University of Utah
UNDERGRADUATE RESEARCH JOURNAL

SPTLC2 DELETION IN ENDOTHELIAL CELLS: IMPLICATIONS FOR ARTERIAL FUNCTION

Lauren Thompson (Caroline Ramous, Kellsey Ly, Kiana Luu, Alex Margetts, Trevor Tippetts, Jae Min Cho, Seul-Ki Park, Ran Hee Choi, John David Symons)
Department of Nutrition and Integrative Physiology

Using pharmacological and genetic approaches to inhibit whole-body ceramide biosynthesis our laboratory showed that this sphingolipid contributes importantly to hypertension and vascular dysfunction associated with diet-induced obesity in mice. Here we tested the hypothesis that inducible, endothelial cell (EC) specific depletion of the rate-limiting enzyme responsible for ceramide biosynthesis i.e., serine palmitoyl transferase light chain 2 (Sptlc2), preserves arterial function in obese mice. Six-week old male mice consumed standard (CON) or high-fat (HF) diet for 14-weeks. After 12-weeks on diet all mice were treated (PO) with tamoxifen. Tamoxifen induces EC-specific Sptlc2 deletion in mice harboring the *VE-Cadherin* Cre promoter (Sptlc2KO^{iEC} mice) but is without effect in *VE-Cadherin* Cre negative mice (wild type; WT). After 14 weeks on diet mice completed metabolic and vascular phenotyping. qPCR results indicated Sptlc2 was depleted > 80% in carotid artery ECs but not vascular smooth muscle cells from CON-Sptlc2KO^{iEC} vs. CON-WT mice. Preliminary results from: (i) glucose, insulin, and pyruvate tolerance tests; (ii) body composition analyses using NMR; and (iii) femoral artery vascular function analyses using isobaric procedures, indicate no differences exist between CON-Sptlc2KO^{iEC} and CON-WT mice. Additional preliminary findings indicate that EC-specific Sptlc2 deletion does not impact the severity of metabolic or vascular dysfunction evoked by HF. For example: (i) glucose, insulin, and pyruvate tolerance tests; (ii) body composition analyses; (iii) non-receptor mediated vasocontraction to potassium chloride, receptor-mediated vasocontraction to phenylephrine, endothelium-dependent vasodilation to acetylcholine, intraluminal flow-mediated vasodilation in response to incremental pressure gradients across the vessel, and endothelium-independent vasodilation to sodium nitroprusside, were similar in femoral arteries from HF-Sptlc2KO^{iEC} and HF-WT mice. Collectively, these preliminary data do not support our original hypothesis that EC-specific Sptlc2 deletion preserves arterial function in the context of diet-induced obesity.