



Keynote Lecture III

PPAR γ in the Complications of Diabetes

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Willa A Hsueh, MD, is Professor of Medicine and Chief of the Division of Endocrinology, Diabetes, and Hypertension at UCLA School of Medicine in Los Angeles, California. Dr Hsueh received her MD cum laude from Ohio State University and performed postgraduate training in Internal Medicine at Johns Hopkins Hospital. She was a clinical fellow in endocrinology at Johns Hopkins Hospital and a research fellow at Stanford University School of Medicine. Her current research interests focus on insulin resistance and mechanisms of cardiovascular disease, nuclear receptors, the renin-angiotensin system, and vascular complications of diabetes mellitus, with the goal of translating observations at the bench to human pathophysiology and prevention of disease. Her group was the first to identify a potentially protective role for ligands to the nuclear receptor, peroxisome proliferator activated receptor γ (PPAR γ) in vascular injury and more recently, in diabetes complications, particularly in regulation of genes that may mediate vascular complications. The PPAR class of therapeutics are emerging as an important strategy in the war against the metabolic syndrome and diabetes. Dr Hsueh and her colleagues also demonstrated that coronary vascular damage occurs in insulin resistance in the absence of traditional cardiovascular disease risk and may be related to adipokine production and inflammatory changes, all of which are improved by PPAR ligands. Her group has also identified mechanisms of angiotensin II tissue damage in insulin resistance and diabetes and recently reported a novel effect to inhibit reverse cholesterol transport.

Dr Hsueh is a fellow of the Council for High Blood Pressure Research of the American Heart Association and presented their Arthur Corcoran Memorial Lectureship. She is a member of numerous other professional societies, including the American Society for Clinical Investigation and the American Association of Physicians. She served on the American Board of Internal Medicine, Endocrinology, Metabolism and Diabetes Committee. Dr Hsueh was listed among *The Best Doctors in America in Endocrinology* from 1998 through 2005, and has received many awards, including a MERIT Award of the National Institute of Arthritis, Metabolism, and Digestive Diseases, the Harry Goldblatt Award for Cardiovascular Research of the American Heart Association, and the Edwin B Astwood Award for Outstanding Research from the Endocrine Society

PPAR γ is a nuclear receptor which has important insulin sensitizing, antianflammatory and antifibrotic activities. It is expressed in multiple tissues where it has direct effects to potentially protect target organs. PPAR γ is also expressed in fat where it increases transcription of adiponectin. PPAR γ ligands attenuate, accelerated atherosclerosis, decrease fibrosis in cardiomyopathic models, and protect the kidney and decrease albuminuria in the diabetic mouse with nephropathy. Many of these tissue actions are mediated by transcriptional down regulation of osteopontin, a large acid phosphoprotein which contributes to macrophage proinflammatory behavior, tissue remodeling and angiogenesis. PPAR γ activation may not only be useful for glucose lowering in diabetes, but for target organ protection as well.