

Emmanuel Farber: In Memoriam (1918–2014)

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On August 3, 2014, the cancer research community lost a giant in the field, Dr. Emmanuel Farber. Emmanuel (Manny) Farber's legacy is his contribution to the science of oncology that is elegantly epitomized in the title of one of his seminal papers: "A New Principle for the Analysis of Chemical Carcinogenesis," in which he introduced the concept that neoplastic disease is the end product of a true biologic process amenable to analysis, as opposed to a series of unrelated accidental (mutagenic) events. In this sense, he also presented the notion that context matters during carcinogenesis as it does in biology at large, suggesting that Darwinian principles could be applied to the analysis of cancer cell populations.

Manny Farber was born in Toronto, Ontario, Canada, on October 19, 1918. He obtained his MD from the University of Toronto in 1942. After completing his residency training in pathology at Hamilton General Hospital, Hamilton, Ontario, he served in the Royal Canadian Medical Corps during World War II and in 1949 obtained his PhD in biochemistry from the University of California, Berkeley. His exposure to liver pathology started in 1950 with a fellowship from the American Cancer Society to work with Dr. Hans Popper, an eminent liver pathologist. This unique combination of biochemistry and pathology made Manny realize, early on, that pathology is dynamic and that it offered tools and opportunities to explore mechanisms of disease processes. Manny used to say that pathology is not a discipline like

biochemistry, pharmacology, or physiology, but it is problem oriented, i.e., the study of disease processes. He strongly believed that understanding the dynamic nature of the disease processes required researchers with various backgrounds, and thus he reached out to chemists, biochemists, physicists, biophysicists, biologists, molecular biologists, microbiologists, cell biologists, and mathematicians, just to mention a few. Now, departments of pathology across the nation have become vibrant platforms for researchers from various disciplines working with a common goal—to understand mechanisms of disease processes. His appreciation of an interdisciplinary approach to study disease propelled him to help develop broad subspecialties of pathology, including experimental pathology, biochemical pathology, and toxicologic pathology. Manny Farber was a pathologist, but he studied pathology as a tool to understand biology and, by extension, life in general, bridging science and philosophy.

Manny Farber's distinguished academic career started in 1950 at Tulane University, New Orleans, Louisiana, and continued at the University of Pittsburgh, Pittsburgh, Pennsylvania, where he was Professor and Chair of Pathology and Professor of Biochemistry (1961–1970). In 1970, he moved to Philadelphia to become the director of the Fels Research Institute and professor of pathology and biochemistry at Temple University School of Medicine. In 1975, he moved to his native city, Toronto, to head the Department of Pathology and was also appointed as professor in the Department of Biochemistry. He served as professor emeritus in the Department of Laboratory Medicine and Pathobiology at the University of Toronto until his death.

In 1975, when Manny came to the University of Toronto, there were four graduate faculty members and about six graduate students. His enthusiasm and inspiration attracted more and more graduate faculty and students. The department has now grown and diversified, to be one of a kind, with 150 graduate faculty and well over 150 graduate students. Dr. Richard Hegele, the current department chair, recalls, "When I was a medical student here, Dr. Farber was the Chairman of Pathology. He was

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an energetic and enthusiastic individual and he was certainly an inspiration for me to pursue pathology as my ultimate career choice in medicine." Manny's inspiration touched each and everyone who came to know of him, let alone those who directly interacted with him. Manny was passionate to teach pathology to undergraduate nonmedical students in the arts and sciences, especially to toxicology students. In the 1970s, teaching pathology to arts and science students was pretty much a no-no. This desire probably stemmed from his belief that understanding disease processes helps us to understand normal biology. Not too surprisingly, he launched a highly successful and most loved "Principles of Pathobiology" course for undergraduate students in the arts and sciences at the University of Toronto.

Manny was always driven by concepts, not techniques. For many years, he had a sign on his desk: *A Fool with a Tool Is Still a Fool*. He had high standards of excellence and scholarship and had little patience for long talks without supporting data. If someone tried to impose on him certain ideas without data, he had some favorite terms for them. But if an idea was backed by data, he was the first one to entertain that idea. He encouraged discussions. At the University of Toronto, every Monday morning we (Manny, Sarma Dittakavi, Rajalakshmi Srinivasan, and Ezio Laconi, with other students and senior colleagues) had group discussions. Often, these discussions were so intense and heated that a passerby not knowing what was happening would be tempted to call the police.

