

## **Phytonutrients as Atheroprotective Compounds – Novel Mechanisms and Targets**

**Reto Asmis, Ph.D.**

**Departments of Clin. Lab. Sciences and Biochemistry, UTHSCSA**

Monocyte diapedesis and macrophage recruitment are chemoattractant-driven responses to vascular injury. We recently showed that hyperlipidemia and hyperglycemia increase the responsiveness of monocytes to chemokine-induced chemotaxis both *ex vivo* and *in vivo*. This gain-of function phenotype acquired by metabolically stressed monocyte appears to directly contribute to increased macrophage recruitment and accelerated atherogenesis in dyslipidemic and diabetic mice but the underlying mechanisms are not known. Our goal is to determine the molecular mechanisms responsible for the enhanced responsiveness of monocytes to chemoattractants induced by metabolic stress and to identify novel therapeutic targets and strategies for the prevention of atherosclerosis. Evidence will be presented demonstrating that the sensitization of monocyte to chemoattractants induced by metabolic stress is mediated by the induction of a novel NADPH oxidase, Nox4, increased intracellular H<sub>2</sub>O<sub>2</sub> formation and protein-S-glutathionylation. This pathway provides a novel mechanism through which metabolic disorders facilitate macrophage recruitment to sites of vascular injury and promote atherogenesis. Finally, new data will be presented, suggesting that selected anti-inflammatory phytonutrients protect blood monocytes from metabolic stress-induced dysfunction and thus may have athero-protective potential.

July 27, 2010