Lipopolysaccharide modulates mitochondrial function in brown adipocytes

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ABSTRACT

Background The rediscovery of brown adipose tissue (BAT) in adult humans opens new avenues for research to ameliorate obesity consequences including metabolic and cardiovascular disease because of its special feature to expend rather than store energy. Lipopolysaccharide (LPS) is known to be elevated in obesity and initiate an inflammatory state, but its effect has not been fully explored in BAT. β3 adrenergic receptor ligands such as CL 316,243 (CL) induce BAT activity through stimulation of UCP1. The interaction between the LPS receptor TLR4 and β3 adrenergic receptors has not been well studied in BAT. Therefore, the objective of this study is to investigate the effect of LPS on the CL response and examine how LPS may alter mitochondrial function in BAT.

Methods Immortalized brown adipocytes were differentiated with or without LPS. After treating cells with CL, RNA and protein were harvested in order to perform qRT-PCR and Western blotting. Mitochondrial respiration was assessed using Seahorse Bioscience XF24 extracellular flux analyzer (Seahorse Bioscience). Reactive oxygen species (ROS) assay was performed to estimate the capacity to prevent cellular damage from oxidative stress.

Results LPS significantly decreased key brown fat genes (CIDEA, UCP1, PGC-1α). Furthermore, LPS-treated cells showed significantly decreased UCP1 induction in response to CL at both protein and gene expression levels. In addition, key mitochondrial genes (ATPase8, CPT1B, CytC, ND1) were significantly reduced by LPS treatment. This implicates LPS acting to impair mitochondrial function and is supported by a reduced O_2 consumption rate in LPS treated cells as well as an increased susceptibility to hydrogen peroxide (oxidative agent).

Conclusions These findings reveal that LPS induces changes in BAT biology including response to b3 ligand as well as negatively affecting mitochondrial function.