

Division of Metabolism, Endocrinology & Diabetes

Peter Arvan, MD

This Division has experienced a number of important milestones this year – beginning with its official name change to the Division of Metabolism, Endocrinology & Diabetes (MEND). Other 2003 highlights are summarized below.

Faculty Awards and Promotions

Peter Arvan M.D., Ph.D., was named Professor and Chief of MEND, replacing interim chief Roger J. Grekin, M.D., Dr. Arvan was also named the first William and Delores Brehm Professor of Metabolism, Endocrinology & Diabetes and this year won the R.R. Bensley Award from the American Association of Anatomists and was honoree of the Sidney Ingbar Memorial Lecture at Harvard Medical School, Beth-Israel Deaconess Hospital, Boston.

Craig Jaffe, M.D., was named the new Clinical Director of the MEND division, promoted to clinical associate professor, and awarded a new R-01 grant from the NIDDK institute of the NIH. Arno K. Kumagai was promoted to clinical associate professor, and he received the Senior Award for his teaching efforts from the graduating medical school class of 2003. Dr. Kumagai also became Director of the Family Centered Experience and Director of the Longitudinal Case Studies, and he continues to direct the Intensive Insulin Therapy Clinic of the U-M Diabetes Center and is co-director of the second-year Medical School course in endocrinology. Robert Lash, M.D., meanwhile, is the Course Director of the Clinical Foundations of Medicine course as he plays a central role in planning and implementing the new teaching curriculum at the Medical School.

Other faculty awards and promotions included: Anne Chang, M.D., as the first recipient of the joint ADA-ASP Young Investigator Innovation Award in Geriatric Endocrinology; Eleni Dimaraki, M.D., who was awarded a VA career development grant; and Jennifer Franzese M.D., who was promoted to Clinical Assistant Professor.

Research Studies

In the laboratory, Roger Grekin, M.D., had shown in prior experimental animal studies that infusion of fatty acids into the hepatic portal vein increased arterial blood pressure – an

observation suggesting that high blood pressure associated with abdominal obesity might be due to increased production of fatty acids by abdominal fat cells. So Grekin's group is now examining the relationship between blood pressure and the production of fatty acid by abdominal fat cells, and they have found that individuals with higher abdominal fatty acid production also have increased renal nerve activity, which is an important regulator of blood pressure. These results suggest that abdominal fatty acid production may contribute to the development of obesity-related hypertension.

Another important study is being conducted by Gary Hammer M.D., Ph.D., who has been studying the differentiation of adrenocortical cells within the adrenal gland, especially the role of the nuclear receptor/transcription factor, steroidogenic factor-1 (SF-1). The Hammer lab is concentrating on the idea that ACTH-stimulated transcriptional activation involves intramolecular (phosphorylation) and intermolecular (transcription complex) interactions of SF-1. These studies led to a grant entitled "Mechanisms of Adrenal Differentiation" being funded by the NIDDK.

Ronald Koenig, M.D., Ph.D. has also launched new studies on the role of retinoic acid (the active metabolite of vitamin A) on inner ear development. His laboratory has established that the essential of retinoic acid for normal inner ear development is due to direct transcriptional repression of the BMP4 gene, which is particularly curious since retinoic acid induces, rather than represses, BMP4 in bone, the inner ear develops in a bony pocket, and the cell types respond in opposite manners. But the Koenig lab identified a novel inner ear specific BMP4 promoter that accounts for the transcriptional repression and these data were published in *Mol Cell Biol.* 2003 23: 2277-2286, which led to a 2003 NIH R-01 grant entitled "Retinoic acid and regulation of BMP4 in development."

Martin Stevens, M.D. has also made considerable progress elucidating potential mechanisms contributing to the development of chronic complications of diabetes. He has developed nuclear medicine techniques to characterize the defects of cardiovascular sympathetic innervation complicating diabetes, demonstrating that the earliest stages in the development of diabetes complications are characterized by augmentation of central sympathetic tone that may result in development of cardiomyopathy, nephropathy, and hypertension. Dr. Stevens' studies are being supported by a new Clinical Research Award from the American Diabetes Association and his

group has initiated a pivotal Juvenile Diabetes Research Foundation clinical trial testing the hypothesis that oxidative stress contributes to the development of microvascular complications in patients with type 1 diabetes – the first study to utilize cardiac imaging techniques developed at the University of Michigan to explore the reversibility of neuropathy, cardiomyopathy and nephropathy.

Finally, William Herman, M.D., as interim Director of the Michigan Diabetes and Training Center, piloted the MDRTC NIH center grant to a successful 5-year renewal, and Chuck Burant, M.D., applied for and received a major American Diabetes Association-sponsored award/grant as part of the new ADA initiative.