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Legends and Legacies Book Chapters

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10-1-2008

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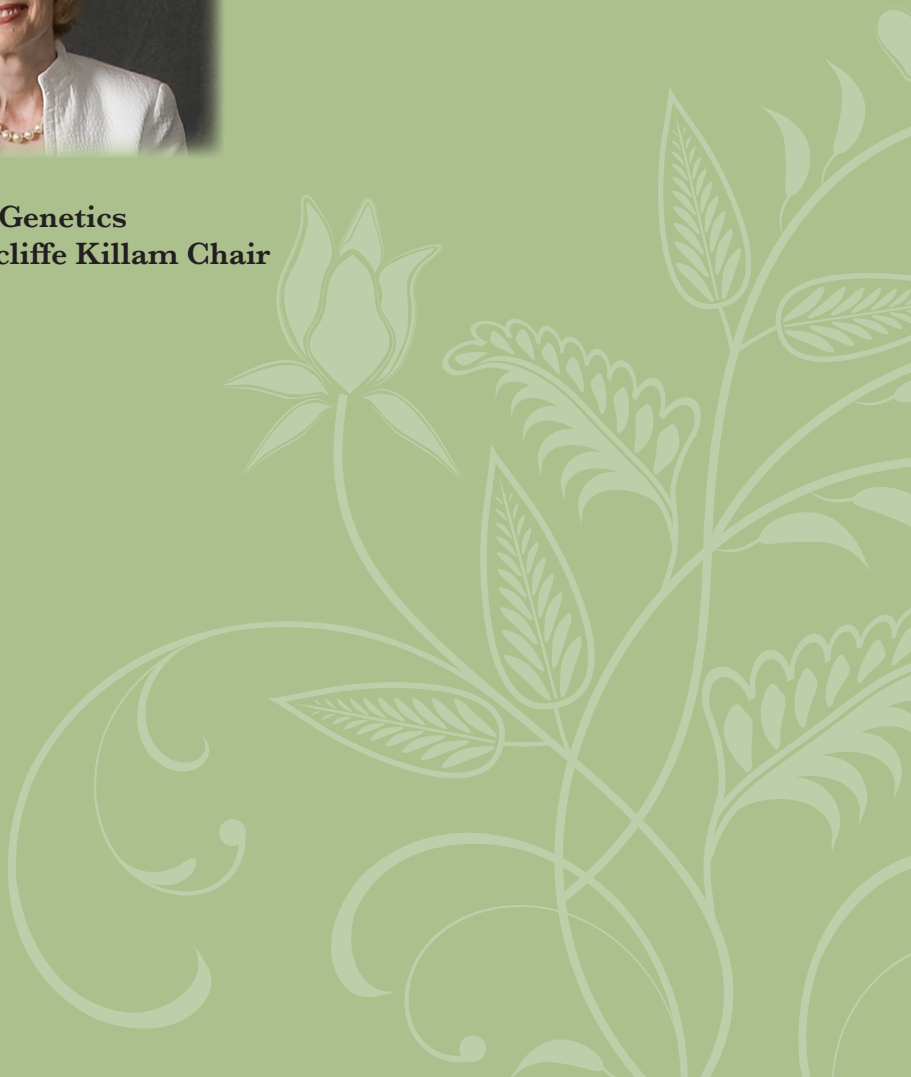
Strong, Louise C., "Louise Connally Strong, MD" (2008). *Legends and Legacies Book Chapters*. 25.  
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*Louise Connally Strong, M.D.*



**Professor of Genetics  
Sue and Radcliffe Killam Chair**





*Louise has fond memories of mentor  
M. Knudson, M.D., Ph.D.,  
who accepted her for a postdoctoral  
fellowship at M. D. Anderson in the  
early 1970s.*



*Collaborating with colleagues in their  
laboratories helped Louise conduct  
landmark studies to detect faulty genes  
that predispose members of certain  
families to cancer.*

(Photo by Beryl Striewski)



