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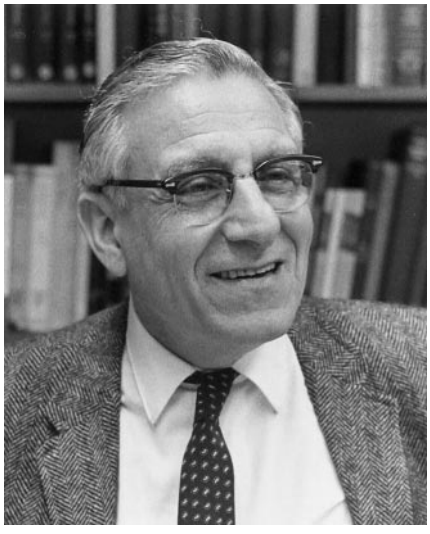
Sidney Weinhouse (1909–2001)



Sidney Weinhouse, one of the world's outstanding biochemists, died on February 9, 2001. Dr. Weinhouse was born in Chicago and received his B.S. in 1933 and his Ph.D. in biochemistry in 1936 from the University of Chicago. In the early years of his postdoctoral work in Chicago, he became well known for his contributions to the field of biochemistry, particularly in studies of two-carbon metabolism in which he pioneered the use of radioactive isotopes. After World War II, he moved to Philadelphia, where he remained for the rest of his career.

He served as Chair of the Division of Biochemistry at the Institute for Cancer Research and Director of the Fels Research Institute at Temple University Medical School. During these years he made significant contributions in the area of isoenzyme expression in cancer tissue. He was recognized for the discovery of the low-affinity hexokinase, called glucokinase, a signal discovery in carbohydrate metabolism. He summarized his work, which had appeared in over 150 articles, in a Clowes Memorial Award Lecture at the AACR Annual meeting in 1972 (*Cancer Res. 32:* 2007–2016, 1972).

During his tenure as editor of *Cancer Research* from 1969 through 1979, he doubled the size of the Editorial Board to ensure that submitted papers were thoroughly and equitably reviewed. He expanded the journal from 2500 pages to over 5300 pages per year, and was widely recognized as having brought the journal to a high level of quality and stature in the cancer field. After his term as Editor, he served as Associate Editor from 1980 to 1987 and served as Cover Editor from 1986 to 1999. To recognize his long-term, extraordinary contributions to the journal, the Editors of *Cancer Research* featured Dr. Weinhouse on the cover four times (January 1980; January 1, 1991; December 15, 1995; and December 1, 1999).

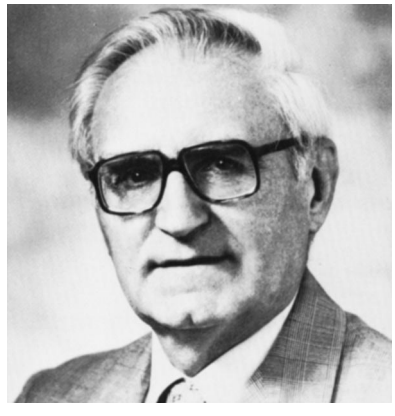
He received numerous national and international honors and awards throughout his long career, including honorary doctoral degrees from the University of Chieti, Italy (1979), the Medical College of Pennsylvania (1973), and Temple University (1975). He was elected to the National Academy of Science in 1979. In 1985, Dr. Weinhouse was elected to honorary membership in the AACR. He joined the AACR as an active member in 1951 and served the association in many capacities, including three 4-year terms and two *ex officio* terms on the Board of Directors between 1957 and 1984 and as AACR President (1981–1982).

Dr. Weinhouse's expertise enhanced the work of many advisory board and councils. He contributed to the Office of Scientific Research and Development during World War II, the National Advisory Council on Research and Clinical Investigation of the American Cancer Society, the Scientific Advisory Board of the Damon Runyon-Walter Winchell Cancer Fund, and the National Advisory Council on Environmental Health Sciences, among others.

Well-known as a mentor throughout his long and productive career, Dr. Weinhouse was always so generous with his time and advice. His long-time associate, Dr. Renato Baserga, Deputy Director of the Kimmel Cancer Center in Philadelphia, notes: "What all these honors and awards cannot convey is the fact that Sidney Weinhouse was one of the most beloved scientists in the scientific community. Universally respected for his integrity, Sidney Weinhouse was an example to colleagues and students alike for his altruism and his devotion to science. He was helpful, fair in his dealings, without violating the principles of good science. He continued to work for the journal *Cancer Research* and to advise younger people until his death at 91. He will always remain an example for all the people and scientists who had the good fortune to know him."

