

Marc G. Caron (1946–2022)

Marc Caron, Ph.D., James B. Duke Professor of Cell Biology and Professor of Neurobiology at Duke University Medical Center died unexpectedly on 25 April 2022 at the age of 75. After receiving his Ph.D. in Biochemistry at the University of Miami in 1973, he joined the Lefkowitz group for a postdoctoral fellowship at Duke University. After an initial two-year stint on the faculty of Laval University, he spent the rest of his 49-year career at Duke, during which time he became a towering figure in the fields of receptor biology and neuroscience.

For a period of almost 15 years early in his career, Marc and I (R.J.L.) were very close collaborators, and up until the end our laboratories were adjacent to each other. Despite this very close, almost 50-year relationship, I must admit that it began with a deception. In 1972, when I was a clinical and research fellow at the Massachusetts General Hospital in Boston and publishing some of my early papers, Marc, then a graduate student, wrote inquiring about the possibility of doing postdoctoral work with me. He also emphasized that as a Canadian citizen he would qualify for a prestigious fellowship from the Medical Research Council of Canada. It was clear from his note that he did not appreciate that I was still a trainee myself but rather thought that I was a faculty member. Immediately recognizing his potential, and hoping that by a year hence I might in fact have landed a faculty job somewhere, I did nothing to disabuse him of this misconception. He got the fellowship, I got a job at Duke and, as they say, the rest is history. Marc's early work focused on developing techniques for studying, purifying, and characterizing what are now known as G-protein-coupled receptors (GPCRs), using the β -adrenergic receptor as a model. He also contributed greatly to the discovery of the mechanisms by which receptor signaling is regulated by kinases and β -arrestins — in particular, how the β -arrestins are involved not only in desensitization but also in endocytosis and signaling. Early on, he developed a particular interest in dopaminergic signaling, which would lead to his laboratory's developing tools for identifying, purifying and cloning the D1 and D2 receptors and clarifying their regulation and signaling mechanisms. In a classic paper, he defined an entirely new mechanism for regulation of behavior by D2 receptor signaling through β -arrestin.



Credit: Kathleen Caron

However, his interests were not confined to postsynaptic mechanisms. Marc's work also addressed many other key features of biogenic amine neurotransmission, and always with a view towards developing therapies for major brain and behavioral disorders. With the cloning and characterization of the dopamine transporter, his group illuminated the mechanisms by which it regulates behavior through elegant studies with knockout mice. These studies not only demonstrated dramatic changes in dopamine-mediated behaviors in the absence of the carrier, but also revealed remarkable adaptive changes in the expression of receptors, enzymes and signaling molecules as the system strains to cope with sustained elevation of extracellular dopamine.

Increasingly, as his work expanded into these new areas, he focused on relating his basic biochemical and cell biological studies to human diseases. For example, he concentrated on the relationship of disordered dopaminergic signaling with Parkinson's disease, as well as on other GPCRs, such as those for ghrelin and neurotensin, whose activities modulate brain dopamine activity. At the time of his death his laboratory was focusing on the development of so-called biased ligands for all three of these GPCRs, with the goal of developing more selective drugs with fewer side effects for the treatment of neurodegenerative diseases such as Parkinson's, or for the non-opioid management of chronic pain. He was also working toward treatments for addiction, depression, schizophrenia, and attention deficit hyperactivity disorder.

In addition to his numerous and seminal scientific contributions, Marc will be remembered as an extraordinary and caring mentor to many generations of trainees. As a mentor, he went above and beyond in his efforts to encourage his trainees to take risks and explore new ideas. He also served as an enthusiastic, unfailing advocate as they transitioned to their own independent scientific careers. Most of all, he conveyed to trainees and colleagues alike his engagement and curiosity, and the great joy he found in doing science. His trainees now carry the flame of his passion for science throughout the world.

Supported by his loving wife Pauline, who predeceased him by four years, he brought a level of attention to their personal as well as professional lives that was quite extraordinary. When candidates would come to interview for positions in his lab, he would pick them up at the airport personally and they would often wind up staying at his home. Trainees were often welcomed to his home for meals and holidays, especially when they were too far from home to easily return for these occasions. He was, in the opinion of many of us who knew him well, as decent a human being as we had ever met, and the quintessential example of what is perfectly captured with the Yiddish word 'mensch'.

Marc's work ethic was legendary and something he passed along to his trainees. However, in addition to his extraordinary scientific productivity (more than 600 published papers) he was a devoted husband, father, and grandfather who always found time for his family. When not busy with professional or family activities he was happiest working the land as a gentleman farmer in Durham, NC, perhaps harking back to his childhood growing up on a dairy and maple syrup farm in a small town in Northern Quebec. ▣

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