

## Eva Klein (1925–2025)

By Maria G. Masucci & Ingemar Ernberg

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**E**va Klein, a pioneer of tumor immunology, died peacefully surrounded by her family on 19 January 2025, three days before her 100th birthday. During a nearly 70-year-long scientific career, Eva made numerous contributions to basic science that have revolutionized immunology and biomedicine. Born in Budapest, Hungary, on 22 January 1925, Eva moved to Sweden in 1947, escaping from the falling ‘Iron Curtain’ with her fellow university student and newlywed husband Georg Klein. In the early 1950s, as young medical students at the Karolinska Institutet in Stockholm, the couple joined the laboratory of Torbjörn Caspersson, known for the development of photoelectric spectrophotometry and the discovery of chromosome banding by quinacrine staining. In this stimulating environment, they began their research on the nucleic acids of tumor cells. Eva became a professor of tumor biology in 1976 and a member of the Swedish Academy of Science in 1987. In 2013, she was elected fellow of the American Association for Cancer Research. She served as a member of the Nobel Assembly at Karolinska Institutet and received numerous recognitions and prizes.

Before the discoveries of DNA structure and the genetic code, the function of nucleic acids, an abundant but mysterious cell component, was the subject of wide speculation. Studying the DNA content of Ehrlich carcinoma ascites cells – a considerable improvement from earlier studies on solid tumors – the Kleins found a correlation between the DNA content and growth properties of malignant cells. Subsequent studies showed that malignancy was associated with chromosomal abnormalities and permanent changes in histocompatibility and other genes. The studies culminated with the discovery, published in 1960, that the pretreatment of syngeneic mice with irradiated sarcoma cells inhibited the growth of methylcholanthrene-induced tumors. Tumor resistance was not achieved by pretreatment with irradiated normal cells, was specific for the challenging tumors, was abolished by total body irradiation before tumor challenge, and correlated with the inhibition of tumor cell growth by lymph node cells from the pretreated mice. The findings were the first conclusive



evidence of endogenous tumor antigens and tumor-specific immune responses.

The Swedish Cancer Foundation saw the potential of the young couple and, through a national fundraising campaign, donated a new research building. Eva sketched a plan on a paper napkin that became the blueprint for the construction. In the Department of Tumor Biology, Eva and Georg created a dynamic and, in many aspects, unique research environment. At a time when modern tumor biology was in its infancy, the Department contributed fundamental discoveries in cancer genetics, tumor immunology, cell biology and virology. It became a sought-after destination for leading scientists from all over the world. In the early 1960s, Eva suggested researching a human tumor. The choice fell on Burkitt’s lymphoma, later shown to carry Epstein–Barr virus (EBV), the first known human tumor virus. A skilled experimentalist, she established several Burkitt’s lymphoma cell lines that were instrumental in the groundbreaking discovery of chromosomal translocations that activate the *MYC* oncogene.

Eva and Georg had very different personalities but complemented each other. Eva provided a creative, unconventional, and somewhat unruly counterbalance to Georg’s unwavering work discipline and absolute focus. Although Eva often stood behind her brilliant husband – in line with the customs of the time and her leading role as homemaker and mother of three children – she pursued independent lines of research, with

a prominent focus on tumor immunology. Her talent for ‘jumping off the bandwagon’ and ‘thinking outside the box’ is best illustrated by the realization that the non-specific cytotoxicity observed in the tumor rejection experiments of Rolf Kiessling, a young PhD student whom she co-supervised together with Hans Wigzell, was not a technical artifact. She named it ‘natural killing’, marking the birth of the natural killer (NK) cells. In a paper published in 1980, the activation of NK-like cytotoxicity by culturing T cells with tumor cells or T cell growth factor (TCGF, now known as interleukin-2) was described and called ‘activated lymphocyte killing’ (ALK). The effectors were later renamed ‘lymphokine-activated killer’ (LAK) cells and became a cornerstone of modern anticancer cell therapies.

For those who had the privilege of being her students and colleagues, Eva was very special: creative, insightful and warm, with a deep understanding of human nature, outspoken, unconventional to almost defiant, and with a profound sense of humor. Science was, for her, ‘above all great fun’. She wrote short essays, and after retirement, while continuing her research as an emeritus professor, she translated poems from Hungarian to Swedish. In the essay *‘Eva Climbs over the Grave’* (in *‘Dear Eva, Dear Georg’*, Karolinska Institutet, 2023), she tells the compelling story of her early life in Budapest. She describes a privileged and creative environment, her dreams of athletics, literature, and art... and the coming of Nazism, racial laws, the escape from deportation and brave rescue of a beloved brother, and the loss of friends and family. She would realize her dreams in a new homeland. Life turned out differently from young Eva’s dreams, but art and science were always intertwined.

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### Competing interests

The authors declare no competing interests.