“Remodeling adipose tissue inflammation to preserve insulin sensitivity in obesity”

A presentation by Sean M. Hartig, Ph.D.

Summary: White adipose tissue (WAT) is an endocrine organ that dynamically expands and contracts to meet the metabolic demands of the organism. However, prolonged excessive caloric intake overwhelms WAT deposits, resulting in peripheral fat deposition, systemic glucose dysregulation, insulin resistance, and type 2 diabetes mellitus. Restoring the capacity of WAT to safely sequester excess energy promotes insulin sensitivity in the face of diet-induced obesity. Our group has recently characterized a microRNA, miR-30a, that promotes fatty acid oxidation and energy expenditure in human adipocytes. In obese humans, miR-30a expression is reduced in subcutaneous WAT isolated from insulin resistant subjects compared to normoglycemic subjects in two independent clinical cohorts, supporting an important role for miR-30a in defending insulin sensitivity. To test the hypothesis that restoration of miR-30a expression in white adipose tissue would improve peripheral insulin insensitivity, we injected adenovirus (Adv) expressing either miR-30a or GFP as a vector control directly into the subcutaneous fat pad of high fat fed, insulin resistant mice. Exogenous miR-30a expression in subcutaneous WAT depots of obese mice improved insulin sensitivity, decreased ectopic liver fat deposition, and reduced WAT inflammation. RNA-Seq coupled with high throughput proteomic profiling indicated that miR-30a targets the transcription factor STAT1 to limit pro-inflammatory programs that would otherwise restrict WAT expansion and decrease insulin sensitivity. Collectively, our observations linking miR-30a expression to insulin sensitivity suggest an uncharacterized pathway that uncouples obesity and the metabolic dysfunction leading to type 2 diabetes mellitus.

Dr. Hartig is Assistant Professor in the Department of Molecular and Cellular Biology at Baylor College of Medicine.

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