LAY ABSTRACT

Overwhelming evidence points to white adipose tissue (WAT) as a major contributor to metabolic regulation body-wide, with WAT dysfunction and obesity associated with poor metabolic health and a higher prevalence of sub-clinical and clinical neuropathy. Many of these phenomena appear to be regulated by factors such as peroxisome proliferator activated receptors (PPARs, including the γ isoform), intracellular proteins that are responsive to metabolic cues and that regulate gene expression. Tissue-specific activities of the PPARs may be controlled in part by circulating blood lipids (lipoproteins), which carry bioactive fatty acids that bind PPARs. However, there is a limited understanding of the interplay between diet, lipoprotein-derived bioactive lipids, and downstream molecular and physiologic events in metabolically-sensitive cells such as fat cells and peripheral neurons. We propose to perform proof-of-concept studies that will test the novel idea that lipoprotein-derived lipids regulate PPARγ-dependent fat cell differentiation, maturation, and inflammatory profiles. These studies will be complemented by work that determines peripheral afferent neuron axonal growth and maturation indices. Our studies will leverage assays that monitor the expression of newly-identified PPAR-responsive genes encoding growth regulator proteins that are, intriguingly, robustly co-expressed in fat and neuron cells. These research areas will have direct relevance toward clarifying the connections between diet, adiposity, and neuropathy, providing a springboard for future grant applications that expand on the work to characterize specific bioactive lipoprotein components and to elucidate the physiological roles of proteins co-residing in fat and neurons.