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It is with great sadness that we mourn the loss of Dr. Marc Caron, PhD., who passed away unexpectedly on Monday, April 25, 2022.

Dr. Caron was the James B. Duke Professor of Cell Biology, Professor of Neurobiology and Professor of Medicine at Duke University Medical Center. He was also a member of the Duke Cancer Institute and Duke Institute for Brain Sciences. Dr. Caron authored more than 650 publications and served as editor or editorial board member for several leading journals including, most recently, the Journal of Clinical Investigation.

Among his many honors, Dr. Caron was an investigator of the Howard Hughes Medical Institute from 1992 to 2004, a member of the American Academy of Arts & Sciences and a fellow of the American Association for the Advancement of Science. In 2005, he received the Julius Axelrod Award from the American Society for Pharmacology and Experimental Therapeutics.

Dr. Caron received his BSc in Chemistry from Laval University and his PhD from the University of Miami. He completed a postdoctoral fellowship at Duke University. He joined the faculty of Laval University School of Medicine (Quebec, Canada) as an assistant professor in 1975, and then returned to join Duke's faculty in 1977 where he was an active faculty member for 45 years.

His main areas of research were neurotransmitter receptors and transporters. In close collaboration with longtime colleague, Dr. Robert Lefkowitz, he pioneered the biochemical techniques that allowed the pharmacological characterization and purification of G-protein coupled receptors (GPCRs). These studies, which began in the mid 1970s, ultimately led to the cloning of the Beta2-Adrenergic receptor in 1986 (Dixon et al. Nature, 1986). He was also involved in the cloning of several other GPCRs including the dopamine D1 receptor. In the GPCR field, Dr. Caron was also a leader in the identification and characterization of G-protein Receptor Kinases (GRKs) and Beta-arrestins (Barrestin). Studies from his lab further showed that Barrestins were not only involved in mediating endocytosis of GPCRs but also mediated additional forms of intracellular signaling following receptor activation.

In parallel to his major contributions to the field of GPCRs, Dr. Caron also made major contributions to the field of transporters, notably by generating genetically modified mouse models lacking or overexpressing neurotransmitter transporters. Among the seminal studies is the paper by Giros et al, (Nature; 1996) describing the initial characterization of animals lacking the dopamine transporter. This was followed by publications on mouse models lacking other key transporters or signaling molecules including NET, VMAT2, GRK2, GRK6, Barrestin-2 and others.

More recently, groundbreaking studies from his team identified a novel mode of signaling for dopamine D2 receptors and much effort was focused on trying to identify better antipsychotics with reduced adverse effects by selectively targeting the Barrestin pathway of the D2 dopamine receptor.

In sum, Dr. Caron contributed to the characterization and cloning of GPCRs, the discovery of GPCR regulation by kinases and arrestins, and the identification of molecular signals for receptor endocytosis and recycling. His genetic gain- and loss-of-function animal models showed the importance of

transporter and GPCR regulation through kinases and arrestins and provided one of the first *in vivo* examples of G protein- versus arrestin-mediated GPCR signaling.

Dr. Caron mentored many trainees and followed them through their own careers with encouragement and advice. We extend our sincerest condolences to Dr. Caron's family, friends and colleagues.