



In Memoriam: David Mangelsdorf, Ph.D.

August 4, 2025

To the UT Southwestern Community:

It is with profound sadness that we inform you of the passing of **David J. Mangelsdorf, Ph.D.**, Chair and Professor of the Department of Pharmacology, who was a visionary scientist, dedicated mentor, and cherished member of our UT Southwestern community for more than 30 years. An Investigator of the Howard Hughes Medical Institute, Dr. Mangelsdorf pioneered the characterization of orphan nuclear receptors (a class of proteins involved in gene regulation) and uncovered key cellular signaling pathways – discoveries that were instrumental in advancing our understanding of diabetes, obesity, cancer, alcohol intoxication, and parasitic infections.

Dr. Mangelsdorf held the Alfred G. Gilman Distinguished Chair in Pharmacology and the Raymond and Ellen Willie Distinguished Chair in Molecular Neuropharmacology in Honor of Harold B. Crasileck, Ph.D., as well as a secondary appointment in the Department of Biochemistry. He was elected to both the National Academy of Sciences (NAS) and the National Academy of Medicine (NAM) – rare and distinguished honors.

Widely known among colleagues and fellow investigators as “Davo,” he had a collegial and curious nature that fostered multidisciplinary collaborations spanning biochemistry, endocrinology, metabolism, neurology, and infectious diseases. His work not only advanced basic science, but also bridged the gap to clinical application, influencing drug development and treatment strategies worldwide. His publications remain among the most cited in the field of molecular pharmacology.

Since 2002, Dr. Mangelsdorf has run a joint laboratory with longtime scientific collaborator Steven Kliewer, Ph.D., Professor of Molecular Biology and Pharmacology, and a fellow member of the NAS. Their early work identifying the ligands and physiological functions of orphan nuclear receptors led to the discovery of two novel signaling pathways mediated by the endocrine factors FGF19 and FGF21, which regulate nutrient metabolism during feeding and fasting. These discoveries revealed promising therapeutic targets for conditions such as cholestasis, type 2 diabetes, and obesity. The Mangelsdorf/Kliewer Lab also uncovered a nuclear receptor pathway in parasitic nematodes and demonstrated that compounds targeting this pathway may represent a new class of antiparasitic agents.

Beyond his scientific achievements, Dr. Mangelsdorf championed excellence through his dedicated service to the UTSW community – as Chair of the Endowed Scholars Committee, longtime Principal Investigator of the Pharmacology training grant, and a committed mentor to numerous faculty members, postdoctoral fellows, and learners within his department and throughout campus.

He earned a Bachelor of Science in Biology and Chemistry from Northern Arizona University in Flagstaff (1981) and his Ph.D. in Biochemistry from the University of Arizona in Tucson (1987), where he and colleagues successfully cloned the gene for the vitamin D receptor. During postdoctoral studies at the Salk Institute for Biological Studies, he defined the orphan nuclear receptor RXR and its ligand, 9-cis retinoic acid. He later characterized ligands and physiologic functions for several mammalian orphan receptors, including the oxysterol receptors (LXRs), the bile acid receptor (FXR), and the dafachronic acid receptor (DAF-12), which governs survival strategies in nematodes.

Dr. Mangelsdorf joined UT Southwestern in 1993 and became Chair of Pharmacology in 2006. He was recruited here by Nobel Laureate Alfred Gilman, M.D., Ph.D., his predecessor as Chair. In 2000, Dr. Mangelsdorf co-founded X-Cepto Therapeutics, Inc., a California-based biotechnology firm focused on discovering compounds that modulate nuclear receptors. The company later became part of Exelixis, Inc.

Dr. Mangelsdorf's scientific excellence was recognized with numerous prestigious awards, including the Endocrine Society's 2025 Edwin B. Astwood Award for Outstanding Research in Basic Science and its Gerald D. Aurbach Award in 2004; the Rolf Luft Award from the Karolinska Institutet, for outstanding contributions in endocrinology and diabetes research (2012); the Edith and Peter O'Donnell Award in Medicine from the Texas Academy of Medicine, Engineering and Science (2007); the Transatlantic Medal from the European Society of Endocrinology (2006); the Heinrich Wieland Prize from the Boehringer Ingelheim Foundation (2003); the Adolf Windaus Prize from the Falk Foundation, for his work in the field of bile acid research (2000); and the John J. Abel Award from the American Society for Pharmacology and Experimental Therapeutics (1997).

Dr. Mangelsdorf is survived by his wife, Katrina Voe Cotton, M.D., Ph.D., M.B.A., their three daughters (Alyssa, Sara, and Laura), two grandsons (James and Henry), as well as a wide circle of family and friends who mourn his loss. On behalf of the entire UT Southwestern community, we extend our heartfelt condolences and will keep them in our thoughts and prayers. A memorial service will take place Saturday, Aug. 9, at 2 p.m. at Zion Lutheran Church, 6121 E. Lovers Lane, Dallas, Texas 75214. All are welcome to attend.

Dr. Mangelsdorf's passing is an immense and painful loss for his family, friends, colleagues, our institution, and the broader field of biomedical science. His work exemplified the spirit of scientific innovation and collaboration that defines UT Southwestern, and his legacy will live on through the investigators he mentored and the lives improved by his discoveries.

Sincerely,

Daniel K. Podolsky, M.D.
President
UT Southwestern Medical Center

W. P. Andrew Lee, M.D.
Executive Vice President for Academic Affairs and Provost
Dean, UT Southwestern Medical School

Joan Conaway, Ph.D.
Vice Provost and Dean of Basic Research