

A Foundational Discovery

Fifty years ago, Peter Nowell and David Hungerford published an article about an unusually small and defective chromosome they found in leukocytes present in patients with a form of blood cancer. Their findings would change the way cancer is understood.



It all started, if Peter C. Nowell, M.D. '52, can be believed, back in 1956, when he embarked on what he has described as “some poorly defined studies of leukemia, looking at the growth and differentiation of human leukemic cells in irradiated mice and *in vitro*.” He has written about his “remarkable lack of manual dexterity in the laboratory.” Once, he even characterized his experiments as “diddling around with leukemic cells in culture.” Not much there, one might assume?

Most observers would beg to differ.

In his more than half a century as a member of Penn's medical faculty, Nowell, the Gaylord P. and Mary Louise Harnwell Emeritus Professor of Pathology and Laboratory Medicine, has made his mark on the School of Medicine, the University of Pennsylvania, and biomedicine in general. He has received many honors – among the most notable the Albert Lasker Medical Research Award, often considered the American Nobel Prize. Other honors include the Parke Davis Award in Experimental Pathology, the Robert de Villiers Award of the Leukemia Society of America,

and the Fred Stewart Award from the Memorial Sloan-Kettering Cancer Center. In addition, he has been elected to the Institute of Medicine, the National Academy of Sciences, and the American Academy of Arts and Sciences.

But 2010 has been a particularly busy time for Nowell, whose work is being celebrated with fresh vigor. The reason? 2010 is the 50th anniversary of the discovery of the Philadelphia chromosome by Nowell and the late David Hungerford, a graduate student at the Institute for Cancer Research in Fox Chase. (He went on to earn his Ph.D. degree from Penn.) Nowell may have written about the first steps toward this major discovery in his characteristically modest way, but there is no doubting the vigor and tenacity with which he and Hungerford developed their finding – or, as subsequently became clear, the significance of the Philadelphia chromosome in medical history.

What they discovered was that cells Nowell had taken from patients with chronic myelogenous leukemia (CML)

had an altered, minute chromosome. They published their finding in *Science* “with caution,” Nowell has written, and the techniques did not exist then to determine whether the minute chromosome results from a deletion or a translocation.

At the time of their discovery, most scientists believed cancer was caused by viruses and did not have a genetic basis. Indeed, the Nowell-Hungerford paper in *Science* was not immediately embraced. But what it showed, according to the Lasker Foundation, was “the first clear evidence that a particular chromosome can lead to a population or clone of identical cells that accumulate in numbers to form a deadly malignancy.” The researchers were the first to describe a consistent cytogenetic abnormality associated with malignancy – subsequently christened the Philadelphia chromosome. John Tomaszewski, M.D. '77, G.M.E. 83, the interim chair of Penn's Department of Pathology and Laboratory Medicine and a former student of Nowell's, describes it as “a discovery that changed in a very significant way how we think about cancer.”



The two discoverers of the Philadelphia chromosome, photographed in the early 1960s. David Hungerford is on the right.

Building on Nowell's work, scientists later discovered the gene that causes CML; more recently, too, scientists were able to produce Gleevec, a drug that can block the effects of the gene and cure the disease in a great proportion of cases.

Honors and More Honors

But back to this year's honors. Philadelphia's Franklin Institute presented Nowell with the 2010 Benjamin Franklin

Medal in Life Science. In addition to noting the impact of the Philadelphia chromosome, the institute also highlighted Nowell's discovery that irradiation allowed improved bone marrow transplants in mice, even when it came from a different species. It also noted that Nowell found that a plant protein called phytohemagglutinin (PHA) could be used to stimulate cell division. As

Nowell described it in his "personal perspective" called "From Chromosomes to Oncogenes" (1993): "Subsequently, . . . PHA combined with improved hypotonic solutions and the air-drying technique, described in collaboration with Paul Moorhead and Bill Mellman as well as Dave Hungerford, became the standard lymphocyte culture method that remains widely used for routine constitutional chromosome studies."

This April also saw a campus symposium in Nowell's honor, "Genetic Basis of Cancer." Experts in the field, both members of the Penn faculty and distinguished scientists from other institutions, spoke. Then, in May, Nowell received an honorary Doctor of Science from the University of Pennsylvania. According to the citation, Nowell's discovery of the Philadelphia chromosome "significantly advanced the world's understanding of the genetic basis of this disease and provided the modern foundation for the fields of cancer biology and cancer genetics."

The citation also made note of Nowell's other forms of service to the School of Medicine and to the University. He was the first director of what is now Penn's Abramson Cancer Center, and he served as chair of the Department of Pathology and Laboratory Medicine for six years.

And no consideration of Nowell as professor would be complete without noting his role in the classroom. As his Lindback Award for Distinguished Teaching demonstrates, he has earned the admiration of his students and colleagues in the sphere of education. As Tomaszewski puts it, "I remember being a medical student in 1974, listening to a chalk talk on clonal evolution in neoplasia by this white-haired professor with a big smile. No slides, just passion and enthusiasm for a concept and the opportunity to convey that concept to students." In addition, as mentor and advisor, Nowell was well known to have a door that was always open to students and colleagues. As he wrote in his "Personal Perspective," he sought to show young researchers the importance of "an environment that allows them to pursue unexpected findings, question accepted dogma, and enjoy the privilege of investigating the complexities that underlie human disease." That outlook is an essential part of Nowell's legacy as well. ♥

— John Shea



Amy Gutmann, Ph.D., Penn's president, reads the citation honoring Peter Nowell at this year's Commencement.