*Posing for a family photo was fun  
for Louise and husband Beeman  
Ewell Strong III, their son Beeman  
and daughter Larkin.*



grew up in Houston in the 1950s, in a traditional home in which my mother was a primary homemaker (chief cook and bottle washer, chauffeur, seamstress and volunteer) and my father was not only the breadwinner but also my first and primary mentor. My older brother and I were always encouraged to excel in whatever we did and to believe that with hard work we could accomplish anything we set out to do. Our parents were big advocates of education, and I knew that I would have their support to pursue whatever path I chose. (They may have had second thoughts when I decided to apply to medical school!) We lived in the area now known as the Memorial Villages — before there were villages with city water and sewerage — and had horses, ducks, chickens, dogs and other animals. For years, my horse was my best friend, and I spent many hours riding throughout the undeveloped areas that now are filled with homes and many cars. My family has deep roots in Texas going back at least four to five generations. My father's family was primarily made up of lawyers, including my father, who served as a Federal District Judge from 1949 until his death in 1975; his father had represented Texas in the U.S. Congress, initially in the House and then in the Senate, from 1928 until 1956. My mother's family was primarily in medicine. Although I never knew my maternal grandfather, I heard many stories about his being the first pediatrician in Texas (he was allergic to the rubber gloves used in surgery so he “failed” in the family tradition of surgery and instead entered the emerging field of pediatrics).

I enjoyed high school, had excellent teachers, studied hard, and was a National Merit Scholar and a valedictorian of my graduating class at Lamar High School. I liked and was good at math, something of a social problem in the days when it was always announced before handing out scores that boys were expected to do well in math, and girls, in verbal skills. I always hid my reverse scores. And although I considered several colleges, I chose to follow in my father's and brother's footsteps at The University of Texas. The timing was great — as an avid football fan, I was there when the UT Longhorns played in their first national championship in 1963.

Though I majored in mathematics, I found myself increasingly interested in biology and genetics, both outstanding programs at UT. I knew I didn't want to be another lawyer in the family! I considered a Ph.D. in genetics, but none of the programs focused on human genetics, so I opted for medical school and enrolled in The University of Texas Medical Branch at Galveston (UTMB) in 1966 with the long-term goal of conducting research in human genetics. My first experience at M. D. Anderson Cancer Center came during the summer of 1967, when I received the Benjamin Stinnett Fellowship in Research Clinical Pathology and learned cytogenetics (human and other) with scientific giants T.C. Hsu, Ph.D., and Jose M. Trujillo, M.D.,

who became lifelong mentors, colleagues and friends.

Medical school for a woman in the 1960s in Galveston, an island off the upper Texas Gulf Coast, was pretty isolating. Women comprised about 5 percent of my class. Socializing and eating at the fraternity houses were not viable options. A friend and I made a pact to keep our sanity — we would play tennis every day no matter what! It might just be 30 minutes, but we would do it. And we did. Being on the island and working hard in a restricted setting, I somehow missed much of the turmoil of the 1960s. There were no marches and no protest movements in the medical school halls. However, I did manage to commute to Houston often enough to meet my future husband, Beeman Ewell Strong III, a UT undergraduate who had received his M.B.A. from Stanford University. He was working in Houston in the petrochemical business when he wasn't writing music or playing the guitar. (I remember how he embarrassed me by paging me throughout the John Sealy Hospital for a date.) We married in January 1970 before my graduation from UTMB that June and spent the first six months living on nearby Jamaica Beach. It became a popular spot for Houston friends to spend the weekend. I still recall leaving home early Sunday mornings when I had to be at the medical school and carefully stepping over bodies sleeping on our floor, some of whom I never saw again. Beeman proudly supported me and was one of only two male spouses recognized at graduation. The next day, my father-in-law told me how proud he was of me for finishing medical school and then advised me that, now that it was done, I could get busy with the important business of taking care of my family.

