Professor Enrico Mihich, 1928–2016

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Photo 1 Enrico (Henry) Mihich (Photo: private)

It was with great sadness that the cancer research community received the news that after a career spanning more than 60 years, Dr. Enrico (“Henry”) Mihich died on December 29, 2016 at 88 years of age. He will be remembered as a leader in the field of cancer research and we are proud to recall that he was one of the first editors of this journal, in 1982 becoming Co-Editor-in-Chief (with Prof. R. Baldwin). Henry was born in Fiume, Italy (now Rijeka, Croatia), surviving the Second World War and its aftermath, narrowly escaping death during the Nazi occupation and later when Communist Yugoslavia took control of the city. He fled as a refugee to Milan in 1945, where he was able to train as a doctor and complete his medical education. He emigrated to the USA and joined the Sloan Kettering Institute in New York City in 1952, where he met Marisa Mustacchi, whom he married in 1954. His mother’s death from cancer in 1955 strengthened his resolve to dedicate his efforts to cancer research in pursuit of a cure of this dreadful disease. To this end, he joined Roswell Park Cancer Institute (RPCI) in Buffalo, New York in 1957, and in 1970 he established a new center for cancer drug and therapy development, the Grace Cancer Drug Center (GCDC)—the first of its kind within a comprehensive cancer center, focusing on translational research, which at the time was a novel approach. He recruited over 25 leading cancer scientists whose work resulted in the introduction of a number of drugs into the clinic, including the development of 5FU-Leucovorin for the treatment of advanced colorectal cancer. At this time, Henry introduced and provided experimental evidence for the counterintuitive idea that lasting therapeutic effects of certain anticancer drugs depend on the drug-induced modulation of immunity against the tumor. This idea met with a degree of skepticism, because it was “obvious” that chemotherapeutics were immunosuppressive—a clear example of a scientific

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paradigm proving very resistant to change, but thereafter following the classic path of new ideas in science and becoming fully accepted as equally as obvious now as it was ridiculous then. Henry's tenacity in promulgating this idea against the resistance of the research community played a major part in its current acceptance.

The GCDC rapidly became a nationally and internationally recognized innovative center for basic and translational cancer research, and a center for advanced training of US and foreign scientists, establishing many durable international collaborations and conferences. Under Henry's 30-year leadership, it was instrumental in bringing new drugs and therapies into clinical trials. The Center's research focused on many of the fundamental concepts which have become the basis for current therapies such as drug resistance, the heterogeneity of tumor cells and the surrounding microenvironment which requires the development of combination therapy, and of course the use of immunologically effective doses and schedules of anti-cancer drugs. Henry was an educator, a mentor, and a role model to many graduate students and scientists who spent time in his department. He was also Chairman of the affiliated graduate program at SUNY Buffalo until 2006. His leadership approach at the GCDC was focused on hiring the best, investing in them to facilitate their success, and then celebrating those successes. He was also a forceful and tireless advocate for international collaboration to advance cancer therapies. In addition to his academic and scientific leadership, Dr. Mihich was active in the American Association for Cancer Research, and was elected to serve as AACR President (1987–1988). He established the ongoing joint scientific and clinical annual conference between the AACR and the JCA (Japanese Cancer Association). In 1999, he led the establishment, and chaired for 20 years, the annual Pezcoller symposium in Trento, Italy, which brings invited scientific leaders to present and discuss major advances in cancer research and treatment. The success of this symposium gave rise to the highly competitive annual AACR-Pezcoller Award to a leading clinical scientist. In fact, the Pezcoller itself is a lasting memorial to Henry's input and influence, and is a good illustration of the respect that he commanded in that numerous luminaries in the field of cancer biomedical research would travel for hours from the nearest airport to two small towns located at the base of the Alps in Northern Italy, Trento and Rovereto, to take part in this symposium. Nonetheless, Henry always made a point of also inviting new investigators to present what he considered provocative novel studies at these regular meetings. In this vein, throughout his career, Henry was actively engaged in establishing channels for collaboration

and exchange globally. Before the break-up of the Soviet Union, he organized and led several symposia in Moscow, Budapest, and Bratislava. With the National Cancer Institute, he went to Argentina to give a course on cancer therapeutics. With the Bender Foundation, he organized and led annual symposia in different parts of the world including China, Thailand, Singapore, Egypt, and Croatia.

Among the many recognitions he received, he was honored by the University of D'Aix Marseilles (France) with a Docteur honoris causa. In 1984, despite his political leanings, he was very proud to have been appointed by then President Ronald Reagan to the National Cancer Advisory Board. After his retirement from RPCI in 2007, he moved to Brookline, MA, and joined the Dana Farber Cancer Institute as a Presidential Scholar—Special Assistant to the President for Sponsored Research.

In addition to his wide-ranging and so influential professional activities, Henry maintained a life-long love for music and opera. As a boy in Fiume during the Nazi occupation, he saw his music teacher, Marcel Tyberg, deported because of his Jewish ancestry. Prior to his disappearance, Tyberg had entrusted the Mihich family with his music compositions, and these Henry eventually took with him to the USA. By great good luck, the wife of the then-director of the RPCI was a professional vocalist with particular interest in twentieth century classical composers. She worked through the music and featured Tyberg's four songs for soprano in English at her next recital; thus, the music of Marcel Tyberg was brought to life in America. This would not have happened without Henry's passion for music and his unshakeable persistence in getting it "discovered". In collaboration with, and with the enthusiastic support of JoAnn Falletta, conductor of the Buffalo Philharmonic Orchestra, and funding through the Buffalo Foundation for Jewish Philanthropies, the music finally came fully to life. Thus, Henry and Ms Falletta together drove the resurrection of interest in the Tyberg repertoire. Henry viewed this as fulfilling a life-long pledge to his beloved music teacher, having studied piano and composition with him before the War. To date, numerous lieder, trios and concertos have been transcribed, performed, and recorded including a performance of Tyberg's Second Symphony by the Croatian National Orchestra in Rijeka in November, 2012.

Persistence, inventiveness, humanity, and humility were critical components of all of this remarkable physician-scientist's extraordinary accomplishments. He will be sorely missed.

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(Co-Editors-in-Chief, *Cancer Immunology, Immunotherapy*)

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Photo 2 Prof. Mihich 2012 at the PIVAC conference in Nottingham (Progress in Vaccination against Cancer, PIVAC 12) (Photo: Gregory Wass)