THE FACULTY OF MEDICINE
Harvard University

Judah Folkman

Judah Folkman was born Moses Judah Folkman in 1933. The son of a rabbi, he became inspired to become a physician as a young boy when visiting ailing members of the congregation with his father. He soon became fascinated with science and medicine, and as a high school student he devised a perfusion system in his basement that maintained the viability of a beating rat heart for days after surgical removal. This led to his admission at age 15 to nearby Ohio State University, where Judah worked part-time all four years in the surgical laboratory of Dr. Robert Zollinger. He quickly mastered surgical skills and became an active participant in the exciting world of academic surgery. Judah entered Harvard Medical School at 19, where he was welcomed into the laboratory of Dr. Robert Gross, then Surgeon-in-Chief at Children's Hospital. There, he invented the first implantable heart pacemaker. Based on his scientific contributions, Judah was elected to the AOA and received the Boylston Medical Prize, Soma Weiss Award, and Borden Undergraduate Research Award in Medicine, when he graduated magna cum laude from HMS in 1957.

Judah became a surgical resident at Massachusetts General Hospital where he had his first introduction to Pediatric Surgery under the mentorship of Dr. W. Hardy Hendren. Midway through his residency, Judah married the love of his life, Paula Prial, who was to become the mother of his wonderful daughters, Marjorie and Laura, and his closest confidant for the remainder of his life. Soon thereafter, Judah enlisted in the United States Navy to fulfill his military obligations for two years. He did research on artificial blood substitutes at the National Naval Medical Center. In the course of this work, he invented the first implantable device for sustained drug-release that was later known as Norplant, which he donated patent-free to the World Population Council for use as a contraceptive. While in the Navy, Judah also observed that tiny fragments of tumor could remain viable, but would not grow beyond approximately one millimeter in diameter, when implanted into an isolated perfused thyroid. This led to his provocative proposal that tumors must stimulate growth of new blood capillaries to provide oxygen and nutrients necessary for their continued proliferation and expansion-a

In tribute to their dedicated efforts to science and medicine, deceased members of the Harvard Faculty of Medicine (those at the rank of full or emeritus professor) receive a review of their life and contributions with a complete reflection, ***a Memorial Minute****.*

process known as “tumor angiogenesis”. He also reasoned that cancer growth might be held in check by inhibiting this process.

Judah Folkman returned to MGH to complete his training in 1962, and became Chief Resident. There, he jury-rigged materials to create a renal dialysis system for a patient with acute renal failure, and saved the patient’s life. He assumed his first faculty position as an Assistant Professor of Surgery on the Harvard Surgical Service at the then Boston City Hospital in 1965. In a tiny laboratory in the basement of the Sears Surgical Building, he began in earnest his career-long study of tumor blood vessels that would ultimately open up the new field of vascular biology. Based on his keen intelligence, outstanding clinical skills and scientific promise, Judah was soon selected to succeed Gross as the Surgeon-in-Chief at Children’s Hospital. However, he chose to acquire six months of additional Pediatric Surgery training under Dr. C. Everett Koop at the Children’s Hospital of Philadelphia, before he assumed this position at the unprecedented young age of 35 in 1967.

As faculty member and surgeon at HMS and Children’s Hospital, Judah was known as a talented and caring surgeon, a gifted teacher, and a master of differential diagnosis. Crowds of students and residents swarmed around him on rounds because of his ability to meld modern biology with clinical practice, and he was the recipient of numerous HMS teaching awards for his introductory lectures to first and second year students. His devotion to patients and families was legendary, as was their appreciation of his technical skills and personal warmth. Judah even made time for those he had never met but who sought his counsel, returning phone calls every day when he returned home from the lab late at night, to be sure that he addressed each patient’s needs. When as a young man, Judah told his father that he would become a physician instead of a rabbi, his father responded, “then you will become a rabbi-like doctor”; and that is exactly what Judah did.

Despite his heavy administrative burden and extensive surgical responsibilities, Judah remained passionate about his mission as physician-scientist, and continued to expand his research efforts focused on tumor angiogenesis. In 1974, Judah changed academic medicine and Harvard University by accepting the first large industrial-funded research grant from Monsanto Company to support his cancer research. As a result, for the first time, Harvard permitted its faculty to submit patents covering medical inventions. Judah’s successful experiment in corporate funding also paved the way for industrial support of academic research laboratories at universities and research institutions across the nation, which is commonplace today.

In 1981, Judah elected to relinquish clinical leadership of the department of Pediatric Surgery to work full-time in his burgeoning laboratory. Although Judah lacked formal expertise in biochemistry or cell biology, he had an uncanny ability to ask penetrating questions, and he had a single-mindedness and tenacity of purpose that was beyond description. He initially attracted HMS students, and gradually postdoctoral fellows and visiting scientists, to work in his Surgical Research Laboratory in the Enders Building at Children’s Hospital, and systematically began to build the case for the tumor angiogenesis hypothesis.