Since my first experience at M. D. Anderson, I had been thinking about cancer. While taking an elective in pediatric oncology there in 1968, I became interested in the etiology of childhood cancer — how could a child have cancer? Ultimately, this question led to my notion of joining two separate interests, genetics and childhood cancer, into a research program. As few thought genetics had anything to do with cancer in the 1960s, it could have been a tough sell. In 1969, I sought advice from the Office of Education at M. D. Anderson and met the director, Alfred G. Knudson, Jr., M.D., Ph.D., who also was dean of The University of Texas Graduate School of Biomedical Sciences (GSBS). I had no idea what he worked on, but I asked him about the possibility of developing a research program in genetics and childhood cancer. He smiled and said he was also interested in that topic and that perhaps I could do a postdoctoral fellowship with him. I have often wondered where I would have gone had he not been in his office that day!

Upon receiving my medical degree, I spent two years in a fellowship with Al Knudson. He had completed his now-landmark two-hit mutation model for retinoblastoma, based on age at tumor onset in heredity and non-heredity

retinoblastoma. My project was to determine whether the two-hit model fit other childhood tumors. We worked first on Wilms' tumor of the kidney. It was very exciting when, in that pre-computer analysis era, together we plotted *by hand* the semi-log graphs of the ages at diagnosis for each Wilms' tumor patient group. We found a pattern similar to that of retinoblastoma. Al and I submitted the manuscript for publication in 1971, and Al departed for Europe for a month. Since that was before electronic communications and faxes, he told me that if the reviews came in during his absence, I should make revisions. Soon after he left, three reviews were returned. There was a short positive review, a short very negative review, and one with detailed suggestions that the research needed more work. Al's assistant indicated she had never seen such a negative review of his work before. I agonized about what to do and rewrote almost every sentence using "suggestive of" rather than our originally confident "demonstrated that" statements. Somewhat to my amazement the manuscript was accepted and published! My first!!

I continued working with Al on neuroblastoma and other childhood cancers until, just as my fellowship ended, there was a brand new focus in my life. I was pregnant! My son, Beeman Connally Strong, was born in May 1973, and I took a rather extended maternity leave. Motherhood was very compelling, and my career goals became cloudy. However, one day Al called to tell me of some exciting new reports. With the advent of chromosome banding and identification of individual chromosomes, Janet D. Rowley, M.D., had reported that the G group chromosome involved in Down's Syndrome (#21) was not the same as the G group chromosome involved in chronic myelogenous leukemia (#22, the Philadelphia chromosome), and, further, that the Philadelphia chromosome was not just a deletion but a translocation. I decided that I wanted to be part of the future of cancer genetics and came back to work part time for the next two years, which carried me through my second pregnancy and the birth of our daughter, Larkin Louise Strong, in November 1974.

Working full time with two small children was harder than I ever anticipated. I was excited to be back in research and foolishly accepted every speaking or writing opportunity that came my way, only to find that I could not handle all the commitments. I experienced a period of recurrent pneumonias over the period of 1976-1978, but eventually I was able to reorder my priorities, have more help at home, and accept that I could not "do it all." (With my X-rays in hand, I finally was able to demonstrate that I was at high risk and should get the pneumococcal vaccine and flu shot generally reserved at that time for the elderly or immune suppressed.)

On returning to work in 1975, I was invited to a National Cancer Institute (NCI) meeting on Genetics of Human Cancer. Having been relatively inactive for several years, I was thrilled to participate and meet



others in the field. After giving my talk under very trying circumstances (my father had just died), I was invited to speak at the National Cancer Advisory Board in 1976. That opportunity was fortuitous because at the meeting a new NCI committee was proposed: the Clearinghouse for Environmental Carcinogens. I was asked to serve on the Data Evaluation/ Human Risk Assessment Subcommittee and did so from 1976-1980. That was the beginning of a long history of almost continuous NCI service.

