

Dana Farber Cancer Institute  
Boston, MA  
September 28, 2008

**Celebration of the Career of Frederick P. Li  
Joseph F. Fraumeni, Jr.,  
National Cancer Institute, NIH**

It is a pleasure to pay tribute to a very dear friend and colleague. I met Fred about 40 years ago when he arrived at the Epidemiology Branch of the National Cancer Institute as a commissioned officer in the U.S. Public Health Service. Fred had been recruited by Bob Miller, our Branch Chief, who served as a wonderful mentor for both of us over the years.

Fred was different from the many young physicians who were flocking to NIH at that time. His background in clinical medicine was matched by a passionate interest in public health. He seemed a natural for epidemiology, and his intellectual curiosity and productivity were evident from the very start. This was not surprising in view of his strong work ethic, which I soon learned was a familial trait transmitted by his parents and reinforced by his accomplished siblings.

Fred had a knack for making important clinical and epidemiological observations, and taking them to the next

level. This often meant crossing disciplines, which in my experience is not always easy, but collaborators were drawn not only to the scientific ideas generated by Fred, but also by his friendly, calm and thoughtful demeanor, and by his generosity of spirit.

At NCI, Fred and I worked together on several projects, but the one that endured long after Fred left for Boston and for Dana-Farber and Harvard is the familial syndrome that came to bear our names. The critical observation was made by Fred who discovered a family with an explosive onset of a wide variety of cancers, affecting children and young adults. Fortunately we were in the midst of a multicenter study of pediatric cancers, and it became possible to identify other families with a similar array of tumors.

In 1969 Fred and I reported the first four families in the *Annals of Internal Medicine*. The title of the article was “Soft-tissue sarcomas, breast cancer, and other neoplasms: A familial syndrome?” We spent more time debating the title than writing the paper. Fred thought we should be conservative and insert a question mark, and he prevailed. But he was more confident later that year when we presented more data in *The Journal of the National Cancer Institute*. The paper was called “Rhabdomyosarcoma in children: epidemiologic study

and identification of a familial cancer syndrome” (with no question mark).

The two papers were met with skepticism in some quarters. At that time genetics was out of the mainstream of cancer research, and family-based studies were on the fringe. In addition, there was a prevailing dogma that any familial tendencies to cancer were site-specific, so that families with different forms of cancer were thought to represent the play of chance, or referral bias, or possibly an environmental factor. During that period the research priority was on the study of tumor viruses, so the possibility was raised that a polyoma-type virus might be on the loose.

The publications generated referrals, and over time we were able to assemble 24 similar families. In a prospective study of these families, we were able to establish the constellation of tumors arising in a dominantly inherited pattern. We are grateful to the remarkable team from Dana-Farber involved in these studies, including Judy Garber who like Fred has roots in our epidemiology program at NCI. In the meantime, new and important insights into the manifestations of the syndrome and the mode of inheritance were coming from Louise Strong at M.D. Anderson Cancer Center in

Houston as well as Jill Birch at the Manchester Children's Hospital in England.

From the start we collected biospecimens from family members in hopes that the syndrome would help uncover a unifying susceptibility mechanism for a variety of cancer types. We looked for immunological, chromosomal and other alterations, but to no avail. However, in 1990 with the arrival of new genetic technology, Stephen Friend and David Malkin at MGH examined specimens in our families and those of Louise Strong. The discovery of germline mutations in the p53 tumor suppressor gene aroused considerable interest in the syndrome, particularly since mutations of p53, the so-called guardian of the genome, was known to occur in the tumor tissue of a high percentage of cancers in the population. Once again Fred took the lead in planning the next generation of studies, which included organizing a series of workshops in which the syndrome served as a prototype for developing recommendations about predictive genetic testing and interventions in cancer-prone families.

As Fred's career blossomed at Dana-Farber and Harvard, his focus extended to several other hereditary cancer syndromes, to the study of late effects of cancer, to preventive strategies in high-risk populations, and more

recently to cancer control research in Asian and other minority populations. What a pleasure it has been to follow the progression of Fred's remarkable career, and his emergence as a leader in the field of cancer epidemiology, genetics, and prevention. The pride that I feel is more than that of a long-standing colleague. Fred has been like a brother to me and I treasure his friendship and that of his wonderful wife, Elaine. In closing, I wish to say that Fred has brought enormous credit not only to Dana-Farber and Harvard, but also to the National Cancer Institute and NIH where his career was launched during the early formative years of our epidemiology program. On behalf of all my colleagues at NCI, I am proud to present Fred with this plaque for a SPECIAL ACHIEVEMENT AWARD. It reads: **TO FREDERICK P. LI, DANA-FARBER CANCER INSTITUTE, IN RECOGNITION OF YOUR PIONEERING SCIENTIFIC CONTRIBUTIONS IN EPIDEMIOLOGY AND GENETICS AT THE NATIONAL CANCER INSTITUTE. DATED SEPTEMBER 26, 2008.**