

November 3-3:30-5:00PM**T-OR-2120-LB****IL-15 improves skeletal muscle oxidative metabolism in association with AMPK pathway activation**Lucien Nadeau *Ottawa Ontario*, Celine Aguer *Ottawa Ontario*

Background: During contraction, skeletal muscle secretes myokines that act on distant tissues to mediate the beneficial effect of exercise on general health. Some myokines also act locally in skeletal muscle in an autocrine/paracrine fashion to facilitate adaptations to physical exercise. Interleukin-15 (IL-15) is highly expressed in skeletal muscle and influences some metabolic parameters that are defective in insulin resistance and obesity. For instance, IL-15 improves muscle glucose uptake and whole body fatty acid oxidation. The aim of this study was to determine the metabolic response of muscle cells to acute IL-15 exposure and the mechanism by which IL-15 acts locally in skeletal muscle. **Methods:** L6 myotubes were exposed to different concentrations of IL-15 and oxygen consumption, fatty acid oxidation and activation of the AMP-activated protein kinase (AMPK) pathway were measured. **Results:** 10 ng/ml and 20 ng/ml IL-15 exposure for 30 min to 3h increased myotube oxygen consumption by 20-30%. Preliminary data also showed that IL-15 increased complete fatty acid oxidation to CO₂ and the ratio of complete/incomplete fatty acid oxidation by 15-30%. The effect of IL-15 on muscle oxidative metabolism seems to involve the AMPK pathway since IL-15 increased the phosphorylation of AMPK and its downstream target acetyl-CoA carboxylase (ACC), known to activate mitochondrial fatty acid oxidation. Current and future experiments are designed to 1) confirm the role of the AMPK pathway in IL-15 mechanism of action by using primary myotubes derived from AMPK α 1/2 knockout mice, 2) study the effect of acute exposure to IL-15 in skeletal muscle ex-vivo, and 3) study the effect of chronic IL-15 exposure on mitochondrial biogenesis and function. **Conclusions:** By increasing the ability of skeletal muscle to completely oxidize fatty acids, IL-15 may prove to be an interesting target to treat metabolic diseases such as obesity and type 2 diabetes.