Also, in 1975, I began to develop an independent research program, initiating a series of studies that continue to this day. In addition to Al Knudson, others who have been significant mentors include David E. Anderson, Ph.D., who shared his office space and resources with me until his retirement in the 1990s, and NCI investigators Robert W. Miller, M.D., Joseph F. Fraumeni, Jr., M.D., and Frederick P. Li, M.D. The NCI epidemiology program on childhood cancer etiology from the 1960s on provided many insights and ideas that have inspired me. I had some funding from a National Institutes of Health (NIH) Medical Genetics Center grant that I used to continue research on retinoblastoma and Wilms' tumor and, following on the work of Li and Fraumeni (1969), initiated a study of cancer in the families of children with soft tissue sarcoma. Li and Fraumeni had demonstrated that there were rare families with unusual patterns of early-onset and multiple primary cancers, distinctly unlike most recognized hereditary cancer syndromes at the time (now referred to as Li-Fraumeni syndrome or LFS). Although the etiology of this syndrome was unknown, I felt that we could further characterize it by studying families of M. D. Anderson patients, hypothesizing, of course, that it was genetic. In this pre-computer and pre-HIPAA (Health Insurance Portability and Accountability Act) age of 1975, we set out to locate the families of childhood sarcoma patients treated at M. D. Anderson from 1944 to 1975. Amazingly, we were able not only to locate the families but also to recruit them to our studies, to document reported cancers, and to develop extended pedigrees. These families have been spectacularly supportive of the research.

In the 1980s, my children were growing up, and life was busy with all the family activities. There were frequent conflicts — we didn't have synchronized electronic personal and professional calendars, so there were occasional missed events with family or late cancellations to meetings. Why were there always NCI advisory board meetings in Bethesda on the Monday after Mother's Day? I also endured the comments by my children that I was not a "normal" mom or an outburst by my daughter that she "would not want my life." But, overall, it was a positive time both personally and professionally.

We were successfully funded to continue our childhood cancer studies. I was awarded tenure and promoted to associate professor and, later, to

professor. In addition, there were unexpected awards, some possibly a rare benefit of being female in a male-dominated faculty. In 1981, I received a letter from Charles A. LeMaistre, M.D., then president of M. D. Anderson, that I had been appointed to the Sue and Radcliffe Killam Professorship; I was the first woman faculty to receive an endowed position. It was a big surprise and honor, since I didn't know such positions existed. A few years later, the professorship was upgraded to the Sue and Radcliffe Killam Chair, which I continue to hold. The Killams not only are generous donors, but they also have been special family friends. Then, in 1984, I received a message that the White House had called. *The White House?* When I called back, I was told by a very impatient voice that President Reagan wanted to appoint me to a six-year term on the National Cancer Advisory Board. I had a few days to consider the offer. Everyone I asked said "take it," so as a young associate professor I did. The other woman scientist on the NCAB was Gertrude (Trudy) Elion, who in 1988 won the Nobel Prize in Physiology or Medicine. Serving on the NCAB was the beginning of six years that introduced me to some wonderful people and to the finances and policies of the NCI. Later in 1984, I received the Texas Federation of Business and Professional Women's Award for Outstanding Achievement in the Field of Oncology. As a multi-generation Texan, I was intrigued to learn that BPW members had a huge role in getting M. D. Anderson established by the Texas Legislature in 1941. Over the years, the BPW has actively supported cancer research conceived and conducted by our women faculty.

My research continued to focus on childhood cancer genetics, primarily retinoblastoma, Wilms' tumor and Li-Fraumeni syndrome, with longitudinal follow-up of families and application of new evolving technology brought by many creative collaborators to unravel the genetics. In addition, as childhood cancer treatment changed and became more successful, I participated in collaborative studies of long-term survivors of childhood cancer, a growing body of individuals who have significant late effects from the treatment. We have been able to maintain continuous NIH funding for these studies in various forms, most notably a P01 (program project grant) from 1984 to the present. Long-time M. D. Anderson collaborators have included the late Grady F. Saunders, Ph.D., for mapping of the Wilms' tumor and aniridia genes; Michael J. Siciliano, Ph.D., on studies of mutation and genome instability; Vicki D. Huff, Ph.D., on studying familial Wilms' tumor and mouse models; Guillermina (Gigi) Lozano, Ph.D., on p53 in human and mouse models; Christopher I. Amos, Ph.D., on statistical genetic analysis, and Michael A. Tainsky, Ph.D. (now at the Barbara Ann Karmanos Cancer Institute), for immortalization and tumorigenesis. Outside collaborators, especially in statistical analysis, include the late Wick Williams, Ph.D., and Ed Lustbader, Ph.D., both from Fox Chase Cancer Center. I also am grateful



for the special relationship with the Retina Research Foundation, a Houston organization founded by Alice R. McPherson, M.D., from whom I have had funding to study retinoblastoma since 1982.

