In Memoriam: Alfred G. Knudson, Jr., MD, PhD

Alfred G. Knudson, Jr., MD, PhD, Fellow of the AACR Academy, died July 10, 2016, at the age of 93. Knudson was a pioneering cancer researcher who is internationally recognized for his groundbreaking “two-hit” hypothesis, which helped provide the basis for our current understanding of the genetic origins of cancer.

Knudson, AACR member since 1976, was distinguished scientist and senior advisor to the president at Fox Chase Cancer Center in Philadelphia, where he served in various leadership positions throughout his career.

Knudson was a world-renowned cancer geneticist and physician who treated children with retinoblastoma. In 1971, after years of observing and treating children with this rare type of cancer, he proposed the two-hit hypothesis to explain the relationship between the hereditary and nonhereditary forms of the disease. The hypothesis predicted that retinoblastoma would develop only if both copies of a key gene are lost, or are inactivated and unable to function. Thus, it predicted the existence of tumor-suppressor genes, which can suppress cancer cell growth.

At the time Knudson proposed the hypothesis, it was based on statistical models he had developed. Five years later, he mapped the retinoblastoma susceptibility gene to chromosome band 13q14. This work laid the foundation for the eventual cloning of RB1, the first tumor-suppressor gene, a decade later, once the molecular technologies needed for gene cloning had become available.

The now-confirmed two-hit hypothesis advanced understanding of the genetic mutations that turn normal cells into cancer cells. It also guided the work of many geneticists and molecular biologists over the years and provided powerful insights into the development of cancer that continue to hold implications for both cancer treatment and prevention.

Knudson’s scientific accomplishments have been widely recognized. He was the recipient of the Charles S. Mott General Motors Cancer Research Foundation Prize in 1988, the American Cancer Society Medal of Honor in 1989, the Canada Gairdner International Award in 1997, the Albert Lasker Award for Clinical Medical Research in 1998, the Distinguished Career Award from the American Society of Pediatric Hematology/Oncology in 1999, the Kyoto Prize in 2004, the Bristol-Myers Squibb Freedom to Discover Award for Distinguished Achievement in Cancer Research in 2005, and the AACR Lifetime Achievement Award in 2005. Knudson was elected a member of the National Academy of Sciences in 1992 and an inaugural Fellow of the AACR Academy in 2013.
In addition to his academic and research contributions, Knudson was an active member of the AACR, serving as associate editor of *Cancer Research* from 1985 to 2000 and on the editorial board of *Cancer Epidemiology, Biomarkers & Prevention* from 1991 to 1998. Additionally, he was a member of the 2012 AACR Award for Lifetime Achievement in Cancer Research Committee.

Born in Los Angeles, Aug. 9, 1922, Knudson received his medical degree at Columbia University in New York and his doctorate in biochemistry and genetics at the California Institute of Technology in Pasadena. He was a senior member of the scientific research staff at Fox Chase Cancer Center since 1976, including serving as director of the Fox Chase Institute for Cancer Research from 1976 until 1982, president of Fox Chase Cancer Center from 1980 to 1982, and scientific director of the cancer center from 1982 to 1983.

Knudson is survived by his wife, Anna Meadows, emeritus member of the AACR and emeritus professor of pediatrics and medicine at the Perelman School of Medicine at the University of Pennsylvania, six children and stepchildren, 10 grandchildren and step grandchildren, and two great grandchildren.

References:
