Anca D. Dobrian, PhD

RESEARCH INTERESTS

Obesity is a growing epidemic and the health costs and morbidities associated with the disease are substantial and projected to increase in the next decades worldwide.

My lab is interested in mechanisms leading to cardiovascular complications of obesity. In particular the research is focused on how inflammation and lipotoxicity in adipose tissue leads to insulin resistance and type2 diabetes. I am also interested in renal mechanisms that contribute to hypertension in obesity.

Angiogenic mechanisms in human adipose tissue
Progressive expansion of adipose tissue in face of excess caloric intake requires adequate blood supply to provide oxygen and nutrients. Therefore, with progressive weight gain in obesity there is a need for new blood vessel formation (angiogenesis). Insufficient blood perfusion due to reduced angiogenesis leads to hypoxia, inflammation and fibrosis that contribute to adipocyte dysfunction and insulin resistance. The regulation of angiogenesis and the role of local factors in different human fat depots (visceral vs. subcutaneous) is unknown. The goal of this project is to establish the angiogenic potential of human adipose tissue from different fat depots and to establish the role of pro-inflammatory lipids in regulation of angiogenesis. A particular focus is on the lipid metabolites generated via the lipoxygenase pathway. This project utilizes a unique resource, human adipose tissue samples collected during bariatric surgery through collaboration with the Sentara Metabolic and Weight Loss Surgery Center at Sentara Norfolk General Hospital. The project is funded by an R15-NIH-NIDDK grant through 2015.

Roles of transcription factors in regulation of inflammation in adipose tissue
Obesity is a state of chronic inflammation and adipose tissue is a major contributor leading to insulin resistance and type2 diabetes. Local control of inflammation is complex and multi-factorial. Immune cell infiltration and activation is one of the key features. Also, adipocyte hypertrophy due to excessive lipid accumulation is a source of adipokines and pro-inflammatory hormones acting in a paracrine and endocrine fashion. Several transcription factors are expressed in both adipocytes and cells of the immune system. Our focus is on two transcription factors that control expression of pro-inflammatory genes in adipocytes and T cells: Signal Transducer and Activator of Transcription (STAT) 4 and Twist-1. In this project we aim to identify the mechanisms by which these transcription factors regulate various target genes responsible for (1) immune cell migration and activation in adipose tissue, and (2) adipocyte metabolism, hypertrophy and inflammation. We utilize various genetic mouse models, including global and adipose tissue specific knockouts and cell culture techniques to establish the mechanisms. This project is a collaboration with Dr. Jerry Nadler's group in the Internal Medicine Department. The project is funded by an RO1 NIH-NIDDK grant through 2016.

Mechanisms of nitric oxide signaling in obesity hypertension
Hypertension that accompanies obesity is a consequence of volume expansion due to excessive sodium retention. Nitric oxide is key for regulation of sodium reabsorption in the renal tubule. We showed that in obesity the proximal renal tubule response to nitric oxide is substantially reduced. Our goal is to investigate the molecular targets responsible for the impaired nitric oxide signaling resulting in blunted natriuresis. These include the cGMP and phosphodiesterases responsible for NO degradation.