Janet Davison Rowley: In Memoriam (1925–2013)

Kathleen H. Goss and Michelle M. Le Beau

"Character is the Sire of Excellence. The accomplishments of mankind are achieved exclusively by men and women of noble character who do nothing mean, small or degrading. They give more than they take."

-Charles B. Huggins

(Mentor and colleague of Dr. Rowley)

Janet Davison Rowley was a pioneer, a humanitarian, and a legend. As the mother of the field of cytogenetics (or as she referred to herself in later years—its grandmother), she laid the foundation for modern cancer molecular genetics and targeted therapy for oncology. Yet, it was her impact as a wife, mother, mentor, teacher, and role model that leaves the broadest footprint on the cancer research community, and every individual fortunate enough to know her. Janet died from complications of ovarian cancer on December 17, 2013. Reflective of the resolve she showed throughout her career, even near the end of her life, she hoped that scientists could learn from her cancer to benefit future patients.

Janet was born in New York City on April 5, 1925, and moved to Chicago as a young child, where she would spend most of her life. Education was a priority to her parents, both University of Chicago (Chicago, IL) graduates, and, at only 15, she entered a program at the University of Chicago for gifted high-school students to begin taking college courses. After earning her bachelor’s degree at 19, Janet was accepted into the University of Chicago medical school but had to defer her admission for a year because the quota for women (3 in a class of 65) was filled for the year. The day after graduation in 1948, she married her medical school classmate, Donald Rowley, who would become a professor at the University of Chicago and a renowned experimental immunologist. Janet and Don would have four boys and, as a young mother, Janet worked part-time at a community clinic, caring for children with developmental disorders. It was here that she was first exposed to the emerging field of cytogenetics and the astounding discovery that Down syndrome was the result of a chromosomal imbalance, namely three copies of chromosome 21. When Janet joined Don on a sabbatical year at Oxford University (Oxford, United Kingdom) in 1961, she was inspired to spend the time learning the newly developed methods of chromosome analysis.

Upon returning to the University of Chicago, she convinced Dr. Leon O. Jacobson, a colleague and mentor, to provide her with a tiny laboratory space, access to a microscope, and a small stipend of $5,000 to cover her expenses for a babysitter. An expert on leukemia, Dr. Jacobson suggested she apply the new technologies to cancer, and she set out to find chromosomal abnormalities in samples from Jacobson’s patients. Although she was spurred on by Nowell and Hungerford’s discovery of “a small minute chromosome” or the “Philadelphia (Ph) chromosome” in the malignant cells from patients with chronic myelogenous leukemia (CML) in 1960, her tireless efforts met with limited success for almost a decade. In 1970, a seismic shift came in the field of cytogenetics with new approaches to stain and, therefore, differentiate chromosomes. Janet learned chromosome banding during a second sabbatical at Oxford University (1970–1971), and would cut out and arrange the fluorescently stained chromosomes on her dining room table, an activity her children referred to as “playing with paper dolls.” In fact, she often reminisced how she would instruct her children not to sneeze, cough, or otherwise disturb the painstakingly arranged karyotypes. It was in her careful analysis of chromosomes from patients with acute myeloid leukemia (AML) in 1972 that she noticed that two chromosomes had exchanged genetic material; specifically, a piece of chromosome 8 had been swapped with material from chromosome 21, and vice versa. Soon thereafter, Janet discovered another translocation, this time an exchange between chromosomes 9 and 22, involving the Ph chromosome in CML. Janet proposed that cancer was a genetic disease and that these recurring chromosomal abnormalities were causative for the cancer phenotype. Like the pioneers of old, Janet took some “arrows in the back.” That is, the concept was not received with enthusiasm by many hematologists and scientists, and she had to be remarkably persistent. By 1977, when Janet and her colleagues discovered a third translocation—in this case the t(15;17) in acute promyelocytic leukemia—the cancer community began to accept the idea that recurring chromosomal abnormalities could drive cancer phenotypes. Nonetheless, it was another decade before the recognition of oncogenes and development of molecular biology technologies led to the cloning of the several translocation breakpoints and identification of the involved oncogenes, thereby ending her decades long crusade to convince the scientific community that chromosomal abnormalities in tumors were the cause of...
the malignant phenotype, rather than irrelevant epiphenomena that occurred as a result of cancer.

Anyone who knew Janet knows that she exemplified independent thinking and perseverance. She herself maintained that the University of Chicago taught her to stick to her convictions, even when others disagree. Thanks to her persistence and a long list of discoveries, her ideas gained credence. Eventually, they brought her widespread recognition, including the Lasker Prize, the National Medal of Science, the Presidential Medal of Freedom, the Japan Prize and, perhaps the most meaningful as they were bestowed by her peers in the American Association of Cancer Research (AACR), the Dorothy P. Landon Foundation Prize for Translational Cancer Research (2005), the Lifetime Achievement Award (2010), and membership in the Inaugural Class of the Academy of the AACR (2013). How she managed to pursue her beliefs and ideas relentlessly—all the while always being informed on all aspects of the particular issue at hand, maintaining impeccable professional and personal grace, and eventually obtaining her goal far more often than not—remains a mystery. These skills allowed her to become a remarkable statesman for the field, particularly when she and other colleagues brought together the leading cytogeneticists and clinicians for a series of international workshops, providing a collaborative forum that showed for the first time that chromosomal abnormalities were independent prognostic factors in leukemia, ultimately transforming the field.

