Martin F. Kagnoff, MD: 1941–2014

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Martin F. Kagnoff

Mucosal immunology lost one of its true pioneers when Marty Kagnoff succumbed to complications of pancreatic cancer on 16 November 2014 at his home in La Jolla, California. He was 73. However, his influence on the field—particularly as personified by the almost 100 students, fellows, and junior faculty members that he was directly responsible for training—will be felt for generations.

Marty grew up in Vancouver, British Columbia, where he finished college and met Marcia, who became his wife. He subsequently moved to the United States to continue his training, matriculating at Harvard Medical School and earning his MD in 1965. He also became a US citizen. He began his clinical training in internal medicine at the Peter Bent Brigham Hospital, but it was interrupted when he accepted a commission in the US Navy and a position as principal investigator at the Armed Forces Radiobiology Research Institute in Bethesda, Maryland. His research there, which focused in part on understanding radiation injury to the intestine, spurred his interest in digestive diseases. Accordingly, when he resumed his clinical training (at New York Hospital and later at Boston University) he elected fellowship training in gastroenterology. This period also brought him into contact with Jerry Trier, and resulted in a publication in *Gastroenterology* on the secretory immunoglobulin A system that cemented his lifelong focus on the mechanisms of mucosal immunology.

In 1972, Marty was recruited by Henry Wheeler as one of the founding gastroenterology faculty members at the fledgling medical school at UC San Diego. It was to be the start of a career-long affiliation. A West Coaster by heritage and temperament, Marty thrived in this new environment, which placed enormous emphasis on understanding the basic mechanisms of disease. His new appointment also carried the opportunity to consolidate his research training in immunology by serving as a visiting scientist with Melvin Cohn at the Salk Institute for Biological Studies from 1972 to 1974. This experience springboarded an extraordinary series of publications in the *Journal of Immunology*, the *Journal of Experimental Medicine*, and *Gastroenterology*, many of them single-authored, that mapped the basic biology of Peyer's patch lymphoid cells and the specifics of the intestinal immune response, including oral tolerance. Marty quickly gained recognition for his ability to conceptualize complex biological systems in a way that opened them for further study. He was also assiduous in linking his basic research to human disease. For example, in the early 1980s, he began to dissect the immunogenetics of celiac disease, at that time a condition that resulted in significant suffering but was often underdiagnosed (even with the proliferation of gluten-free foods on

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grocery shelves, one might argue that to some extent that is still true today). His growing reputation in the area led him to be sought out not only by other scientists but also by many parents of children who were failing to thrive and who were subsequently revealed to be suffering from celiac disease.

In the late 1980s, Marty gathered a group of collaborators at UC San Diego to apply for a National Institutes of Health Program Project Grant on host–environment interactions at the level of the intestinal mucosa. This award was funded for 25 years. His work during that period and into the 1990s was substantially informed by the novel proposal that the intestinal epithelium is an active participant in mucosal immunity as well as by emerging concepts of the innate immune system. He showed that epithelial cells respond directly to interactions with bacteria and pathogens with a phenotypic shift and the production of specific cytokines, chemokines, and antimicrobial products, thereby orchestrating host defenses. This concept is now well accepted, of course, and forms the cornerstone of our understanding of a variety of digestive disorders, including inflammatory bowel diseases. He also published some of the earliest reports of the ways in which epithelial function is compromised by HIV infection. As always, this line of research was inspired by his clinical interactions with the burgeoning number of AIDS patients suffering from devastating gastrointestinal complications of the newly emerged disease, for which at the time little help could be offered. Indeed, Marty was always fearless in seeking out and applying new approaches to his work that might yield more definitive insights. A sabbatical spent in Paris in 2001, for example, enabled him to apply the newly developed Cre-loxP technology to studying the intestinal epithelium. This paved the way for a seminal series of studies that probed the links between epithelial nuclear factor-kB signaling, inflammation, and cancer.

In 2005, Marty received a significant philanthropic gift to found the William K. Warren Medical Research Center for Celiac Disease at UC San Diego, thereby returning to one of his earliest scientific interests. The center has greatly enhanced not only the basic understanding of the disease and its protean manifestations but also patient education and public understanding. Based in part on his growing responsibilities as director of the center, in 2007 Marty decided to retire from his academic positions as professor of medicine and pediatrics and focus full-time on his research activities without the distractions of teaching and university committees. Indeed, his wet lab was still active through June 2014, until his sudden diagnosis with pancreatic cancer.

Marty's myriad colleagues worldwide, as well as those who worked with him in San Diego, knew him as a passionate advocate for science with an incredibly incisive intellect. He was famously thrifty with money but supremely generous with his time as a mentor and colleague. He was particularly dedicated to the need to educate legislators about the importance of biomedical research, and he spent a period on leave from UC San Diego in Washington, DC, doing just that. Not only did he have a substantial impact on the field of mucosal immunology through his own research (with almost 15,000 lifetime citations and an h-index of 64), but he also shaped the field through his tireless contributions in organizing meetings and in editorial roles. For example, he was editor-in-chief of both the *Journal of Clinical Investigation* and the *American Journal of Physiology—Gastrointestinal and Liver Physiology*.

He loved to travel worldwide, but he was also a deeply committed family man, never happier than when spending time in La Jolla or at his beloved second home on the island of Kauai, Hawaii, surrounded by his wife, children, and grandchildren. He is survived by Marcia, his partner of more than 50 years, who herself enjoyed a distinguished career as a psychologist and hospital administrator with Marty's great support; their son Michael, a La Jolla attorney, and daughter-in-law Lisa and their two sons, Jacob and Drew; and daughter Melissa, a neurologist in San Diego.

The field has lost a giant, but we have all been enriched, both scientifically and personally, by Marty's many legacies, both tangible and intangible.