



No quality is more important for a scientist than curiosity, and Thomas O'Halloran, PhD, Associate Director for Basic Sciences for the Lurie Cancer Center, has it in spades. The eldest of nine children, O'Halloran says, "At a very early age, I was fascinated with chemistry and molecules and life, and how things worked." He and a friend combined their home chemistry sets to create a "Jacob's ladder"-- a high voltage traveling arc that generated 20,000 volts of electricity. Further experiments resulted in laughing gas and disappearing ink, which they sold to their classmates, and a failed attempt to make trinitrotoluene (TNT). "We had too much fun!" he recalls.

As an adult, that same curiosity continues to serve him well. In addition to his position at the Lurie Cancer Center, O'Halloran is the Charles E. and Emma H. Morrison Professor in the Department of Chemistry and in the Department of Biochemistry, Molecular Biology and Cell Biology at Northwestern University. He also serves as Director of the new Chemistry of Life Processes Institute (CLP), a research center on the Evanston campus dedicated to fostering interdisciplinary studies in chemistry, biology, engineering and medicine. His multiple roles on both of Northwestern's campuses have helped O'Halloran increase the interaction among scientists in different fields and promote interdisciplinary efforts. "There's a beautiful spectrum of research expertise that cuts across the two campuses," he says.

Examples of these efforts to foster collaboration include the design of Silverman Hall, the new building that will soon house the CLP. In the new facility, scientists from different disciplines will work in close physical proximity to one another, facilitating interaction and breaking down barriers associated with the more common “silo” arrangement of academic disciplines. “There are still a lot of rich scientific pastures to plow at the interfaces between classical disciplines,” O’Halloran says. And he is hopeful that Silverman Hall will help that happen. He also expects the new facility and the CLP to play “a very important role in implementing the Lurie Cancer Center’s vision of stimulating new types of basic research in the fields of cancer detection, treatment and prevention.”

Discovering Metals: Early Research Experience

O’Halloran came to cancer research by an unusual path. After his freshman year at the University of Missouri at Columbia, he “talked his way into” a summer job at one of the school’s research laboratories, “and they let me start mixing things,” he says. “I didn’t make any TNT, but I did start crystallizing cobalt complexes of deep purples, reds and greens, and iron complexes—and I fell in love with it.” His work that summer stoked O’Halloran’s interest in metals and their functions in the human body. “Metals were clearly needed by living cells,” he learned, “but no one had paid much attention to how they got to where they were going.” After graduating, O’Halloran studied the chemistry of platinum drugs at Columbia University in New York where he earned his PhD. He performed his postdoctoral studies at MIT, and, in 1986, was recruited by Northwestern.

O’Halloran’s research at Northwestern focuses on the regulatory biology and chemistry of transition metal receptors involved in homeostasis and oxidative stress pathways. He is especially interested in the intracellular chemistry of elements essential for growth and proliferation, nanoscale drug delivery systems and the mechanisms of anticancer agents based on arsenic, molybdenum and platinum chemistry.

Targeting Cancer

O’Halloran recently started moving part of his lab forward from examining the basic way molecules work in living systems to creating new drugs that kill cancer cells. As project

leader for a Center of Cancer Nanotechnology Excellence (NU-CCNE) study on targeted delivery of multifunctional therapeutic agents, O’Halloran and his team have developed tiny drug delivery vehicles called nanobins that carry drugs directly to malignant cells, where they bind and then unload their drug cargo, killing the cancer cells. (Funding for this study comes from a National Cancer Institute Nanotechnology Excellence Grant.)

To keep drugs from leaking out of these “smart” nanobins, O’Halloran and his team also devised a liposome bilayer that surrounds the vehicles, making them a safe and effective way to get toxic substances to the cancer cells without destroying healthy ones. Along the way, the team discovered a way to reduce the toxicity of arsenic trioxide, a toxic but effective cancer killer that has been used in traditional Chinese medicine for thousands of years, and is one of the drugs transported by the nanobins. The hope is that higher doses will mean more effective treatment and better patient outcomes. (Arsenic trioxide is currently FDA-approved to treat acute promyelocytic leukemia.)

O’Halloran is enthusiastic about the progress they are making and the value of collaboration in their ultimate success. “I simply can’t progress to the next stage with the tools of basic science alone,” he says. “We can’t move these ideas forward without the context of the Lurie Cancer Center, the participation of our clinical colleagues and the phenomenal support of basic cancer research provided by Ann Lurie and groups like the H Foundation, a Chicago-based philanthropic organization.”

In another example of this cooperation, O’Halloran notes that the CLP and the Lurie Cancer Center are working together to recruit a thought leader in the field of proteomics, a branch of molecular biology focused on the study of proteins, and a growing area of cancer research. “Proteomics is an emerging field that is important to both clinical cancer and basic science research, so the CLP and the Lurie Cancer Center are working hard to recruit a senior level faculty member with expertise in this area,” he says. And, once again emphasizing the importance of teamwork, O’Halloran says they are looking for “someone who will work with us arm-in-arm to build something far greater than what we are capable of as individuals toiling away on separate problems.”

O'Halloran credits Lurie Cancer Center Director, Steve Rosen, with fostering this collaborative culture and showing him how to engage colleagues on a personal as well as an intellectual level. "Steve always makes it interesting and fun to join him in a project," he says. "And I'm trying to employ that skill to bridge really different disciplines in the basic sciences and the medical community."

Career as Privilege

O'Halloran's many roles don't leave him much free time, but he carves out what he can for hiking, camping and fly fishing in the Boundary Waters between Canada and the US. Reflecting on his career, O'Halloran says he is grateful to be able to do the work he does. "It's such a privilege to be able to explore in these ways, to have our curiosity unleashed on very fundamental questions," he says. "And, every now and then, when a moment of idle curiosity develops into an obsession and, ultimately, into a discovery that helps cancer patients, you really appreciate how lucky you are."