Transcriptional regulation of Brown Adipose Tissue Thermogenesis

Ji Suk Chang, Ph.D.

Assistant Professor
Laboratory of Gene Regulation and Metabolism
Pennington Biomedical Research Center, Baton Rouge, LA 70808, USA

Activation of brown adipose tissue (BAT) thermogenesis can reduce obesity and diabetes by increasing energy expenditure and improving blood glucose clearance. The transcriptional coactivator PGC-1α regulates the transcription program of adaptive thermogenesis in BAT. We have recently identified a splice variant of the PGC-1α gene that encodes the N-terminal isoform of PGC-1α (NT-PGC-1α). NT-PGC-1α expression in brown adipocytes increases mitochondrial number and activity by inducing the expression of a number of mitochondrial genes involved in thermogenesis, fatty acid transport and β-oxidation, TCA cycle, and electron transport system. In agreement with in vitro data, NT-PGC-1α is sufficient to activate BAT thermogenesis in PGC-1α-deficient mice in response to cold and high-fat diet. Furthermore, NT-PGC-1α activation resulting from PGC-1α ablation enhances the capacity of BAT to oxidize fatty acids and dissipate energy as heat. This compensatory adaptation results in attenuation of diet-induced obesity. In contrast, loss of NT-PGC-1α in BAT decreases fatty acid oxidation, reducing BAT thermogenesis in response to cold. Collectively, our data highlight an important role for NT-PGC-1α in the regulation of adaptive thermogenesis in BAT.