Manny always felt that while exploring the dynamics of the disease processes, one should not lose focus on biology. In the years when molecular approaches were in high gear, he constantly reminded us of the importance of integrative biologic analysis. Using liver carcinogenesis models, Manny and his group demonstrated that the bulk of the tissue needed to be compromised for the "initiated hepatocyte" to emerge and possibly progress to cancer. Subsequently, one of us (Ezio Laconi) demonstrated that transplanting normal hepatocytes into the carcinogen-damaged livers decreased the progression of "initiated hepatocytes and hepatic nodules." How correct you were, Manny, in your conviction, wisdom, and vision!

Many of today's generation may not know that Manny Farber was greatly instrumental for today's smoke-free environment. Manny served from 1961 to 1964 on the Surgeon General's first Advisory Committee on Smoking and Health, which produced some of the most conclusive evidence that years of smoking cigarettes could cause cancer. Manny Farber made a seminal observation that chemical carcinogens interact with nucleic acids and form DNA adducts. These early groundbreaking studies led to the concept that chemical carcinogenesis is a sequential process and that cancer could be induced through a series of step-by-step chemical treatments. Because of these pioneering observations and his expertise in chemical carcinogenesis, Manny's arguments weighed heavily in issuing the report that has done more to prevent tobacco use and educate public about smoking risk than any other preventive measure. This committee's report was a paradigm shift in the way Americans live today. Thanks, Manny, for your efforts to keep today's environment relatively smoke free.

During his distinguished and colorful career, Manny published over 400 peer-reviewed papers, books, book chapters, and reviews. He trained several scientists from all over the world, and many of them are in important and high-ranking academic positions with excellent research accomplishments. This is truly a precious legacy we owe to Manny Farber.

Manny was a most accomplished individual. His career was laced with innumerable awards presented to him by his colleagues at home and abroad in the fields of cancer and pathology. He received several awards from the American Association for Cancer Research (AACR), including the G.H.A. Clowes Memorial Award. In 2010, he received the Lifetime Achievement Award in Cancer Research. In 2013, he was elected as an inaugural fellow of the Academy of the American Association for Cancer Research. Manny served the AACR in several capacities, including as its president (1972–1973) and vice president; he was also a member of the board of directors, an associate editor of *Cancer Research*, and a member of the Pennsylvania (East) State Legislative Committee and the Molecular Epidemiology Working Group. The American Society for Experimental Pathology lauded him with the Parke-Davis Award. His other honors included the Rous-Whipple Award from the American Association of Pathologists and the Gold-Headed Cane Award from the American Society for Investigative Pathology. In addition, the Society of Toxicologic Pathologists granted him an honorary membership, the highest recognition that this professional group can bestow. Manny was elected vice president and president of the American Society of Experimental Pathology. Manny Farber's recognition goes beyond North America. For example, the University of Torino, Italy, awarded him Doctor of Medicine and Surgery, *Honoris Causa*; CARSO, University of Bari, Italy, presented him with the Golden Plate Award for Excellence in Oncological Research. He was also bestowed with honorary memberships from the Japanese Cancer Association and the Pathological Society of Great Britain and Ireland. In 1984, Manny Farber was appointed as a fellow of the Royal Society of Canada, an award that recognizes outstanding Canadians.

Manny was married to Ruth Farber until her death in 1993. He later married Henrietta Keller Farber, who died in 2011. He is survived by his daughter, Dr. Naomi Farber, his son-in-law, Professor Steven Grosby, and a beloved grandson, Sam Grosby. Talking about her father, Naomi recalls, that "Manny was a very attentive and involved father. He encouraged me to explore and follow my interests, and often joined me. He held high standards for excellence in those activities that truly interested me. My father was my professional model, and it is because of him that I likely sought a life as an academic. He was a model of intellectual passion, deep ethical standards and integrity, and independence. Finally, my father was an absolutely devoted and reliable parent who, along with my mother Ruth, would have sacrificed anything for me. My mother fully supported his work and was a devoted partner throughout their marriage of 50 years. He was a loyal and caring husband." Sam Grosby recalls that his grandfather was "always so eager to be close to those whom he loved and to share his life and love with them. I was lucky to spend 21 years with my grandfather, sharing his life and love so often. He really was omnipresent in my childhood, as was his love."

Manny never rested on his laurels. He was always on the move looking for new ideas. One of us (Sarma Dittakavi) spoke with him when he had reached the age of 90 years. He was still the same Manny, full of energy and vibrancy. Many of us wish that we had his energy. Manny was a pioneer and a legend. His eloquence, contagious enthusiasm, and no-nonsense attitude to science continue to play an important role in the lives of those privileged ones who have known him.

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