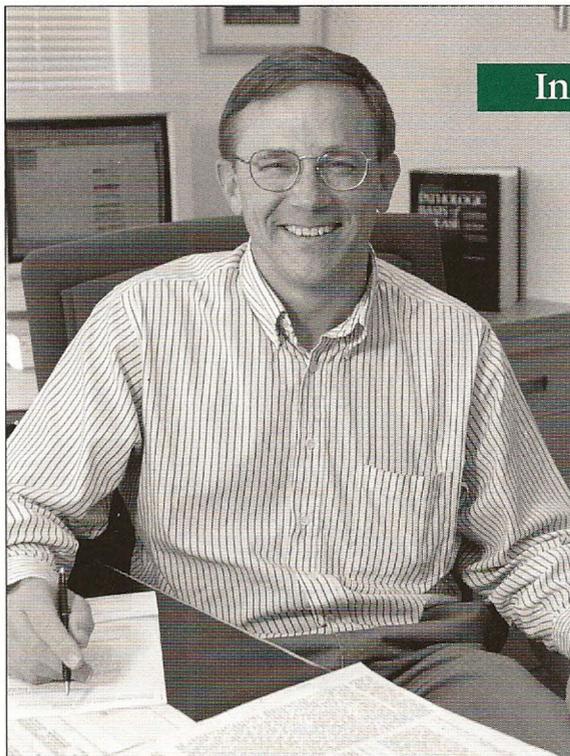


DANA-FARBER
CANCER INSTITUTE

SCIENTIFIC REPORT 2005

In Memoriam



Stanley J. Korsmeyer, MD
June 8, 1950 to March 31, 2005

Although he was a visionary scientist
and a natural leader, he was even
more so a compassionate human being
whose mission was to heal.

Stanley J. Korsmeyer, MD, a scientific leader at Dana-Farber and among the most admired figures in cancer research, died on March 31, 2005, from complications of lung cancer. He had never smoked. Known universally as “Stan,” he was hailed as a scientist of powerful insight and industry, and is remembered with deep fondness as a role model, mentor, husband, father, and friend.

Dr. Korsmeyer's untimely death at age 54 was a blow to the Dana-Farber community and to colleagues throughout the cancer research enterprise. An entirely new avenue in understanding and treating the disease opened with his recognition, based on findings published in 1985, that cancer reflects not only uncontrolled cell growth, but also the body's failure to eliminate unwanted, dangerous cells through apoptosis, or programmed cell death.

Pursuing this insight led Dr. Korsmeyer and others through a cascade of discoveries about a molecular family that regulates apoptosis and, in cancer, allows damaged cells to survive instead of self-destructing for the good of the individual. At the time of his death, he and members of his lab were beginning to see the dawn of a new therapeutic era based on manipulating cell death and survival.

“Stan Korsmeyer was one of the world's great scientists and one of its greatest people,” said Edward J. Benz Jr., MD, president of Dana-Farber. “He was admired and loved for who he was, even more than for what he accomplished. Even in the face of his illness, he was determined to take care of and support his family and those who depended on him in his lab. We will all miss him profoundly.”

Dr. Korsmeyer headed the Program in Molecular Oncology within the Department of Cancer Immunology and AIDS, and, as chair of the Executive Research Committee, was an important voice in the Institute's new Strategic Plan for Research. At Harvard Medical School, he was the Sidney Farber Professor of Pathology and Professor of Medicine.

Dr. Korsmeyer's research had been supported by the Howard Hughes Medical Institute, of which he was an investigator, since 1986, when he moved to Washington University in St. Louis from his previous post at the National Cancer Institute. In 1998 he was recruited to join the Dana-Farber faculty.

Following his diagnosis in early 2004 and through the ups and downs of chemotherapy, Dr. Korsmeyer continued to do research, write papers, and lead his large laboratory. “He was very tough scientifically, and that toughness applied to how he fought his disease,” recalled Loren Walensky, MD,

Dr. Korsmeyer's research on *Bcl-2* and other regulators of apoptosis
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PhD, a member of the lab, who is translating the knowledge gained about apoptosis and cancer into new cancer drug candidates.

