

Obituary

Christopher J. Michejda

Christopher J. Michejda, member of the editorial board of the *Molecular Cancer Therapeutics* and an eminent biomedical chemist, died of a heart attack on January 9, 2007 while attending the annual retreat of intramural researchers at the National Cancer Institute (NCI) in Bethesda, MD.

Born in Poland in 1937, Chris grew up in Chicago, IL as his parents settled in the United States shortly after World War II. Chris attended the University of Illinois and then the University of Rochester where he received his Ph.D. degree in physical organic chemistry in 1963. Following a postdoctoral training at Harvard University with Professor Paul Bartlett, Dr. Michejda became an assistant professor at the University of Nebraska, progressing later to the rank of full professor. His tenure in Nebraska was marked by seminal contributions to the field of chemical carcinogenesis, including the elucidation of the mechanism of the metabolic activation of nitrosamines to alkylating agents and the demonstration of the fundamental roles of these reactive species in the processes of mutagenesis and carcinogenesis. From 1971 to 1972, Dr. Michejda spent a sabbatical year at the ETH in Zurich, Switzerland, which he recalled later as a turning point in his interests in chemical biology. Subsequently, he went to the National Science Foundation in Washington, DC for 2 years, serving as a Program Administrator and an ardent advocate for support of chemistry as a multidisciplinary component of biomedical research. In the late 1970s, Dr. Michejda joined the NCI, where he initially continued working in the field of carcinogenesis but soon expanded his research into the area of therapeutics. As a head of the Molecular Aspects of Drug Design section from 1978 until his death (operating first under the ABL-Basic Research Program and then the NCI Structural Biophysics Laboratory), Chris became wholly committed to the rational design of innovative anticancer, and later, antiviral agents as well. His early investigations at the NCI provided fundamental information on the metabolism and DNA reactivity of several important classes of anticancer agents. But it was the interdisciplinary integration of approaches that has become a "signature" of his creative efforts to discover new anticancer and anti-HIV strategies. Dr. Michejda's research typically involved extensive biochemical/biophysical characterizations of potential targets that would drive computational/structural/synthetic chemistry studies on new drug candidate molecules and in-depth investigations of their interactions with



intended targets, all combined with thorough evaluation of biological activities *in vitro* and *in vivo*.

In the quest for innovative "targeted therapeutics" to enhance selective toxicity for cancer cells, Dr. Michejda was a strong proponent of strategies based on cytotoxic small molecules, notably including advanced DNA binding agents. A firm believer that rationally designed cytotoxic agents have unexploited potential for selectivity, he successfully conducted various proof-of-principle studies showing the utility of such agents in unconventional strategies for attacking specific features of cancer cells or viral processes. Chris pioneered, for example, the targeted delivery of toxic small molecules to tumors through receptors overexpressed on the surface of cancer cells. He and his coworkers tested this strategy using conjugates of cytotoxic drugs with small peptides or peptide-mimicking molecules targeted at cancer-specific receptors. Other classes of small molecules discovered and developed by his research team took advantage of new targeting opportunities stemming from progress in DNA replication, DNA repair, and transcription. Examples of such drugs include the imidazoacridones, compounds with promising anticancer and anti-HIV activities that combine DNA intercalation with minor groove binding. Because this mode of binding features large interaction surfaces, Dr. Michejda

envisaged that such complexes would allow for the distortion of specific protein-DNA interactions and for interference with the functions of critical DNA-processing proteins in anticancer and anti-HIV/AIDS strategies.

Chris was a master at interfacing chemistry with other disciplines. Being erudite and having an uncommonly broad knowledge, he was equally at ease as “a medicinal chemist among molecular biologists and translational researchers” or, reciprocally, as a “biochemist and molecular biologist among chemists.” This trait, along with his unselfish personality, made him widely valued by his NCI colleagues and by cancer researchers elsewhere as a willing and creative collaborator and source of inspiration. Dr. Michejda’s scientific accomplishments are reflected by more than 150 publications in highly regarded scientific journals and 15 patents (several of which were licensed outside of the NIH) for innovative biologically active molecules and new therapeutic strategies.

Dr. Michejda was always eager to share his expertise and views but he was also an attentive listener, keen to hear more about emerging scientific opportunities applicable to drug development. Untiring as a participant and discussant often raising unconventional yet pointed questions, with his prominent posture and a smiling face, Chris became a characteristic figure at gatherings attended by the anticancer drug development community in the U.S. and abroad. In addition to his tenure on the editorial board of *Molecular Cancer Therapeutics* (since the inception of this journal), Chris was an associate editor of *Cancer Research* and a member of the editorial boards of several other scientific publications. Serving the research community in a multitude of ways, he was also a member of numerous advisory panels, organizing committees for scientific meetings and other working groups. He was a vitally important force in organizing the Chemistry in Cancer Research group of the AACR and in prompting efforts to elevate chemical biology in the structure and priorities of the NCI. Chris was a beloved mentor to many biomedical students

and postdoctoral fellows, who were not only inspired by his scientific passion but also cherished the always positive, encouraging outlook, and most importantly, care, that he invariably showed to others. Chris’ warmth, benevolent wit, and a magic ability to make everyone feel comfortable were legendary.

Chris’ caring personality and broad interests transcended science. He was a prominent member of various Polish-American groups and was awarded Poland’s Cavalier Cross of the Order of Merit for the assistance that he extended on American soil to the Solidarity movement prior to the fall of communism.

On January 9, straight from the NCI retreat in Bethesda, Chris was supposed to fly to Grand Rapids, MI to attend a workshop brainstorming new approaches to anticancer therapies. Chris was physically and metaphorically at the very heart of American biomedical research when his biological heart stopped... Emblematic for Chris’ whole life, his unselfish dedication to science, to his Polish roots, and, first and foremost, to the elementary values of humanity, his family has established the memorial Christopher Michejda Fund at the Kosciuszko Foundation, which is dedicated to sponsoring the training of young Polish biomedical scientists in the U.S.

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