My research highlight to date was the finding of germline mutations in the tumor suppressor gene TP53 underlying LFS. During the 1980s, it had become clear from clinical and statistical data that these rare families seemed to have an inherited cancer susceptibility likely due to a single gene. The question was which gene. Several observations combined to make p53 a strong candidate. Michael Tainsky and I collaborated with Li and Fraumeni and with the laboratory of Stephen H. Friend, M.D., Ph.D., to identify mutations in p53 in the first five of five families studied. This was an important and highly visible scientific finding, published in the journal *Science* in 1990. But that is not why it is my “highlight.” It was an overwhelming, almost scary feeling to know “the gene” for which a minor change could produce such a devastating effect and to realize that I knew such vital information about our research participants that they did not know about themselves. Almost immediately, the NCI held a conference to bring together ethicists, clinicians of many types (screening, diagnosis, treatment, prevention), geneticists, behavioral scientists, lawyers and genetic counselors to examine how we could effectively use this powerful new information. One of our research participants attended as a patient advocate. Issues of testing children, of imaging, of legal implications and other concerns were discussed, and guidelines for testing and counseling developed. At M. D. Anderson, we developed a research program to provide educational materials, counseling and testing to our research participants, and to determine what information people at risk wanted and how it would be used. The initial uptake on testing in the 1990s was low, although it has increased significantly since 2000. A personal benefit, and highlight, of this effort has been the opportunity to reconnect with the families who have been participants (in fact, almost collaborators) over the years. Many I knew from the 1970s, others I knew only from the telephone and the pedigrees. For some, I know the history for four to five generations. I’ve been privileged to share their histories and to see their families grow over another generation. These wonderful people have been my professional family. And now, finally, we had information that we could give back. We were able to bring family members together to discuss the risks with a genetic counselor and in some cases to take preventive measures. Unfortunately, given the range of tumors that occur with LFS, we have not been able to offer effective screening recommendations. For some, the genetic information is unwanted or seems more a burden than a benefit. The biggest disappointment to date is that we still do not have proven effective preventive/surveillance/management strategies for the individuals at risk.

For me personally, the 1990s brought the “empty nest,” as my children went off to college. It had been fun to visit several schools with them, see the campuses, and, more important, see how they made decisions about continuing their education. My son went to UT, majoring in electrical engineering and computer science, and my daughter to Middlebury College, then Brown University, majoring in biology. Somehow college brought a blissful end to the teenage period and restored the closeness and communication of earlier years.

I had some interesting opportunities arise in the 1990s. M. D. Anderson had initiated a program of Faculty Achievement Awards, and I received the first award in Cancer Prevention. I became involved in the new Faculty Senate, the faculty governance body mandated by the UT System. This experience was very valuable; we (faculty) often see the institution through the tunnel vision of our day-to-day activities and associations, unaware of the many other faculty and missions that go on in other sectors. The Faculty Senate is the one organization that brings together an elected body from all departments and divisions and addresses faculty issues from the “faculty as a whole” perspective. While there have been many notable accomplishments of the Faculty Senate, clearly one from which I and probably others in this book benefit is the compensation review that initially revealed a pattern of strikingly lower salaries among women and minorities.

Outside the institution, there were also new opportunities. Like many other faculty at M. D. Anderson, I was a member of the American Association for Cancer Research (AACR), which is the largest cancer research organization in the world. It is the one professional organization that brings together all disciplines in the broad cancer research community with a focus on communication and fostering of science and public education. After being elected to the AACR Board of Directors, I became president in 1996–1997. One of the goals of my year was public education about cancer — not the media or marketing hype, but the current status and potential. At the annual meeting, we held the first public education session to provide a forum of experts to exchange information with the public, to present the opportunities and to hear the public concerns. This was a pilot; we had no idea what the level of interest might be on a Saturday morning, and didn’t know whether to expect a handful or hundreds of participants. Fortunately, our local organizers in San Diego did a great job and really brought out the public. We had a full house with attendees staying beyond the scheduled time and thanking us for the session. It was terrific, people were so interested and so grateful, and we were touched. Those sessions now are standard at AACR annual meetings.

