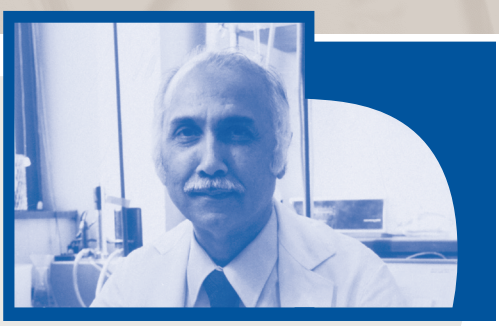
Wright State University

The Partab T. Varandani Memorial Lecture



Thursday, April 14, 2016

2 p.m., Gandhi Auditorium, White Hall
Wright State University

Alfred G. Gilman Distinguished Chair in Pharmacology
University of Texas Southwest Medical Center
Investigator, Howard Hughes Medical Institute
Member, National Academy of Sciences

"Neuroendocrine Regulation of Nutrient Metabolism by FGF21"

DAVID J. MANGELSDORF, Ph.D.

Dr. David Mangelsdorf is a leader in the field of nuclear receptors, a family of transcription factors that have universal roles governing transcriptional programs during development, reproduction, and metabolism. These receptors have become important therapeutic targets for diseases such as cancer, diabetes, metabolic syndrome, atherosclerosis, and parasitism. Stemming from his discovery of the retinoic acid X receptor (RXR) and its ligand (9-cis-retinoic acid, a derivative of vitamin A), Dr. Mangelsdorf has since characterized ligands and physiologic functions for other so-called "orphan receptors" – receptors whose functions and ligands are unknown. In the mid-1990s his laboratory published seminal papers in *Nature* and *Cell* where he identified oxysterols as ligands for the liver X receptors (LXR), and defined their essential role in cholesterol homeostasis, establishing these receptors as potential therapeutic targets for atherosclerosis and cancer. Fast on the heels of the LXR discovery, Dr. Mangelsdorf reported that bile acids are the ligands for the receptor FXR, which he published in *Science* and *Molecular Cell*, and that LXR and FXR work in tandem to control and reset lipid metabolism after a meal. He further characterized peroxisome-proliferator activated receptors (PPARs) that bind fatty acids and have become important clinical targets for anti-diabetic drugs. More recently, his laboratory has elucidated the roles of the endocrine fibroblast growth factors (FGF) in bile acid, lipid, and carbohydrate metabolism. FGF21 is now in clinical trials for treating obesity. He has since focused his attention on nematodes and discovered the DAF-12 endocrine signaling pathway (*Cell:* 2006), which regulates development and is required for regulating the infectious stage in parasitic nematodes (*PNAS:* 2009). Collectively these studies have identified new therapeutic targets for a multitude of metabolic diseases and parasitism.

David Mangelsdorf received his BS in Biology and Chemistry from Northern Arizona University in Flagstaff (1981) and his PhD in Biochemistry from the University of Arizona in Tucson (1987). He began his work on nuclear receptor proteins as a postdoctoral fellow in the laboratory of Dr. Ronald Evans, an HHMI investigator, at The Salk Institute for Biological Studies.

In 1993 he joined Nobel laureates Michael Brown and Joseph Goldstein at UT Southwestern Medical Center, which has an outstanding history in cholesterol and steroid research. Following his pioneering work with LXR, Dr. Mangelsdorf notes "*It was at this point that I made probably the best move of my career—I recruited Steven Kliewer, a former colleague from the Evans lab who had gone to work at GlaxoSmithKline. Like Brown and Goldstein, we run a joint lab, working on how these receptors regulate metabolism.*" Since 2005, their joint efforts on the discovery of ligands and physiologic functions for nuclear receptors has generated insights into obesity and metabolic syndrome, and their associated disease consequences. As a member and principal investigator for the Nuclear Receptor Signaling Atlas (NURSA), a multi-institutional consortium sponsored by NIH, Dr. Mangelsdorf has been instrumental in developing nuclear receptor expression profiling as a resource to investigate numerous physiologic and pathologic conditions and has promoted new paradigms for basic research and clinical use.

David Mangelsdorf has published 219 scientific articles and holds 11 patents. Dr. Mangelsdorf is the recipient of numerous accolades including the John J. Abel Award in Pharmacology (1997); the1998 Richard E. Weitzman Memorial Award and the 2004 Gerald D. Aurbach Award (from The Endocrine Society); the Adolf Windaus Prize for Bile Acid Research (2000); the 2003 Heinrich-Wieland-Preis, Chemisches Staatsinstitut of Munich University, Germany; the 2007 O'Donnell Award in Medicine (from The Academy of Medicine, Engineering and Science of Texas); and the 2012 Rolf Luft Award in Endocrinology and Diabetes, Karolinska Institutet. In 2008, David Mangelsdorf was elected as a member to the prestigious National Academy of Sciences. Currently, he serves on the editorial board for *PNAS* and *Cell Metabolism*, and is a member of the NIH Endocrine Study Section. In addition to his funding as an investigator for the Howard Hughes Medical Institute, his laboratory is currently funded by the National Institutes of Health (3 awards), the Robert A. Welch Foundation, and the Cancer Prevention Research Institute of Texas.

Sponsored by the *Department of Biochemistry and Molecular Biology*, the *College of Science and Mathematics*, the *Boonshoft School of Medicine*, the *Biomedical Sciences Ph.D. Program*, the *V.P. for Research and Dean of Graduate School*, and the *Office of the Provost*.

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For more information, please contact the Department of Biochemistry and Molecular Biology at (937) 775-3041.

This event is free and open to the public.

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