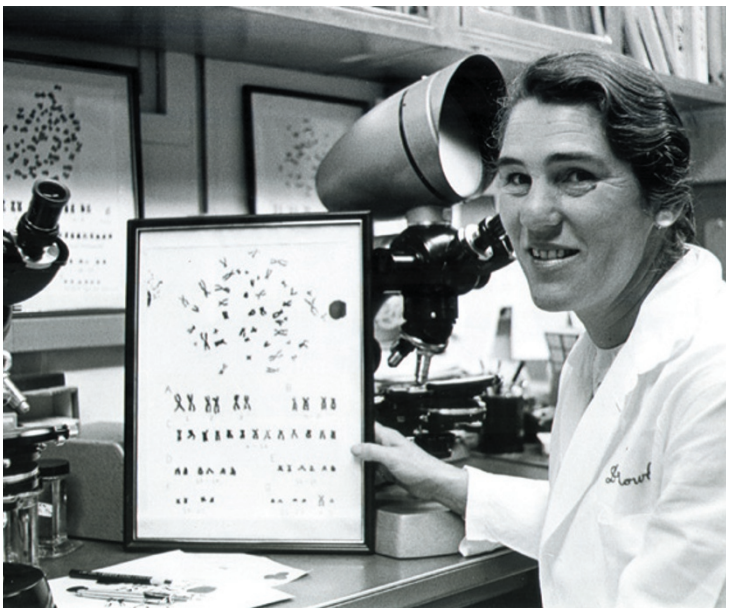
Janet Rowley

(1925–2013)

Geneticist who discovered that broken chromosomes cause cancer.

Janet Rowley, the 'matriarch of modern cancer genetics', transformed our understanding of cancer. In the 1960s she would cut out 'paper dolls' at the dining room table — but not for her children to play with. These photographs of human chromosomes eventually yielded discoveries that established the genetic basis of cancer and led to targeted cancer therapies.



UNIV. CHICAGO MEDICINE

Janet Davison was born in New York City on 5 April 1925 and spent most of her life in Chicago, Illinois. Encouraged by her mother, a high-school teacher and librarian, Janet received her bachelor's degree from the University of Chicago at the age of 19. Accepted subsequently to the university's medical school, she had to wait nine months to enrol because the school had already reached its quota of women: three in a class of 65. The day after her graduation in 1948, she married a classmate, Donald Rowley, who later became a distinguished pathologist.

In 1955, Janet began working part-time in a local clinic, where she treated children with Down's syndrome. The developmental disorder was linked in 1959 to an extra copy of chromosome 21, and Rowley became fascinated with inherited genetic diseases. When her husband took a sabbatical in England in 1961, she arranged to study with Laszlo Lajtha, a haematologist at the Churchill Hospital in Oxford. There, she began to examine chromosomes in the laboratory.

Returning to the United States in 1962, she secured a job with Leon Jacobson, a haematologist at the University of Chicago. Rowley asked for a darkroom, a microscope and a salary sufficient to pay a babysitter. Over the next decade, she scoured cells from people with leukaemia, looking for chromosomal abnormalities.

During a second sabbatical in Oxford, she perfected techniques to stain chromosomes, making it easier to identify them. She was the first to realize that bits of chromosomes in some human cancer cells had broken off and swapped places — a phenomenon known as translocation. The translocation that she identified between chromosomes 8 and 21 is now known to account for up to 12% of cases of acute myeloid leukaemia. She published the work in a singly authored paper in June 1973 (J. D. Rowley *Ann. Genet.* **16,** 109–112; 1973). The same month, she published a paper in *Nature* (J. D. Rowley *Nature* **243,** 290–293; 1973) that characterized a genetic abnormality found in people with chronic myeloid leukaemia.

Rowley showed that the 'Philadelphia chromosome', an aberrant version of chromosome 22 (named after the city where researchers identified the abnormality) was a genetic swap: the truncated chromosome 22 was accompanied by an elongated chromosome 9. Previously, a large genetic deletion had been thought to be involved. In 1977, she identified a third translocation, in people with acute promyelocytic leukaemia.

Her work was met with a chorus of scepticism and wonder that anyone would bother to study chromosome abnormalities, which were then considered to be an effect of disease rather than a cause. By the 1980s, however, each of the abnormalities had been molecularly characterized, revealing that translocations create 'fusion' proteins that drive cell growth. Since then, dozens of translocations have been found in other cancers.

For acute promyelocytic leukaemia, Rowley's discovery helped to uncover the mechanism behind an effective drug: retinoic acid. A derivative of vitamin A, the drug restores normal function to its disrupted protein receptor.

For chronic myeloid leukaemia, a disease that was once a death sentence, Rowley's discovery enabled work that led to new, effective treatments including imatinib, approved in the United States in 2001. She received numerous prestigious prizes for her research.

I first met Janet in 2000, when the efficacy of imatinib was well known. Aged 75, instead of dwelling on her seminal work on chronic myeloid leukaemia, she told me about new pathogenetic mechanisms of acute myeloid leukaemia that she was working on, and that she swam regularly in Lake Michigan and cycled to and from work.

Janet was also outspoken about her beliefs. Despite serving on former US President George W. Bush's Council on Bioethics, she was highly critical of the administration's policy that barred federal funding of embryonic stem-cell research. In 2009, she stood next to President Barack Obama when he lifted the ban.

In 2012, Janet, Nicholas Lydon and I were awarded the Japan Prize for work that led to imatinib. By the last evening of the week-long events surrounding the prize, I was spent. Janet, 30 years my senior and recovering from chemotherapy for ovarian cancer, was still going strong. I asked her how she managed. With a twinkle in her eye, she replied that I had had to chase my three children around while she had been able to rest.

That summed up Janet. She had incredible energy and curiosity and was gracious and humble, with the ability to make others around her feel good about themselves. ■

Brian J. Druker *is director of the Knight Cancer Institute at Oregon Health & Science University, Portland, Oregon, and a Howard Hughes Medical Institute investigator. He shared the 2012 Japan Prize with Janet Rowley and Nicholas Lydon.*
e-mail: drukerb@ohsu.edu