Of course, education is always an important part of academics. Over the years, I have been on many graduate students’ committees. Often I have

partnered with my laboratory collaborators, recommending that the students seek mentors with a “wet lab” so they can learn marketable skills but work with projects on which I am a collaborator. This approach was especially productive with the Grady Saunders lab. Students and postdocs who have contributed significantly to my program directly include Melissa L. Bondy, Ph.D., Sara S. Strom, Ph.D., Li Cheng, Ph.D., and Shih-Jen Hwang, Ph.D. I find that teaching is such an essential part of academic life; so many times in preparing a lecture or answering a student’s question, I come up with a new idea or new hypothesis to test.

During the 1990s, new cancer genes involving relatively common cancers were identified, beginning with the breast cancer susceptibility genes BRCA1 and 2. These findings initially drove the development of clinical cancer genetics, a service offering genetic counseling and testing to concerned individuals. Over the last two decades, many new cancer susceptibility genes have been identified and rapidly incorporated into the program, and many students have trained in cancer genetics counseling. I very much enjoy working with the counselors but have to remember that my “historic approach” may not be so fascinating to everyone. The new trainees can’t remember a time when we didn’t know about such genes!

My most rewarding personal experiences have been from my family: with my husband, seeing our son and daughter grow up, graduate from college, get married, enter promising careers, start their own families — and, most important, maintain a close relationship with us. Our children are great individuals, and we have learned so much from them. This past year has brought the thrill of grandparenthood. On graduating from UT, my son took a job in Portland, Oregon, with Intel in chip architecture and design. Initially, we thought that would last a few years, and that he would, of course, come back to Texas. However, he has become an Oregonian, and we have loved getting to know Oregon. We anticipate increased visits there since he and his wife, Kirsten Healey, an artist and teacher, in April 2008 welcomed our second grandchild, a precious little boy named Beeman Driscoll Strong.

At one time it appeared that we would not have any Strong descendents in Texas. My daughter Larkin had moved from the northeast (Providence, Rhode Island) to the northwest (University of Washington in Seattle) in 2001 for graduate school. While there she met her husband Paul Scheet, also a graduate student, who was studying statistical genetics. They completed their Ph.D.s in health services/public health (Larkin) and statistics (Paul) in 2006 and moved to Ann Arbor, Michigan, for postdoctoral fellowships. In December 2007, they had our first grandchild, a beautiful little girl named Linnea Connally Scheet. I have to admit that I never knew I would be so excited about being a grandmother, but it is absolutely thrilling. I spent most

of December in Michigan — and I really don't like cold weather — and returned to babysit in February. The great news for me is that Paul and Larkin completed their postdocs and joined M. D. Anderson in the summer of 2008 in the Department of Epidemiology. Imagine the joy of coming to work in the morning with the possibility of running into your daughter or son-in-law when the elevator opens or in the lunch line. And imagine stopping off on the way home to play with your granddaughter!

My career has not followed the traditional academic mode. I broke a cardinal rule: instead of the usual movement from one institution to another in an effort to advance up the career ladder, I have been at M. D. Anderson my entire career, without even a sabbatical. Perhaps had I been better informed about the “traditional” career path and what one needed to do to succeed, I would have considered other opportunities. And yet I have been happy with my research, and my choice worked for me and my family to stay in Houston. It certainly worked for my science, as I could never have conducted the longitudinal studies of M. D. Anderson patients and families elsewhere. It also worked as new technologies were developed and applied rapidly over these years at M. D. Anderson. I have had the fantastic opportunity to do what I loved without worrying about the “establishment” career path. One could hardly ask for more.

