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OBITUARY

Obituary: J. David Leander, Ph.D.

(April 8, 1944–November 14, 2014)

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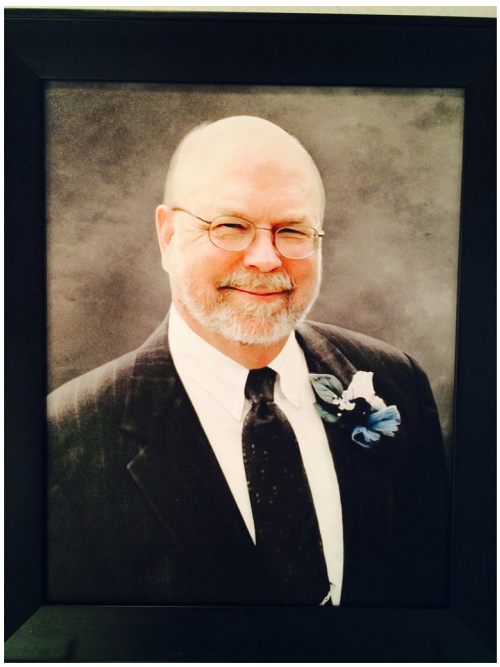

John David Leander, a pioneering behavioral pharmacologist, who dedicated his extraordinary wisdom and curiosity to the search for new drugs to treat psychiatric and neurological disorders died on November 14, 2014 at the age of 70. Dave grew up in Mt. Vernon, Washington, on his family's dairy farm, and moved east to pursue his graduate training at the University of Florida in Gainesville where he graduated in 1971 with a Ph.D. in psychology. It was his postdoctoral fellowship with Donald E. McMillan at the University of North Carolina, Chapel Hill that launched his career as a behavioral pharmacologist and his subsequent research at Eli Lilly and Company that laid the foundation for his many contributions in the drug development arena. Throughout his career, Dave maintained close personal relationships with his scientific colleagues and his wife Kathleen and the families of his three children Sven, Eric, and Lisa were his greatest joy. His obituary in the Indianapolis Star recalls his characteristic response to social events, including a remark he made in anticipation of his own memorial service, which was "For heaven's sake, keep it simple." Yet, his scientific contributions are far more complex.

Dave was a prolific scientist, as revealed by over 200 published manuscripts in multiple areas, including the behavioral and pharmacological effects of drugs that target opioid, dopamine, and NMDA receptors. He was a huge advocate of and creative developer of in vivo assays to establish the pharmacodynamics and on-target actions of drugs. In this capacity, he pioneered a host of assays still widely accepted today (e.g., NMDA-induced lethality, kappa agonist-induced urination, and suppression of operant behaviors for antagonism studies). Subsequently, he made excellent use of his expertise in behavioral pharmacology when he joined Eli Lilly and Company in Indianapolis, Indiana in 1981. There, he made multiple contributions to the discovery and development of drugs for clinical situations as diverse as depression, attention-deficit-hyperactivity disorder, anxiety, schizophrenia, epilepsy, Parkinson's disease, and stroke. As a consultant after his retirement from Lilly in 2002, he rapidly brought molecules to Phase 2 proof of concept working with a number of start-up biopharmaceutical companies. In addition to Dave's contributions in drug development, he will be remembered for his mentorship of several

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pharmacologists who have carried on the tradition of excellence in behavioral pharmacology.

Dave focused a good deal of attention during his career on investigations of behavioral effects of opioids. One of his most compelling observations was a series of studies showing that the opioid analgesic meperidine had pharmacological actions and behavioral effects that could not be accounted for by its interactions with mu opioid receptors. Dave's carefully crafted experiments led to the unexpected observation that meperidine's effects on schedule-controlled responding of pigeons and rats were not prevented by opioid antagonists, one of the defining characteristics of opioid action. In subsequent experiments, Dave established the unique behavioral effects of meperidine and brought a greater understanding to its side-effect profile, which often led to serious consequences in clinical situations (e.g., incoordination, tremors, and convulsions).

Work by Dave and his colleagues on the discovery of a novel series of kappa opioid receptor antagonists led to the generation of an assay (urinary output) that not only was specific for kappa receptors, but also detected partial kappa agonism and was sensitive to blockade by kappa receptor antagonists.

One focus of Dave's research at Eli Lilly and Company was the identification of the efficacy, side-effect profile, and in vivo target engagement of NMDA receptors. In this context, Dave provided fundamental data for identifying the potential psychotomimetic-like effects of these molecules and provided the foundation for the development of an in vivo assay for detection of NMDA receptor blockade.

Dave's research had a direct impact on the discovery of drugs such as the antidepressants, fluoxetine and duloxetine; the antipsychotic, olanzapine; a peripherally-restricted opioid receptor antagonist to prevent post-operative ileus (alvimopan); and drugs to treat Parkinson's disease (pergolide) and attention-deficit-hyperactivity disorder (atomoxetine). Other discovery efforts led to a host of prototypical compounds for investigation of NMDA receptors, kappa opioid receptors, serotonin 1A receptors, and others; some of which advanced into clinical development or formed the basis of venture capital-backed companies.

After retirement in 2002, Leander started his own scientific consulting group. A crowning achievement of those efforts is exemplified in the strategic and creative planning as Chief Scientific Advisor for the biopharmaceutical company Naurex in successfully progressing a novel molecule (rapastinel; GLYX-13) rapidly through Phase 1 and Phase 2 clinical investigations in treatment-resistant depression, an area of great unmet medical need and much current scientific interest.

During Dave's tenure at Lilly, he attained the position of Lilly Research Fellow and served as Chair of the Neuroscience Discovery Strategy Group. Among his many well-deserved awards are Distinguished Alumnus Awards from Western Washington University and the University of Florida, as well as membership in several scientific societies, including the American College of Neuropsychopharmacology, the American Society of Pharmacology and Experimental Therapeutics, the Behavioral Pharmacology Society, and the Society for Neuroscience.

Beyond these awards, Dave will remain an inspiring figure to us as an extraordinary scientist and visionary behavioral pharmacologist who transformed our understanding of how behavioral events can be used to inform and elaborate the neurobiology of the brain and apply these understandings to the discovery and development of novel therapeutic agents. We will also remember him as a dedicated mentor and an endearing friend and will continue to be inspired by the values that he instilled in his colleagues, including sincerity, thoughtfulness, and scientific rigor.