PGC-1α and PGC-1β regulate protein synthesis in C2C12 myotubes

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Skeletal muscle atrophy is characterised by increased rates of protein degradation and/or decreased rates of protein synthesis. Overexpression of peroxisome proliferator-activated receptor γ co-activator-1α (PGC-1α) or PGC-1β can attenuate muscle atrophy, and this has been attributed to a decrease in protein degradation (Brault, Jespersen & Goldberg, 2010; Sandri *et al.*, 2006).

This study investigated the role of PGC-1α and PGC-1β in protein synthesis in C2C12 myotubes. Myotubes were infected with GFP, PGC-1α, or PGC-1β adenoviruses, and protein synthesis was measured at basal levels and with dexamethasone treatment, by the uptake of [^{3}H]-tyrosine.

PGC-1α or PGC-1β overexpression resulted in a 25-28% increase in protein synthesis. Dexamethasone decreased protein synthesis by 15% in the GFP-infected myotubes. However, overexpression of PGC-1α or PGC-1β was able to prevent the dexamethasone-induced decrease. Treatment with LY294, an inhibitor of PI3K/Akt, did not prevent the PGC-1α or PGC-1β driven increase in protein synthesis. This effect was therefore independent of Akt, a major kinase involved in muscle growth.

Another potential mechanism for the PGC-1α and PGC-1β driven increase in protein synthesis may be *via* their regulation of microRNAs (miRNAs). The expression of miR-1 and miR-133a, two miRNAs that are thought to play a role in muscle hypertrophy, were downregulated by PGC-1α or PGC-1β overexpression. Further studies will determine if these two miRNAs are involved in the regulation of protein synthesis with PGC-1α and PGC-1β overexpression.

Brault JJ, Jespersen JG & Goldberg AL. (2010) Peroxisome proliferator-activated receptor γ coactivator 1α or 1β overexpression inhibits muscle protein degradation, induction of ubiquitin ligases, and disuse atrophy. *Journal of Biological Chemistry* **285,** 19460-71.

Sandri M, Lin J, Handschin C, Yang W, Arany ZP, Lecker SH, Goldberg AL & Spiegelman BM. (2006). PGC-1alpha protects skeletal muscle from atrophy by suppressing FoxO3 action and atrophy-specific gene transcription. *Proceedings of the National Academy of Sciences USA* **103,** 16260-16265.