Indeed, since his death earlier this year, Sidney Weinhouse has been sorely missed not only by his research colleagues, but also by his many friends at the AACR. He was a constant inspiration to both junior and senior members of the AACR staff who never stopped marvelling at his intellect, proficiency, and energy. The cancer community has lost a great scientist, teacher, and friend; however, Sidney Weinhouse leaves an amazing legacy of people who have been positively influenced by him, professionally and personally. (Contributors to this tribute include Gerald Litwack, Thomas Jefferson University, Philadelphia; Renato Baserga, Kimmel Cancer Center, Philadelphia; Margaret Foti, AACR.)

Pietro M. Gullino (1919–2001)



Pietro M. Gullino, a champion of host-tumor interaction, died on May 28, 2001, in Saluzzo, Italy. For nearly 50 years, he delved deeply into the world of solid tumors and provided startling insight into its complexity with unparalleled clarity. In an era of reductionism, he took the controversial stand that "a solid tumor is not a bag of cancer cells," but rather an organ composed of vascular, interstitial and cellular compartments, with its own set of rules. He believed that only an integrative understanding of tumor pathophysiology would improve the probability of cancer prevention and cure.

After finishing his medical degree summa cum laude at the University of Torino in 1943 and receiving his diploma from the Italian Board of Pathology in 1952, Pietro Gullino did his postdoctoral training at the Technische Hochschule in Munich in biochemistry. He arrived at the National Cancer Institute in Bethesda in 1954 as a Fellow of the Italian League against Cancer and worked there for 29 years. When he entered

the field of tumor biology, the norm was to excise tissue, grind it up and measure gross biochemical parameters. However, his dream was to open the "black box" by studying tumors *in vivo* in their natural environment in an intact host. To this end, he developed an elegant tumor model with a single artery and a single vein connected to the host's vasculature so that nutrients, waste products, drugs and blood flowing into and out of the tumor could be directly quantified. This model provided unprecedented insight into host-tumor interaction and the tumor microenvironment, a fertile area of research today. The first day I met Pietro Gullino, he reinforced the idea of studying tumors *in vivo* by posing a simple question. How do you measure the amount of milk consumed by a family? You need to count the number of milk bottles dropped off and empty bottles retrieved from their home on a weekly basis and, from the difference, calculate the milk consumption in a natural environment. Alternatively, you could fill a swimming pool with milk, dunk the family into it and measure how much milk they drank in a week in an "unnatural" environment. The former method requires more patience, but is more "*in vivo*." His message was clear: *in vivo veritas.*

Using his *in vivo* approach, he presented unequivocal data refuting Nobel Laureate Warberg's contention that neoplasia and anaerobic energy metabolism are inextricably linked. Gullino showed that, unlike tissue slices *in vitro*, tumors *in vivo* avidly consume oxygen. In addition to clearing up this confusion in the field of metabolic physiology, he made seminal contributions to the areas of lymphatic function and metastasis in tumors. He was again ahead of his time. For example, he showed that 5 to 10% of blood plasma entering the tumor circulation oozes out from the tumor's periphery, presumably due to the lack of a functional lymphatic network. Using the same isolated tumor model, he later demonstrated that tumors shed more than a million cells per day per gram (of tumor) into the outgoing blood and yet may not lead to visible metastasis. These circulating shed cells may in the future allow for the molecular diagnosis of primary tumors and their metastases before they are clinically detectable.

To analyze the environment where cancer cells live *in vivo*, Gullino developed a micropore capsule to collect the very fluid that bathes cancer cells (interstitial fluid). Using this deceptively simple device, he investigated the internal milieu of tumors and the accessibility of drugs (including DNA) from the vascular to the interstitial compartment. In 1971, when he did not observe a significant amount of DNA in the capsule, he recognized that tumors present barriers to the delivery of DNA. This finding has major implications for today's proposed gene therapy as well as for other anti-cancer treatments.

Among his many fruitful collaborations with bioengineers was the development of a device to grow cells on "artificial" capillaries in 1972. An *in vitro* organ-like structure was created. This formed the foundation of the new field of tissue engineering and has served as a useful device for testing novel anti-cancer agents.

