Janet Davison Rowley, M.D. (1925–2013)

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As she said in writing about Theodore Puck in 2006, "it is impossible to write a comprehensive obituary of [Janet Rowley] in less than a dozen pages.[1]" Leading pioneer in cancer research and matriarch of cancer genetics and cytogenetics, Janet Davison Rowley, M.D. (Figure 1), died at her home from complications of ovarian cancer on December 17, 2013. How ironic that a woman whose numerous cancer research discoveries led to lifesaving treatments for so many cancer patients succumbed to cancer. Dr. Rowley joined the American Society of Human Genetics (ASHG) in 1963 and was an active member; she served on the board of directors from 1985 to 1988 and as president from 1992 to 1993. "Janet Rowley's work established that cancer is a genetic disease," said Mary-Claire King, professor of genetics and medicine in the Division of Medical Genetics at the University of Washington and past president (2012) of ASHG. "She demonstrated that mutations in critical genes lead to specific forms of leukemia and lymphoma and that one can determine the form of cancer present in a patient directly from the genetic changes in the cancer. We are still working from her paradigm." For her groundbreaking studies in cancer genetics and cytogenetics, in 1991 Dr. Rowley was corecipient (with Alfred G. Knudson Jr., M.D., Ph.D.) of the Allen Award, the preeminent prize awarded by ASHG. At the 2009 ASHG meeting, Dr. Rowley received the prestigious Peter and Patricia Gruber Foundation Genetics Prize, awarded for trailblazing research that "provides new models that inspire and enable fundamental shifts in knowledge and culture." An excellent writer, she made her earliest contribution to the *American Journal of Human Genetics* with a book review in 1974. She was published thrice more in *The Journal*: in 1994 for her 1993 presidential address,[2] in 2003 for her introductory speech for Albert de la Chapelle (the 2002 William Allen Award winner),[3] and in 2006 for her memorial to Theodore Puck.[1]

Professors Janet Rowley and Felix Mitelman cofounded and served as co-editors-in-chief of the journal *Genes, Chromosomes & Cancer* for 25 years. *Genes, Chromosomes & Cancer* continues to provide rapid publication of high-quality studies in cancer genetics and cytogenetics, advancing the fields that Dr. Rowley shaped.

The only child of Ethel and Hurford Davison, Janet Davison was born on April 5, 1925, in New York City. Her parents, both graduates of the University of Chicago (U of C), moved back to the south side of Chicago to accept positions as educators when Janet was a toddler. After 2 years of high school, Janet earned a scholarship to enroll in the Hutchins College at the U of C, which combined the last 2 years of high school with the first 2 years of college. "The U of C," she later recalled, "taught me to stick to my convictions if I really thought that I was correct, even when others disagreed." Janet completed her college degree at the U of C in 1944 and was accepted into the U of C medical school but had to wait to matriculate because the quota for women—three per class of 65—was already filled. "So I had to wait 9 months," she said in an interview, "I was only 19 at the time, so it wasn't a great tragedy." At the age of 23, Janet Davison graduated from medical school, and the next day, she married fellow medical student Donald Rowley, M.D., who would become an eminent professor of pathology at the U of C. Dr. Janet Rowley completed her internship at the United States Public Health Service's Marine Hospital in Chicago in 1951. She spent the next 20 years raising her family, composed

Figure 1. Janet Davison Rowley
Photo by Jason Smith. Courtesy of the University of Chicago (U of C) Medicine.

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Figure 2. Dr. Rowley at Her Microscope
Courtesy of the U of C Medicine.

of four sons, while working part time at various Chicago clinics, including one that provided specialized care for children with trisomy 21 (Down syndrome). The Rowley family spent a year at Oxford University while Donald did a sabbatical and Janet learned the newly developed techniques of chromosome analysis from Marco Fraccaro. When Janet Rowley returned to Chicago in 1962, her colleague and mentor, Leon Jacobson, M.D., suggested that she apply her new knowledge to study the chromosomes from patients with leukemia. He offered a lab bench, a microscope, and a small salary to examine chromosomes from his leukemia patients. For the next decade, she labored over the microscope in the search for consistent chromosome abnormalities amid the seeming genetic chaos of leukemic cells, a daunting task in the era prior to chromosome banding (Figure 2).

