

# Stanley J. Korsmeyer

## 1950–2005

Stanley J. Korsmeyer, a pioneer and leader in the field of programmed cell death, died of lung cancer on 31 March 2005. Widely recognized as one of the world's leading cancer biologists, Korsmeyer will also be remembered as one of this generation's greatest role models and mentors by those fortunate enough to have worked with him.

Korsmeyer, known as 'Stan' to all, was raised on a livestock farm in Illinois. He distinguished himself at the early age of 14 by showing a pair of hogs and winning the Governor's Trophy at the Illinois State Fair. Early on he studied for a career in veterinary medicine, but a wise veterinarian guided him into a career in medicine. He completed a BA in biology from the University of Illinois-Urbana (1972), and an MD at the University of Illinois-Chicago (1976). After a residency at the University of California, San Francisco, he became an associate and then a senior investigator at the National Cancer Institute.

During this time, along with others, he cloned the *BCL2* gene (Bakhshi, M. *et al. Cell* 41, 899–906; 1985) and began studying how the protein product was involved in follicular lymphoma. After moving to Washington University in 1986 as a Howard Hughes Medical Institute investigator, Stan embarked on studies that would transform the landscape of cancer biology along with many other fields. Building on earlier work of Vaux, Cory and Adams (Vaux, D. L. *et al. Nature* 335, 440–442; 1988) he developed both transgenic and knockout mice that conclusively showed a role for Bcl2 in blocking cell death (McDonnell, T. J. *et al. Cell* 57, 79–88; 1989; *Cell* 75, 229–240; 1993). Moreover, Bcl2-expressing transgenic mice developed lymphoma, establishing inhibition of cell death as a new pathway in oncogenesis (McDonnell, T. J. *Nature* 349, 254–257; 1991). His laboratory established that Bcl2 was a mitochondrial protein (Hockenbery, D. M. *Nature* 348, 334–336; 1990) that interacted with and inhibited another class of Bcl2 homologues — including proapoptotic proteins such as Bax — preventing mitochondrial permeabilization, cytochrome c and caspase activation, and ultimately cell death (Oltvai, Z. *Cell* 74, 609–619; 1993). He popularized the notion that the Bcl2 family homo- and heterodimers function as rheostats controlling cell death and survival. His laboratory went on to clone many other *Bcl2* family members and defined pathways that were pivotal to not only cancer biology but several other fields including immunology, neuronal survival, chemotherapeutic action, and oxidant-induced stress. In 1998 he was recruited from his post as director of the Division of Molecular Oncology at Washington University to the Dana Farber Cancer Institute, where he served as the Sidney Farber professor of pathology and professor of medicine at Harvard Medical School.

Korsmeyer is best known for his work in cell death but he was also a leader in other areas of cancer biology. His laboratory cloned the *MLL* gene that is rearranged in mixed-lineage leukaemias (Domer, P. H. *et al. Proc. Natl Acad. Sci. USA* 90, 7884–7888; 1993), and showed that it regulated *Hox* gene expression (Yu, B. D. *et al. Nature* 378, 505–508; 1995). Subsequent microarray and functional studies from his laboratory confirmed a role for *Hox* gene deregulation in leukaemias harbouring



*MLL* rearrangements (Armstrong, S. A. *Nature Genet.* 30, 41–47; 2002). All told, he published over 300 chapters and scientific papers, and, with over 46,000 citations, is one of the most cited biomedical researchers. He was elected to the National Academy of Sciences in 1995, the Academy of Arts and Sciences in 2000, and received numerous honours including the Bristol Myers Squibb award for Cancer Research and the Charles S. Mott Prize of the General Motors Cancer Research Foundation. Many expected he would eventually receive a Nobel Prize.

People meeting Stan for the first time were often surprised at how unpretentious and affable he was. "How ya doing, guy?" he would say, often with a pat on the shoulder but always with an infectious smile. He made visitors feel at ease and spoke often of his family, his wife Susan and sons Jason and Evan, and of his mid-western roots. It did not take much time with Stan to realize that he also operated on a much higher intellectual plain than most of us. He spoke and wrote with great eloquence and precision, reflecting his clear thinking and extraordinary intellect. He was curious about everything and had a special knack for asking questions that hit right at the heart of the issue. He was extremely focused, hard working and optimistic, and highly intolerant of self-doubt or procrastination. He was gifted at selecting the right people and inspiring them to get the job done.

People of Stan's greatness, who bring out the best in everyone around them, are rare. He taught us that honesty, hard work, determination and optimism are the makings of success, both in science and in life. We would do well to remember these lessons and pass them on to future generations.

JAY L. HESS

University of Pennsylvania School of Medicine, 413b Stellar Chance Laboratories, 422 Curie Boulevard, Philadelphia, PA 19104, USA.  
e-mail: jhess@mail.med.upenn.edu