In addition to his major scientific discoveries, his key positions allowed him to influence research directions and policy during the course of his career. He was the Chief of the Laboratory of Tumor Pathophysiology at the National Cancer Institute from 1973 to 1985 and served as chairman of the U.S. Presidential Task Force on Breast Cancer from 1975 to 1979. True to form, he did not mince words when advocating prevention, treatment, and research efforts.

He promised his wife that he would return to their place of birth, Saluzzo, after his retirement, and he did. From 1985 to 1998, he served as Professor of Pathological Anatomy at the University of Torino, Italy. There he continued his work on two unexpected approaches to controlling tumor angiogenesis: modulating copper ions and gangliosides. Many years after Gullino discovered inhibition of angiogenesis by reducing copper in the diet, clinical trials on copper are now underway for the treatment of solid tumors.

Of all the contributions he made to the understanding of tumor biology, the most prominent was his discovery 25 years ago that cells in tissue acquire angiogenic capacity in the process of neoplastic transformation. This seminal finding, confirmed later by elegant genetic experiments, offers the possibility of cancer prevention. Someday, when cancer can be prevented by antiangiogenic approaches, the vision of Pietro Gullino will be realized.

Pietro Gullino was a modest and self-effacing man. He had no patience for pretension or pompous behavior. His thinking was clear and innovative. Indeed, his ideas on prevention by anti-angiogenesis and his emphasis on *in vivo* microenvironment and integrative biology were ahead of their time. He was a great educator and mentor throughout his lifetime. Beginning in 1986, for six years Pietro Gullino and I ran a week-long intensive workshop on tumor angiogenesis and metastasis where he gave eight 90-minute lectures (up to the age of 72). He also enjoyed teaching people outside the lab, discussing the subtleties of the 164 rose bushes that he planted and tended at his home in Italy, or introducing people to the nuances of the spectrum of fine Italian red wines and fabrics. Pietro Gullino approached life as a learning experience both inside and outside of the laboratory and made it a challenging and memorable experience to those fortunate enough to have shared it with him. (Rakesh K. Jain, Harvard Medical School and Massachusetts General Hospital, Boston, MA.)

Thomas S. Argyris (1923–2001)

Thomas S. Argyris, a member of the American Association for Cancer Research since 1960, died suddenly on April 29, 2001. Tom received his Ph.D. from Brown University with William Montagna in 1953, and after a postdoctoral fellowship with George Wislocki at Harvard Medical School, joined the faculty in the Zoology Department at Syracuse University in 1955. In 1972, having risen to the rank of professor, Tom moved to the Upstate Medical Center as Professor of Pathology, and retired from active research and teaching from that institution as Emeritus Professor of Pathology in 1985.

Tom's research interests centered on understanding how developmental processes were reactivated and recapitulated in the adult. During his career, he focused on three systems - stimulation of hair follicle growth and differentiation, wound healing in the skin, and adaptive growth due to functional stimulation in the liver and kidney. In each, he meticulously dissected the cellular response, and sought to understand how the machinery of macromolecular synthesis - RNA and protein - was recruited to initiate and support the complex developmental biology that regenerated or reformed the tissue. Perhaps his most important research came later in his career, when, in a series of 13 papers published from 1981 through 1985, he enunciated and established that induced hyperplasia in the skin was the common mechanism of tumor promotion induced by chemical and physical insult.

Many of us were surprised by the premature retirement of an active and imaginative intellect, but he told me that he had said what he had to say, and that it was all there in the literature. In this regard, as we emerge from an extended period of dissection of regulation and recruitment of individual genes during morphogenesis and tumorigenesis, we would be wise to remember and revisit Tom's focus on the biology of systems and activation of general biochemical mechanisms as fundamental to our understanding of these processes.

Tom was a respected and truly engaging teacher, whose style reflected his love for his subject. This attracted more than 30 graduate and medical students to his tutelage, and some dozen undergraduate students. His knowledge and enthusiasm were complemented by his warmth and kindness, and we were privileged to have had the opportunity to begin our careers in his care before being tossed into the wringer of this competitive sport.

Tom leaves behind his wife and collaborator, Bertie Argyris, also retired from a distinguished academic career at Upstate Medical Center as Emeritus Professor of Immunology. Other survivors are his brother Peter Argyris and his twin brother Chris Argyris, Emeritus Professor at Harvard University. (Len Augenlicht; Albert Einstein College of Medicine and Cancer Center, Bronx, NY)

(This obituary also appeared in the ASIP Bulletin 4:2 (October) 2001.)