Knowing Dr. Janet Rowley as we do, it is not surprising that she made her first big scientific discovery at home. A second sabbatical in Oxford, this time with Walter Bodmer from 1970 to 1971, enabled her to learn new fluorescent staining techniques to highlight chromosomal bands and facilitate differentiation between the various chromosomes. Dr. Rowley began to photograph the banded chromosomes from leukemia patients by using the fluorescence microscope. She would take the pictures home to examine. Her children often teased her about getting paid to play with paper dolls as she sat at their dining room table while using surgical scissors to cut each chromosome out of the photographs and carefully arranging them in pairs. In the spring of 1972, in her Hyde Park home, Rowley "lined up the chromosomes from leukemia cells on a table and told [her] kids not to sneeze." She noticed that the chromosomes from a patient with acute myeloid leukemia (AML) had two abnormalities. Chromosomes 8 and 21 appeared to have made a trade. The bottom of one chromosome 21 had broken off and moved to the bottom of one chromosome 8, and the bottom of that chromosome 8 had moved to the bottom of that chromosome 21—an apparently reciprocal exchange we now know as t(8;21)(q22;q22). When she looked at more patients with this same kind of leukemia, she saw the same translocation. Assuming that this finding had already been published, she went to the library, and to her surprise, it hadn't been reported in the literature. The realization that she had discovered that leukemia was associated with a genetic alteration was reportedly "one of the greatest moments" in her life, but like most breakthroughs, her finding was greeted with skepticism by the scientific community. Later that year, Dr. Rowley noticed that patients with another form of leukemia, chronic myelogenous leukemia (CML), had a different translocation. The bottom of one chromosome 22 had been exchanged for a piece of the bottom of one chromosome 9. This translocation, which we now know as t(9;22)(q34;q11.2), causes important genes that regulate cell growth and division to no longer be in their normal position, resulting in the uncontrolled cellular proliferation that is cancer. The observation of two consistent translocations in leukemia, one in AML and one in CML (both published in 1973), argued that such translocations were tied to specific types of leukemia.[4,5] Yet, because of chromosomal instability, variant translocations, and additional chromosomal alterations in patients with leukemia, many scientists remained skeptical. "It was generally thought that chromosome abnormalities were a consequence of the cancer, not the cause," Rowley recalled. In 1977, Rowley and colleagues identified a third consistent chromosomal alteration in leukemia, the t(15;17)(q24.1;q21) translocation, which causes acute promyelocytic leukemia, a rare disease but one in which every patient has the same genetic rearrangement.[6] "That made me a believer," she later recalled. "That was the frosting on the cake."

Following her lead that specific translocations defined specific forms of cancer, scientists around the world joined the search for chromosomal alterations in cancer. Others used the translocations as roadmaps to find specific genes disrupted by chromosome damage, thus opening up the current era of cancer genetics. By 1990, more than 70 translocations had been identified and linked to different cancers. "This was a time of excitement and wonder that is hard to describe," Dr. Rowley wrote in an essay. At age 47, after publishing the AML and CML studies, her 19th and 20th publications, respectively,[4,5] her 21st publication was a report on chromosomal patterns in myelocytic leukemia in the *New England Journal of Medicine*.[7] Her career skyrocketed. Her resume now lists 509 publications in leading scientific journals. More recent discoveries include cloning a gene rearrangement that occurs in leukemias seen in infants and the recognition that deletions of chromosomes 5 and 7 are associated with therapy-related leukemia in patients previously treated with particular anticancer drugs. Janet Rowley rose quickly through the

Figure 3. Authors Susanne Gollin, Left, and Shalini Reshmi, Right, with Dr. Rowley after Breakfast Together during the 2003 ASHG Meeting in Los Angeles

Figure 4. Dr. Rowley on Her Bicycle at the U of C
Courtesy of the U of C Medicine.

ranks at the U of C from research associate (assistant professor) in 1962 to associate professor in 1969, professor in 1977, and distinguished service professor in 1984. Although she should have retired at some point around age 70, Dr. Rowley accepted the position of Interim Deputy Dean for Science in the Division of the Biological Sciences at the U of C from January 2001 to November 2002. She continued to be active in science and traveled extensively to present lectures and receive awards.

The awards began in the early 1980s with the Lasker Award and the National Medal of Science, the nation's highest scientific honor, in 1998. Others included the Presidential Medal of Freedom, America's highest civilian honor, in 2009; the Lifetime Achievement Award from the American Association for Cancer Research in 2010; the Japan Prize for Healthcare and Medical Technology in 2012; and the Albany Medical Center Prize in 2013. Janet Rowley received honorary doctor of science degrees from 14 institutions, including Oxford, Harvard University, Yale University, the University of Pennsylvania, and Dartmouth College. Dr. Rowley was elected as a member of numerous scientific and honorary societies, including the National Academy of Sciences, the Institute of Medicine, the American Philosophical Society, and the American Academy of Arts & Sciences.

