

POSTER 38

PGC-1 α OVEREXPRESSION IN PRIMARY HEPATOCYTES INCREASES FATTY ACID OXIDATION AND MITOCHONDRIAL CONTENT

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The role of peroxisome proliferator-activated receptor- γ coactivator-1 α (PGC-1 α) in increasing mitochondrial content and fatty acid oxidation (FAO) in skeletal muscle has been well described. Often, this increase in mitochondrial content and FAO is observed to associate with increased skeletal muscle and systemic insulin sensitivity. However, to date no studies have documented the effect of elevated PGC-1 α protein expression on hepatocyte mitochondrial function and FAO. Therefore, we examined whether adenoviral PGC-1 α protein overexpression would result in increased markers of mitochondrial content and FAO in primary hepatocytes. Additionally, would the increased mitochondrial content and FAO be associated with protection of hepatocyte insulin signaling following chronic exposure to lipids. We examined protein markers of mitochondrial content, FAO, and insulin signaling in primary hepatocytes isolated from the Sprague-Dawley rats transduced with PGC-1 α or β -gal adenovirus. PGC-1 α overexpressing (PGC o/e) primary hepatocytes were observed to have greater protein expression of the mitochondrial markers, CPS-1 and mtTFA. Also, PGCo/e hepatocytes demonstrate 2-fold higher FAO to CO₂ than β -gal controls, while no difference is observed in total FAO (acid soluble metabolite + CO₂). Finally, PGCo/e hepatocytes were observed to maintain insulin stimulated Akt phosphorylation following overnight lipid exposure, with a decrease in signaling observed in the β -gal control hepatocytes. In conclusion, isolated primary hepatocytes overexpressing PGC-1 α are observed to have higher mitochondrial content, twice the FAO to CO₂, and maintenance of insulin signaling in response to lipid exposure. These data suggest that increased hepatic mitochondrial content and FAO to CO₂ is protective of hepatic insulin action.