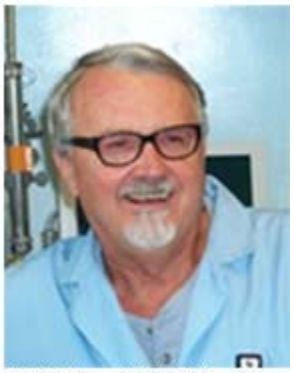
March 2007
Volume 6

CENTER FOR CANCER RESEARCH
frontiers
IN SCIENCE

IN REMEMBRANCE

In Remembrance: Christopher J. Michejda, PhD


Christopher J. Michejda, PhD

The CCR research community mourns the loss of Christopher J. Michejda, PhD, whose recent and unexpected death at age 69 has been deeply felt by his friends and colleagues. R. Andrew Byrd, PhD, Chief of CCR's Structural Biophysics Laboratory, expressed the sense of loss felt by the entire community. "Chris Michejda was both a very dear friend and an able scientist. His dedication to research and to NCI was unbounded. He fostered an interdisciplinary approach, as evidenced by all of his collaborations and his willingness to plan and implement joint conferences. He will be missed." CCR Director Robert Wiltrout, PhD, said, "Chris was always generous with his time in support of any project that would make NCI a better scientific community. His standard answer to most requests for help was, 'Okay mate, we'll make it happen.' We'll all miss hearing those words."

An internationally recognized research scientist and head of the Molecular Aspects of Drug Design Section within the Structural Biophysics Laboratory, Chris's initial studies at NCI focused on chemical carcinogenesis and nitrosamines. This seminal work helped to identify the mechanism of activation and metabolic pathways used by these environmental carcinogens to cause cancer. Based on this early work and his expert knowledge of triazene chemistry, Chris and his team developed effective antitumor agents based on triazene derivatives. Eventually, this research led him to an interest in the fundamental problems involved in developing drugs against cancer and viral diseases, such as AIDS.

A Pioneering Scientist

Under Chris's direction, his research group at NCI became known for its ability to develop new therapies by combining data from biological studies of disease stages with structural data on potential drug targets within these stages. He pioneered the development of receptor-targeted small molecule toxins that selectively eliminate tumor cells without harming healthy tissue. This approach, now followed by many research labs, has made possible the design of new drugs with better selectivity and low toxicity. Most recently, together with Nadya Tarasova, PhD, Chris discovered a rational approach to specific inhibition of integral membrane proteins that has led to the development of promising novel drug candidates.

The Michejda group's pioneering work with bisimidazoacridones resulted in a new class of compounds potently cytotoxic to liver and pancreatic cancers as well as leukemias. One of these agents is being readied for proposed clinical trials as a treatment for gastrointestinal cancers. Chris's collaborative work with Susan Keay, MD, PhD, of the University of Maryland, resulted in discovery of a so-called antiproliferative factor (APF) in the bladder epithelium of patients who suffer from interstitial cystitis, which unraveled the cause of this disease. By identifying the elements necessary for APF to inhibit normal epithelial growth, the Michejda group paved the way for APF to evolve as a potent inhibitor of bladder and renal cancer. Another collaboration, with Brian Carr, MD, FRCP, PhD, of the University of Pittsburgh, led to the discovery of a new class of highly selective phosphatase inhibitors that are potently active against liver cancer in animal models.

An Exceptional Mentor

Devoted to the broad scientific community, Chris was an exceptional mentor, training many postdoctoral fellows and predoctoral and medical students. The extraordinary breadth of his knowledge ranged from theoretical chemistry to molecular signaling mechanisms. More importantly, Chris had a warm and engaging personality that made all his staff members feel welcome. Susan Holbeck, PhD, a former fellow, recalled, "I met Chris 14 years ago, when I was a postdoc in Frederick, and our interactions continued when I joined DTP (the NCI Developmental Therapeutics Program). His enthusiasm was contagious—it was great fun talking science with Chris. He always put a smile on my face." Another former fellow, Wei Yao, PhD, remembered Chris's kindness. "I first met Chris in 2001 when I was applying for a postdoc position in his lab. That was my first presentation in English in my life. When I struggled to finish all the slides with my broken English and was so nervous, Chris gave me his warm smile and said 'That was great! I can't talk science in Chinese.' I was so lucky to be a member of his lab. He was like a father to me and so many young people from abroad."

One of Chris's long-time colleagues, David Farnsworth, remembered his willingness to discuss science. "Chris was always willing to talk, especially if you had new results to share. He seemed to enjoy most the data that didn't initially make sense or that didn't fit one's hypothesis." Dr. Tarasova said that "Chris was a scientist with a vision and an encyclopedic knowledge in huge areas encompassing organic chemistry and tumor and cell biology. His scientific enthusiasm and energy were infectious as he was trying to make a difference working on novel approaches in anticancer drug development with amazing devotion. And he did make a difference because many of the approaches he suggested turned out to be vastly successful and are very likely to save lives in the near future."

A Highly Respected Leader

Chris published more than 160 articles in prominent scientific journals and held 15 patents for new therapeutic compounds or concepts. He also served as an associate editor for *Cancer Research* and on the editorial boards of *Molecular Cancer Therapeutics*, *Cancer Epidemiology, Biomarkers, & Prevention*, and *Chemical Research in Toxicology*. Highly respected in his field, he was an invited speaker at many local and international conferences

and symposiums. Most recently, Chris played a key role in organizing the joint American Chemical Society and American Association for Cancer Research Conference on Chemistry in Cancer Research, held in February. This meeting featured lectures by prominent leaders in key chemically oriented areas of cancer research, including drug discovery, proteomics, the chemical biology of carcinogenesis, biomarkers and analytical chemistry, modeling and bioinformatics, and structural biology.

As Chair of the Chemistry and Structural Biology Faculty, Chris led CCR's efforts to establish the Program in Interdisciplinary Training in Chemistry for postdoctoral fellows and graduates. He was also an active member of several other NCI faculties and committees and served for many years as a scientific advisor to *CCR Frontiers in Science.*

A close friend and colleague, Larry Keefer, PhD, stated that Chris was "a man whose influence will most assuredly live on. His published research contributions will remain available in libraries and online for all to see. Initiatives he has worked to establish as means to foster interdisciplinary research and to achieve recognition of chemistry's irreplaceable role in the life sciences will continue."

Chris Michejda's scientific innovations, his outstanding mentoring and leadership skills, and his warmth and generosity will always be remembered by his friends and colleagues here at the CCR.