These seminal discoveries, most of which were made when she was well into her 50s or after, were just the beginning of Janet’s impact on the cancer genetics field. She and her colleagues described numerous recurring translocations in the hematologic malignant diseases, as well as the association of abnormalities leading to loss of genetic material from chromosomes 5 and 7 with therapy-related myeloid neoplasms. Her laboratory cloned the breakpoint of the common translocations of 11q23 that she named MLL for myeloid–lymphoid leukemia (now referred to as KMT2A), work that ultimately led to the cloning of nearly 75 MLL translocation partner genes, as well as the characterization of the role of lysine methyltransferases in cancer. Her most recent research efforts focused on the role of microRNAs in human leukemia, and the molecular basis and consequence of epigenetic modifications in MLL-rearranged leukemia. She truly enjoyed watching the field and accompanying technologies evolve, but also warned that as more chromosomal alterations are identified in tumors, it will be increasingly important to distinguish those that are drivers, rather than passengers.

Janet’s legacy in cancer research includes her contributions to our understanding that cancer is not one disease, but is instead composed of many distinct subtypes characterized by unique genetic abnormalities. This is a concept often taken for granted in this post-genomics era, but was not widely accepted during the time of Janet’s early work. Moreover, her scientific achievements provided the groundwork for personalized (also known as precision or genomics-driven) oncology (i.e., exploiting the distinct molecular features of a tumor for rational treatment that is tailored to individual patients). To this day, imatinib (marketed as Gleevec), stands as one of the true success stories in targeted therapies for cancer. This ABL1 tyrosine kinase small-molecule inhibitor was approved for use in CML in 2001, four decades after the discovery of the Ph chromosome, and dramatically improved patient survival, changing the natural history of this disease. Even as researchers continue to unravel the mechanisms of relapse and drug resistance, it is clear that these developments would not have been possible without Janet’s characterization of the genetic basis of cancer. As she recently described in a perspective piece in Science on discoveries in pursuit of personalized medicine approaches for cancer, “There will be many surprises along the way, and paradigms will be discarded. Nevertheless, the goal will always be the same—to treat disease and benefit the patient.”

Beyond her impact on the scientific community, Janet will be remembered for the way she lived her life with humility, grace, wonder, vigor, and generosity. She was a mentor who had the rare gift of both showing her enthusiasm for each small accomplishment in the laboratory and staying laser-focused on the major questions and big picture. Janet had a passion for science and what it could do for humanity. Up until her death, she fought for federal research funding and worked tirelessly to help her colleagues secure support for their research. Over the years, she shared her pure love of discovery with over a hundred trainees and paved the way for many scientists, serving as an exemplary role model for women in science and medicine.

Importantly, Janet always encouraged individualism, professional freedom, and thinking outside the box. This was one secret to her success in science, and she gladly passed on its value to her students, fellows, and colleagues.

As a postdoctoral fellow in Janet’s laboratory, one of the authors (M.M. Le Beau) witnessed Janet’s finesse in addressing the challenges in academia on many occasions, but one particular event stands out. In the early 1980s, our group defined a new clinical–morphologic–cytogenetic subset of AML characterized by the inv(16)(p13.1q22) [now recognized by the World Health Organization (WHO) Classification as an entity within “AML with recurrent genetic abnormalities’’) and submitted the description to a preeminent journal, only to receive a polite rejection, accompanied by a scathing review, questioning the existence of this new cytogenetic entity and suggesting that we “could not karyotype our way out of a paper bag.” As a young researcher, this review was devastating, causing me to question my chance of success in this career. Janet only laughed, and patiently reminded me of the clinical and scientific importance of the finding, after which she quietly spoke to the editor of the journal and secured the review of a revised manuscript. When we received notification from the journal of the acceptance of the article shortly thereafter, Janet’s simple response was memorable: “Virtue triumphs!”

Despite her professional success, Janet’s family was always one of her highest priorities. She worked part-time for more than 20 years to raise her children and often attributed her success in science to her life–work balance and the richness of
her life outside of science. In addition to her family, her beautiful (and award-winning) garden, traveling, and the opera were her passions. Janet is survived by three of her four sons and five beloved grandchildren, who also lost their father and grandfather, Don, last year. Humankind has been enriched by Janet's work, and those who knew her are richer for her life. Virtue does indeed triumph!

Kathleen H. Goss
Michelle M. Le Beau
University of Chicago Medicine Comprehensive Cancer Center
Chicago, IL

Published OnlineFirst March 25, 2014.
Janet Davison Rowley: In Memoriam (1925–2013)

Kathleen H. Goss and Michelle M. Le Beau


Updated version  Access the most recent version of this article at:
doi:10.1158/0008-5472.CAN-14-0519

E-mail alerts  Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions  To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions  To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.