Isaiah Joshua ('Josh') Fidler 1936–2020

On 8 May 2020, Josh Fidler passed away at this home in Houston, Texas. Born on 4 December 1936 in Jerusalem to Shoshana Stern and Pinchas Fidler, he grew up in the Palestine Mandate. His father, a renowned soccer player who captained the Mandatory Palestine National team, tragically died in the Arab–Israeli war in 1948. His mother, who worked in the newly formed government, inspired him to seek a higher education at a time when most young people in Israel were being asked to consider farming and construction.

After finishing his early education and serving in the Israel defense forces, Josh left Israel for Stillwater, Oklahoma, where he earned his doctorate in veterinary medicine from Oklahoma State University in 1963. He then moved to Philadelphia, where he worked as a surgical oncologist at the University of Pennsylvania School of Veterinary Medicine, eventually earning his doctoral degree in human pathology, which set the stage for his seminal contributions to cancer biology and metastasis.

Josh was convinced that metastasis is an organized set of genetic and cellular events, and unraveling the molecular underpinnings of this process became his lifelong quest. In 1975, he joined the National Cancer Institute to lead the newly formed metastasis research program at the Frederick Cancer Research and Development Center (now the National Cancer Institute at Frederick). While there he published a series of papers in *Nature* and *Science* that had a transformative impact on the field of cancer metastasis, and he launched a renewed effort to determine the fundamental underlying biology of cancer metastasis and to develop specific therapies.

In 1983, the University of Texas MD Anderson Cancer Center (UT MDACC) recruited him as a professor and Chair of the Department of Cell Biology to initiate a research program in cancer biology and metastasis. In 1984, in recognition of the growing interest in translating the evolving knowledge of metastasis into the clinic and the need to train the next generation of physician-scientists, Josh started the Metastasis Research Center at the UT MDACC. The center was endowed by a gift from Vivian and R.E. Bob Smith, and he was named the incumbent R.E. Bob Smith Distinguished Chair in Cancer Biology. In a visionary move, he consolidated basic and translational cancer research at UT MDACC and became the founding chair of the first 'Department of Cancer Biology'.

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This new department fostered exploration of the mechanisms of cancer metastasis and the role of the tumor microenvironment in cancer progression. Together with work by Judah Folkman and others, it contributed to illuminating the impact of tumor angiogenesis on metastasis. During the next couple of decades, Josh continued his seminal research and further expanded the understanding of the clonal heterogeneity of cancer and its direct impact on metastatic potential. His contributions include establishment of the B16F (Fidler) series of mouse melanoma cell lines that have distinct metastatic potential. These cell lines have helped elucidate mechanisms associated with different steps of metastasis and remain valuable experimental reagents for the community at large.

Josh contributed to the basic understanding of how cancer spreads to other organs and exploits the local environment to grow, and he offered fundamental evidence for the 'seed and soil' hypothesis of Stephen Paget. He explored the origins of metastases and identified mechanisms surrounding their therapy-recalcitrant nature. His most recent work focused on brain cancer, where he identified the key role of astrocytes in aiding metastasis. Decades of molecular biology, genomic and cell biology research by many laboratories validated the conceptual framework of stepwise

metastasis that he proposed in 1980. Josh had a strong commitment to scientific rigor and excellence and the need for science to benefit humanity. He was passionate about education and training, and he mentored many scientists and physician-scientists who now hold faculty leadership positions around the world. His yearly laboratory course on experimental models of metastasis as part of the cancer biology graduate program and his lectures on cancer metastasis for the graduate students were full of passion and instructive brilliance.

Josh published over 800 peer-reviewed research papers in a career of more than 50 years. He served as president of the American Association for Cancer Research and was the founding editor of *Cancer and Metastasis Reviews*. He received countless awards that recognized his excellence and valued expertise in metastasis research, including the American Cancer Society's Distinguished Service Award and Medal of Honor in Basic Research in 2013, the 2016 Gold-Headed Cane Award from the American Society for Investigative Pathology, and the American Association for Cancer Research's Margaret Foti Award for Leadership and Extraordinary Achievements in Cancer Research in 2018.

Josh was a trailblazer with an uncompromising mission to unravel cancer metastasis. His lifelong work elucidating

why and how tumors spread to other organs has given the scientific community an important blueprint for continuing his efforts with a path to identifying novel therapies. Josh was a beloved family man, and his kindness, personal strength and effervescent personality will always be cherished by all who worked with him and knew him. He will be fondly remembered as

people walk the corridors of the Department of Cancer Biology and appreciate his many photos of the spring blooms of Texas that decorate the hallways to the labs, where his legacy will continue to flourish. For the wider cancer community, he will be forever remembered as the modern-day father of metastasis research, and his work will continue to inspire for decades to come. □

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