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TITLE

Endothelial Sampling and Molecular Analysis Coupled to Reactive Hyperemia Peripheral Arterial Tone Index: a Novel Approach to Study Endothelial Dysfunction and Vascular Inflammation in Diabetic Patients

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Diabetes is major accelerator of macro vascular disease. Pathogenetic mechanisms in diabetes-associated macrovascular disease include endothelial dysfunction, accentuated vascular inflammation and increased oxidative stress. Advanced Glycation End-products (AGEs) are highly expressed in diabetic tissues and endothelial activation. The receptor for AGEs (RAGE) has been implicated in the pathogenesis of atherosclerosis in animal and in-vitro studies. Hyperglycemia promotes expression of Monocyte chemoattractant protein-1 (MCP-1) and Early Growth Response-1 (EGR-1) in cultured cells. MCP-1 has pivotal role in the diabetic vasculopathy and EGR-1 induces RAGE expression. However, limited availability of endothelial tissue is a major constraint, when studying the cellular mechanisms of diabetic vasculopathy in humans. We validated an innovative and minimally invasive approach allowing characterization of vascular ECs' molecular phenotype in human subjects. By using this approach, we showed elevated MCP-1, EGR-1 and RAGE gene expression in the venous endothelium of both Type 1 and Type 2 diabetic patients vs. age-matched healthy volunteers. This data suggest that the venous endothelium chronicles the systemic activation of endothelial oxidative/inflammatory programs in patients with diabetes presenting EC inflammation in case of poorly controlled hyperglycemia. More recently, we studied 11 healthy volunteers between 32-54 yrs old (42±7.5 yrs old, 5 males) and showed that endothelial dysfunction (by means of reactive hyperemia index and gene expression) increases with ageing, particularly in females, with high BMI index, and in Hispanics. Our work may lead to approaches detecting EC dysfunction in early and even preclinical diabetes and may ultimately pave the way toward more predictive and personalized medicine.

Biography

Dr.Duygu Onat received her BS and MS in Molecular Biology and Genetics from Bogazici University, Istanbul, Turkey and her PhD in Molecular Biology and Biochemistry from Düsseldorf University, Düsseldorf, Germany. After working in Germany, Switzerland and Italy with UNESCO, FEBS and SFFR Awards, Dr. Onat is awarded by AHA Postdoctoral Award to work in the Department of Medicine, Columbia University. In 2006, she joined the Faculty in Columbia University and is Principle Investigator of an Irving Institute/Clinical Trials Pilot Award and Co-PI in external/NIH funded awards. She also serves in the review board of the Irving Institute/CTO Pilot Awards Program.