation of the strength of my case, the more I discussed the promotion with Dr. Bast. On January 30, 1998, he called to say that they had found a slot, and in September of that year, I received the coveted tenured position. The process had been a nightmare, but the outcome was a dream!

Until I joined a newly formed space committee, I did not know about the inequalities that existed in the distribution of laboratory space, a vital resource for scientists. When committee chairman Dr. Bill Klein learned that I did not have any assigned independent laboratory space, he encouraged me to obtain some, and together we formulated a plan for doing so. I gathered and presented information to Dr. Reuben Lotan, the deputy head of research for the Division of Cancer Medicine, who in turn discussed the idea with Dr. Kripke. I received laboratory space with the valuable help of these individuals.

Overall, it was not easy for me to procure resources or to progress in the cancer center's hierarchy for two main reasons. First, I continued to work in the same organization where I had been trained, and, second, my department lacked a permanent chairperson who could have advocated my case. Perhaps it would have been easier if I had moved to a new institution, at which point I would have received, upfront, a tenured position and laboratory space. My experience suggests that junior faculty interested in

being promoted and in obtaining additional resources ought to look beyond their current organizations for opportunities.

All of these experiences have formed a foundation upon which I continue to build my career. Perhaps the narratives of my progress in life and work can be of some use to scientists who are at various stages of their careers — whether discovering the competitive field of cancer research, establishing themselves in their careers, or serving as advisors and role models to up-and-coming scientists.

I came from a city that had one public library (which was open only two or three days a week), electrical power shortages during the summer, and limited hours of running water each day. As a result, I never took for granted the incredible resources available in the United States. For me, it was — literally and figuratively — a rags-to-riches transition. I have been to many countries, and what the United States has to offer to a hungry and curious mind surpasses what is available in any other place. My education and training have benefited enormously from this country's wealth, and I see no reason why scientists who come to this country from other nations cannot make the most of state-of-the-art facilities and training opportunities.

I would also encourage foreign scientists, especially women, to network with colleagues who are knowledgeable about working in America. Not only are these colleagues cognizant of the operating procedures and the rules of the game at every step in an academic career — grant and manuscript writing, promotions, serving on committees, and vying for awards and honors, to name a few — but also they can act as conduits for these steps. I would not be where I am today without the superb support of Drs. Waun Ki Hong, Hagop Kantarjian, Michael Keating, Bill Klein, Margaret Kripke, Reuben Lotan, Bill Plunkett, Garth Powis, Steve Rosen and Liz Travis.

To junior faculty, the cancer research road may appear winding, difficult and scary. Successful scientists have all experienced the frustrations and sorrows of rejected manuscripts, unfunded grants and incorrect hypotheses. Do not let these discourage you, as cancer research is creative, enjoyable and rewarding. At this early professional phase, find the cancer field that fascinates you, and pursue projects that become your passion. It does not matter what you select; what matters is how passionate you are about your chosen field. Become industrious and productive in your research area, and strive to publish papers and obtain grant funding. Publications and grants will substantially enhance your curriculum vita, and in terms of career advancement, nothing can substitute for an outstanding CV. It acts as an advocate, a campaigner and a recommendation letter. Finally, select your mentors wisely, and remain connected with them — and I will underscore that I used the plural, not singular, form of the word. Yes, you will need more than one mentor to assist, guide, motivate and push you.

Collaborating with other scientists is critical in cancer research and easily feasible for mid-career scientists. Cancer is complex, and cancer research calls for multidisciplinary efforts. As we grow more focused on our research areas, we become specialists in particular fields; at the same time, our overall base of scientific knowledge narrows. With the amount of literature germane to each area of cancer research, it is almost impossible to keep up with your own field, let alone learn about others. Institutions ought to recognize the importance of collaborative, collegial and collective efforts, allowing mid-career scientists with varying specialties to combine their expertise and resources.

To senior faculty members — especially women, who have the inherent capability to care and give — let your research goals encompass teaching and mentoring. I serve as the director of education and faculty development for the Department of Experimental Therapeutics, and I feel that it is of paramount importance to inspire and educate students and trainees who will carry on our mission of making cancer history: combating and hopefully curing cancer. This is a monumental task, and therefore, we must ensure that the next generation of interested, inquisitive and intelligent researchers is ready to roll.

If you have read this chapter to its finale, you now know how my circumstances and interests have shaped my academic career. I have been incredibly lucky to have such a great professional life. It is doing what I love and loving what I do; it involves encountering challenges that make each project unique and surprises that make each day interesting; it has been full of motivating mentors and great lab team members; and, perhaps most important, it consists of translational research, which impacts the lives of patients.

Every morning I enter M. D. Anderson through the Clark Clinic lobby. I see patients sitting and waiting with their loved ones. Their eyes are filled with the hope that they have arrived at the best possible place for their cancers to be conquered. But soon enough many realize that cancer is cruel and that even the best cancer center may not be good enough to cure their disease. This is what drives me to work harder and more efficiently every day — both alongside and with my lab team members and my wonderful colleagues — to find new remedies, new regimens and new drug combinations for their diseases. Even the best cancer center has to become better to conquer cancer.