Judah’s angiogenesis theory was initially met with great skepticism because he proposed that cancers secrete a ‘tumor angiogenesis factor’ to stimulate neovascularization, but it had not yet been identified or purified. He realized that the major obstacle was the lack of bioassays to identify this activity. As a great innovator, Judah developed multiple new experimental systems to measure and study angiogenesis factors, including the first capillary endothelial cell cultures, in vitro angiogenesis models, and sustained

release polymers for testing of putative angiogenesis modulators in rabbit corneas. The availability of these assays led to the purification of the first tumor angiogenesis factor, basic fibroblast growth factor in 1984. This discovery was followed by the isolation and cloning of multiple angiogenic factors by researchers around the world, which confirmed the critical role of angiogenesis for tumor growth as well as many other diseases. Thanks to Judah's perseverance, admonition quickly became admiration and, as he used to say, "my critics soon became my competitors".

Judah's tumor angiogenesis hypothesis launched an era of discovery and validation, during which his team at Children's Hospital discovered numerous additional angiogenic factors, as well endogenous molecules that inhibit capillary growth, including angiostatin, endostatin, and angiostatic steroids, and they began deciphering the molecular basis of angiogenic control. This work led to development of numerous anti-angiogenic drugs, some of which entered human clinical trials, including TNP-470, Thalidomide, and Endostatin. There are now multiple angiogenesis inhibitors approved for clinical use, which are benefiting more than one million people worldwide. Judah's impact on cancer alone was impressive in that the FDA now recognizes anti-angiogenesis as an entirely new modality for the treatment of cancer, along with chemotherapy, radiation therapy and surgery. Equally impressive is that angiogenesis inhibitors have restored sight in patients who are blind due to age-related macular degeneration; these drugs have become the clinical standard of care in Opthalmology.

Judah authored some 400 peer-reviewed papers and more than 100 book chapters and monographs. Over 38,000 articles have been published on angiogenesis, the field that he pioneered. He received scores of awards and honors for his distinguished research, including the National Institutes of Health's Christopher Columbus Discovery Award in Biomedical Research, American Cancer Society's Medal of Honor for Basic Science, Bristol-Myers Squibb's Award For Distinguished Achievement in Cancer Research, HMS's Warren Alpert Prize, Canada's Gairdner Foundation International Award, Israel's Wolf Foundation Prize in Medicine, Germany's Ernst Schering Prize, the Italian Association of Cancer Research in Rome's Gold Medal, the United Kingdom Society for Endocrinology's Dale Medal, and Switzerland's Dr. Josef Steiner Cancer Research Award. Judah also was elected to the National Academy of Sciences, Institute of Medicine, American Academy of Arts and Sciences, American Philosophical Society, and membership on the President's Cancer Advisory Board, in addition to receiving numerous honorary degrees from leading universities around the world. The research lab he founded with a single assistant when he arrived at Children's Hospital in 1967 had, by the time of his death, grown into a 125 scientist-strong Vascular Biology Program. And, more than 1000 labs around the world are now pursuing angiogenesis research, yielding thousands of angiogenesis-related publications each year.

Judah's contributions in the laboratory have permanently transformed our thinking about cancer and many other diseases, and they have pointed the way to novel strategies for their treatment. But Judah also was known for illuminating lectures that left his listeners spellbound, whether experts or novices, and that created innumerable new scientific converts as he traveled around the globe spreading his vision. His lecture style was enthralling, his enthusiasm contagious, and his self-deprecating humor a foil for the seriousness of his subject. Judah always shared his latest insights and unpublished data because he did not see his scientific competitors as enemies, but as potential allies. To Judah, the enemy was the disease he was trying to cure, or the technology he strived to develop to overcome obstacles that stood in his way.

Judah Folkman was an inspirational leader in everything that he did. For those of us who were blessed

with the chance to work closely with him, we remember Judah best for his warmth, his humor, and his incredible mentoring skills. He mentored from the first light of day until his head hit the pillow and probably thereafter in his dreams. Most of all, however, Judah mentored by the example of his perseverance, his willingness to move in different directions, and his sheer boyish delight in discovery. Whereas most people saw a lump of coal and spurned others who strived to look further, Judah walked forth boldly, turned it over and found a diamond. He did this with experiments, but more importantly, he did this with people, whether patients, students, technicians, workmen, colleagues or competitors. His death on January 14, 2008 was a terrible loss to our community, and to the entire world. We will all miss him greatly.

Donald Ingber, MD,PhD (*Chair*, Folkman Memorial Minute Committee)
Patricia Donahoe, MD
Michael Gimbrone, MD
W. Hardy Hendren, MD
Michael Klagsbrun, PhD
Marsha Moses, PhD