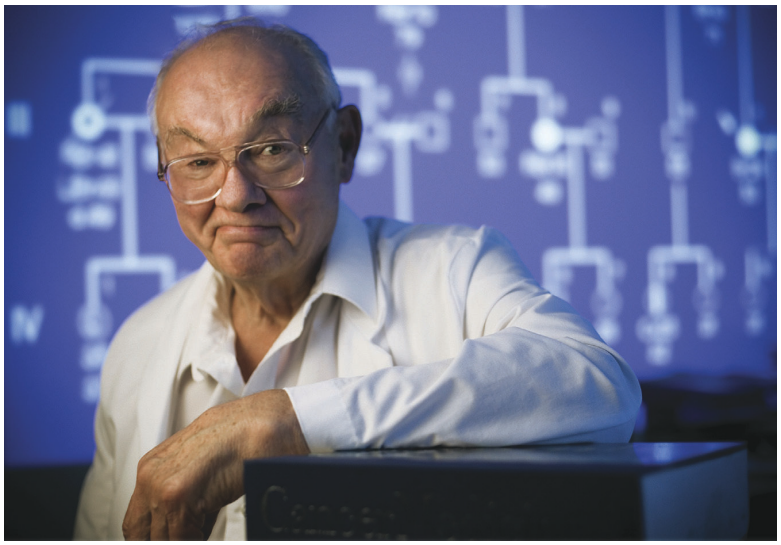
Henry T. Lynch, MD (January 4, 1928–June 2, 2019)

On June 2, 2019, the field of cancer genetics lost one of its most remarkable visionaries, who virtually created the field in the 1960s before any cancer-related problem could be solved on a genetic basis. He died of congestive heart failure in a hospice associated with Creighton University at age 91.

Henry T. Lynch was born on January 4, 1928, in Lawrence, Massachusetts, and grew up in Manhattan during the Depression in a world of little privilege. He left high school at age 14, and joined the Navy to fight in the European and Pacific Theaters in World War II from 1944 to 1946—starting at age 16! When fully grown, he stood 6 feet 5 inches tall and had pugilistic skills (he was known as Hammerin' Hank during a brief professional boxing career), so no one questioned his age, which was borrowed from a cousin. After completing his time as a Naval gunner (receiving the Philippine Liberation Ribbon) and a brief boxing career, he went to college, earned a Master's degree in Psychology, and started working on a PhD in human genetics to better understand the nature of psychiatric disorders. He changed course and obtained an MD degree from the University of Texas Medical Branch (Galveston) in 1960, and completed his clinical training in Nebraska. Since 1967, he enjoyed a successful career at the Creighton University School of Medicine in Omaha, Nebraska, as Professor of Medicine, Director of the Cancer Center (1994–2002), and Chairman of the Department of Preventive Medicine (1968–2019).

Henry always carried a passion for genetics, and focused his talents on the familial aspects of cancer. Although he initially had few proponents, he pioneered a field by virtue of his "shoe leather research," which involved traveling in the field, identifying and interviewing families with clusters of cancer, carefully assembling clinical documentation and constructing pedigrees, collecting samples of blood and tissue (which were later critical in solving the genetic bases of these diseases), and offering his observations to the medical community.

Throughout the 1960s, despite publishing prolifically, his ideas were not widely embraced, and it would not be until the mid-1980s that the first genes were identified and linked to familial cancers. Once this threshold was breached, the diseases fell one after another to the molecular biologists, and many of Henry's brilliant predictions were proven to be true, often by virtue of the samples of DNA he had carefully obtained and curated.



Henry T. Lynch, MD

I first encountered Henry in 1972 while working on my MD thesis. I had identified 2 families who seemed to have too many cancers at too early an age for this to represent simple "bad luck," which was the prevailing interpretation of familial clustering at the time. I came across Henry's publications, wrote him a letter, and received stacks of pedigrees, advice, and encouragement. It would be another 15 years before I would meet him, but he welcomed me like a long-lost son when I finally made it to Creighton. He never stopped bringing encouragement and enthusiasm.

While I was doing my research, I came across a little-known monograph written by Henry called "Hereditary Factors in Carcinoma," published in 1967.[1] In this book consisting of 12 chapters, he catalogued the familial linkages between gastrointestinal and endometrial cancers (which he initially called "cancer families," but were given many names over the years[2]), and the relationships among other cancers that clustered in families. This book also contained a chapter about the emotional toll these familial syndromes create, and a chapter on genetic counseling. He was ahead of his time, had a broad vision of the role he was to play in this discipline, and he frequently traveled throughout the United States and around the world to collect data and counsel families (Figure 1).

Henry was not the first to recognize familial clusters of colorectal, endometrial, gastric and other cancers. That recognition falls to Aldred S. Warthin, MD, PhD, Chairman of Pathology at the University of Michigan, who first noted familial clustering of cancer in his seamstress' family, and reported this in 1913.[3] However, in the late 1960s, Henry traveled to Michigan, organized a family reunion of "Cancer Family G" and updated the pedigrees and collected blood samples for future research.[4] This family has been repeatedly followed up in the literature, and was eventually linked to a germline mutation in the *MSH2* gene.[5]

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JHU 2276
Merck Sharp v. Johns Hopkins
IPR2024-00648

Figure 1. Henry Lynch, in his characteristic mode, providing counsel to families.

The term Lynch syndrome was first used in 1984 in an attempt to subdivide these cancer families based on specific organ risks, but the term was not widely embraced at that time.[6] In 1993–1996, mutations in the DNA mismatch repair genes were identified as the cause of this disease, as the families could be identified by the presence of microsatellite instability in the tumors.[7,8] However, not all familial clusters of colorectal and other cancers could be linked to these genes. Out of convenience, in November 1997[9] it was informally voted upon at an National Cancer Institute–sponsored workshop to use the term "Lynch syndrome" for those families with a germline mutation in a DNA mismatch repair gene—a term to use until we knew more about the disease. The term has largely been accepted in Henry's honor, but other monikers are still used by some. Interestingly, the initial reporting of familial clustering of breast and ovarian cancers—first appreciated by Henry[10]—is not called Lynch syndrome. Such is life. I never heard him complain about it.

As his career and the field of genetics research matured, there was a beautiful collision between the clinical observations and DNA that Henry had collected and the ability to use linkage analysis to localize and eventually clone the germline mutations responsible for hereditary cancer syndromes. Henry had multiple collaborative publications with Bert Vogelstein on the hereditary colorectal cancer problem and with others on the hereditary breast and ovarian cancer issue, just to name a few. Each time candidate genes were proposed as the cause of one of the familial syndromes, Henry had a ready cache of pedigrees and DNA samples to be tested. Time has been very kind to Henry; so many of his predictions have been confirmed. What were once thought to be casual anecdotes from frightened families ended up being the substrate for some of the most important discoveries of the twentieth century. Henry published more than a thousand papers and has been honored with more awards than can be possibly listed here, including from the American Gastroenterological Association and virtually all of the professional cancer and genetics societies. After all is tallied up, it is fair to say that he was indeed the "father of cancer genetics," and he deserves every honor that has been bestowed on him.

Henry's beloved wife of 60 years and research collaborator Jane (Smith) Lynch died in 2012. Henry is survived by a son, Patrick Lynch (a well-known familial cancer researcher at MD Anderson in Houston), 2 daughters Kathy Pinder and Ann Kelly, 10 grandchildren, and 9 great grandchildren.

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