

Calcium and IL-6 mediated contraction-induced IL-6 synthesis in the contracting skeletal muscle: could it be used as a treatment for obesity?

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Introduction

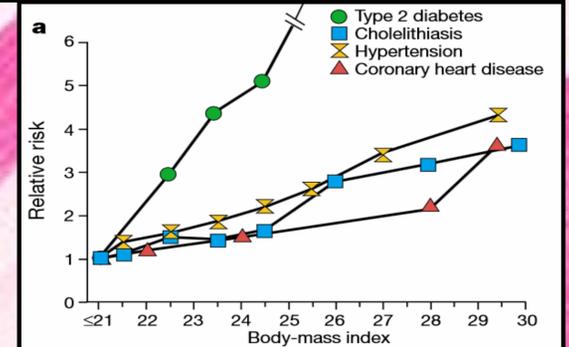
Obesity and its associated medical conditions are a worldwide medical problem taking up to 3% of a countries medical care budget. IL-6 has been reported to act as an exercise factor, and ever since the discovery of this novel function, there has been research focused on clarifying the signals that regulate its expression in the skeletal muscle, being the involvement of calcium signaling a consistent result.

Methodology

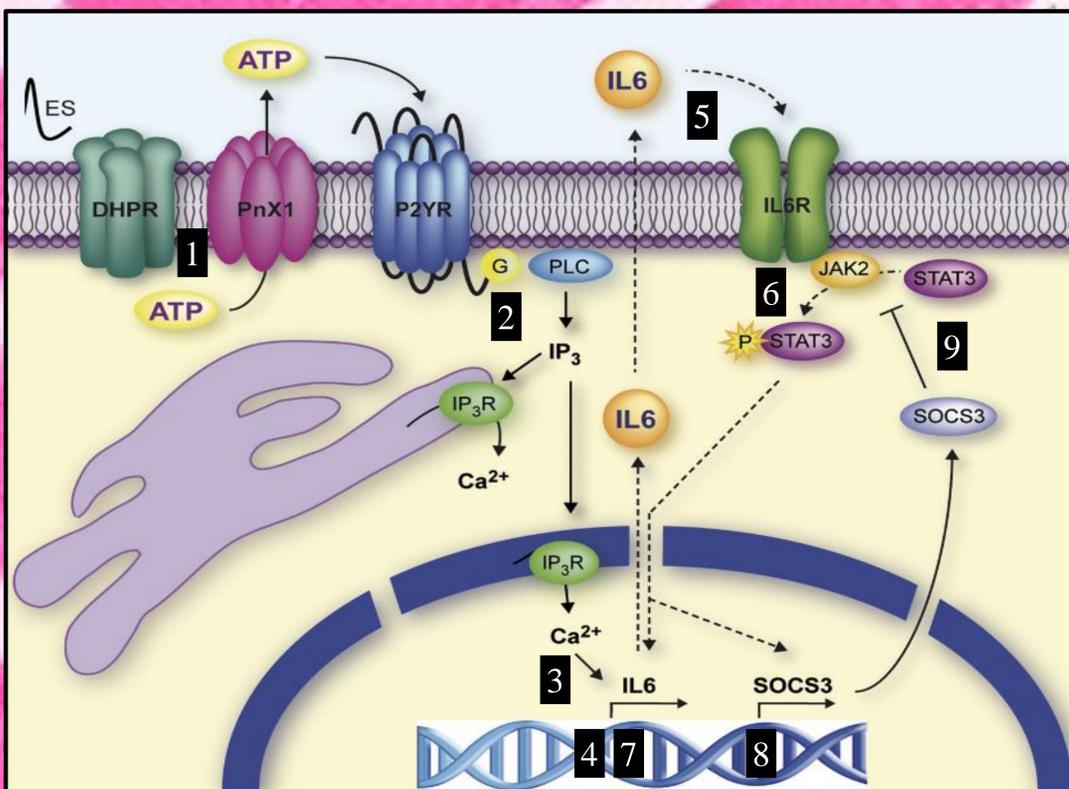
The methodology followed consisted in the extraction of information from both review and research scientific papers obtained from the Google Scholar and PubMed databases.

Objective

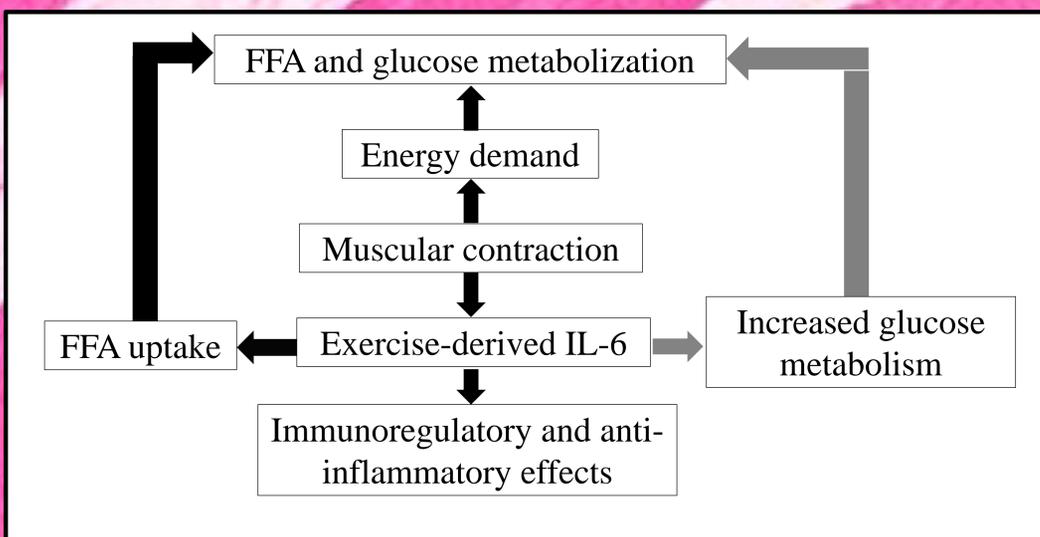
The objective is to asses whether IL-6 upregulation in the skeletal muscle could be used to treat obesity



Results



1. Contraction-induced ATP release into the extracellular medium through Pannexin
2. ATP-dependent P2Y-induced IP₃ signalling
3. Activation of calcium downstream transcription factors
4. Calcium-mediated IL-6 gene transcription.
5. IL-6 release and IL-6 receptor activation.
6. JAK2/STAT3 pathway activation
7. IL-6-dependent IL-6 gene transcription
8. SOCS3 gene transcription
9. JAK2 inhibition by SOCS3



Contraction-derived IL-6 acts as an exercise factor increasing FFA uptake in the skeletal muscle and presumably increasing whole body glucose metabolism, this occurs in response to an energy demand on the contracting muscle

Conclusions

1. The ATP and Ca²⁺ pathway is too inespecific to be modified to artificially upregulate IL-6
2. The IL-6-dependent pathway is more specific and simple, therefore, it could be a good candidate to artificially upregulate IL-6.
3. The mechanism I propose consists in low-dose IL-6 administrations into the skeletal muscle to activate the IL-6 autocrine loop
4. Would it have the desired effect?
 - RhIL-6 infusions have demonstrated an increased FFA blood levels
 - Without the energy demand FFA do not get metabolized and create ectopic fat deposits in the skeletal muscle
 - Increased intramuscular fat deposits have been positively correlated to insulin resistivity

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