Throughout his stellar and much-honored career, Dr. Korsmeyer was regarded as a powerful and focused scientific visionary with an iron core of determination, tempered by a sunny, upbeat disposition. As a mentor, he guided the early careers of many postdoctoral fellows, graduate students, and technicians.

Stanley Joel Korsmeyer was born in 1950 on his family's livestock farm in southwestern Illinois. His first claim to fame was the Governor's Trophy he won at 14 by showing a pair of hogs at the Illinois State Fair. Thoughts of becoming a veterinarian turned instead toward medicine on the advice of a local vet.

"What an incredibly good piece of advice that would turn out to be," wrote Timothy J. Ley, MD, associate director of the cancer center and professor of medicine at Washington University, in a tribute in *Science*. Though the young Korsmeyer had no idea how to pursue such a goal, Ley continued, "His parents prepared him for life with the bedrock values of farming: thoughtful preparation, hard work, personal integrity, and neighborly kindness."

After receiving his BA in biology from the University of Illinois-Urbana and his MD from the University of Illinois-Chicago, Dr. Korsmeyer did a residency at the University of California, San Francisco. It was in San Francisco that he met his future wife, Susan Reynard, an oncology nurse.

Beginning his research career at the National Cancer Institute, Dr. Korsmeyer collaborated with Thomas Waldmann, MD, Philip Leder, MD, and others to define immunoglobulin gene rearrangements in normal and diseased B lymphocytes. This work led, after Dr. Korsmeyer had joined the faculty at Washington University, to his most important discovery, one that would set the direction of his future research.

In 1985, he and his colleagues identified a gene, *Bcl-2*, that was abnormally activated by an accidental rearrangement of chromosomes in follicular lymphoma cells, enabling them to survive despite signals commanding the unwanted cells to die.

An editorial in *Nature Immunology* honoring Dr. Korsmeyer described the significance of the findings: "*Bcl-2* turned out to be a highly conserved 'master regulator'

of cell survival," suggesting that "the first step of oncogenesis might be a failure to execute apoptosis. This idea not only changed prevailing views of oncogenesis but opened new vistas for therapeutic intervention in the clinic."

At Washington University, and after he moved to Dana-Farber in 1988, Dr. Korsmeyer led his laboratory teams in studying the function and regulation of *Bcl-2*, the founding member of a family of proteins that regulate apoptosis. These proteins include the proapoptotic molecules BAX, BID, and BAD, and antiapoptotic factors that are "now known to be essential for normal lymphocyte development, homeostasis, and effector function. Thus the identification of *Bcl-2* has opened up new areas for investigation of how the immune system regulates life and death," said the *Nature Immunology* editorial.

Dr. Korsmeyer's career was strewn with honors and accolades. Among them were membership in the National Academy of Sciences, the Institute of Medicine, and the American Philosophical Society; the Bristol-Myers Squibb Award, and the Charles S. Mott Prize of the General Motors Cancer Research Foundation. Dr. Korsmeyer also received the 2000 Louisa Gross Horwitz Prize, the first annual Wiley Prize in the Biomedical Sciences, the Leukemia & Lymphoma Society's de Villiers International Achievement Award, and the International Award for Cancer Research from the Pezcoller Foundation and the American Association for Cancer Research. Dr. Korsmeyer was especially pleased to receive the A. Clifford Barger Excellence in Mentoring Award from Harvard Medical School in 2004.

His own mentor as a medical student was the noted hematologist Paul Heller, MD, who was a Holocaust survivor. Dr. Heller had "rebounded from that adversity with such reverence for life and belief in individuals that he developed an unending optimism that the next experiment could improve the lot of mankind," said Dr. Korsmeyer, whose life, work, and teaching were imbued with a similar spirit of hopefulness.

Despite all of these awards, wrote Dr. Ley in the *Science* retrospective, Dr. Korsmeyer's source of greatest pride was his family. His wife of 25 years, Susan, and his sons, Jason and Evan, were the most important people in his life." Dr. Ley continued: "Although he was a visionary scientist and a natural leader, he was even more so a compassionate human being whose mission was to heal."