Janet Rowley was not only a distinguished researcher and steadfast colleague but also an attentive and encouraging mentor and often a mother figure to her trainees, staff, and others whom she took under her wing (Figure 3). She routinely advised young (and older) investigators not to give up. "Take risks," she had said. "Do something different if it looks interesting… I didn't do anything noteworthy until I was 50. Success often involves a great deal of luck. Some people don't like to hear that because it means there are things out of their control. But that's the way it is." She would often sign emails, "Good luck!! Janet." Janet Rowley mentored nearly 100 graduate students, postdocs, and fellows and gave anyone interested in science an opportunity to carry out research projects in her laboratory, irrespective of funding, because she would always find funding to support aspiring students. No matter how busy she was, when a trainee needed a letter of reference, Dr. Rowley was always there for him or her. She treated every human being with respect, regardless of their lot in life. She played an important role on national ethics and cancer advisory committees by clearly stating her views on controversial matters, such as stem cell research, and making clear that funding for "observation-driven" cancer research like her own should also be funded in this era of funding for only "hypothesis-driven" science.

An avid gardener, Dr. Rowley spent her rare free moments tending to her urban flower and vegetable garden at her home near the U of C campus. Her garden was the place where she claimed to have done some of her best thinking. Dr. Rowley would stop in her tracks midconversation to remove a weed from a neighbor's garden. The Janet Rowley Memorial Garden at the west end of Bond Chapel near the center of the U of C campus is sure to remain weed free. Dr. Rowley also enjoyed her indoor garden in her sunroom at home. We often spoke of our mutual love of orchid plants. Her other interests included the opera and traveling worldwide to hike, camp, observe wildlife, and become acquainted with the indigenous peoples. Dr. Rowley exercised by swimming in Lake Michigan and in bodies of water around the world, including swimming in the Pacific Ocean with her grandchildren during the 2009 ASHG meeting in Hawaii. She continued to bicycle daily from her Hyde Park home to her laboratory into her late 80s, regardless of the weather conditions (Figure 4). Needless to say, Dr. Rowley had limitless energy. During a meeting on fluorescence in situ hybridization in Colorado, upon returning to the lodge after a day of skiing, Dr. Rowley was looking for companions to join her on a snowshoeing expedition. Dr. Rowley also enjoyed spending time with her family at their cottage in the Porter Beach community, overlooking Lake Michigan. Additions to their cottage were built to accommodate their growing family of grandchildren, and some of the furniture was designed and built by Dr. Rowley's husband. There, surrounded by the Indiana Dunes State Park and overlooking the Indiana Dunes National Lakeshore with a clear view of

the downtown Chicago skyline, she gardened, swam in the lake, read while sitting on the deck, and hosted guests for recreation, relaxation, and delicious home-cooked meals.

Dr. Rowley remained a proud yet humble woman with a keen sense of style and grace and a terrific sense of humor. She often shunned the limelight and deflected accolades to her coworkers by indicating that her later research findings were the result of a team effort. According to speakers at her memorial service, including her son Robert, Dr. Rowley apologized to her colleague for putting him in the difficult position of having to give her the diagnosis of ovarian cancer. She donated her cancer tissue to science in the hope that researchers might learn from it so that someday, they might be able to prolong the life of other women afflicted with this devastating disease. Near the end of her life, as remembered by her son David at her memorial service, she was barely able to walk up to the dais to accept the Partners in Discovery Award from the Women's Board of the U of C Cancer Research Foundation in November 2013, but she proceeded to put on her "game face" to rally for more funding for scientific research.

Dr. Rowley's beloved husband, Donald, died in March 2013. Although they had experienced the loss of a son in an accident at Porter Beach, the loss of her husband of 65 years was extremely difficult for her. Dr. Rowley is survived by three sons, David, Robert, and Roger, and five grandchildren, Jason, Jenny, Gia, Anra, and Ian. David Rowley said, "Both my parents served as exemplary role models for their approaches to science, to life, to others, and to family." "My mother was an inspiration to all of her family through her generosity and her caring and doing whatever was in her power to help each of us achieve our own individual goals. She will be dearly missed by her family, including five grandchildren." David, you and your family should know that Janet Davison Rowley will be dearly missed not only by her family but also by her friends, neighbors, colleagues, trainees, and countless people whose lives she touched directly and indirectly by her contributions to science, medicine, and humanity. As Peter Aplan wrote in an email exchange among editors and editorial board members of her beloved journal, *Genes, Chromosomes & Cancer*, "Although we are all poorer for this loss, we are all richer for her life." Further, as Brian Druker, director of the Oregon Health & Science University Knight Cancer Institute, who shared the Japan Prize with Janet Rowley for development of Gleevec said, "Her spirit will live on in all of the people who have benefitted from her work."

Acknowledgments

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