Attenuation of glucose uptake is associated with reduced levels of striated activator of Rho signalling (STARS) in L6 myotubes

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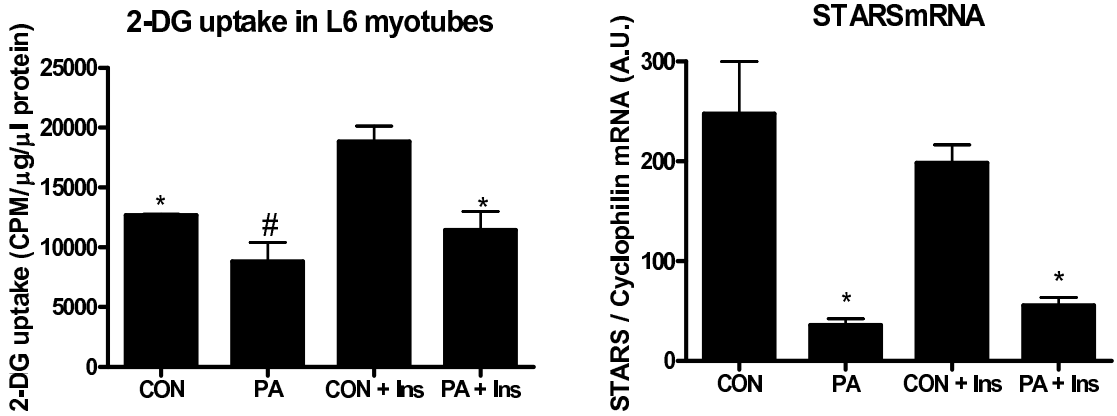
Introduction. STARS is a novel actin-binding protein specifically expressed in cardiac and skeletal muscle (Arai *et al.*, 2002). STARS binds to the I-band of the sarcomere and to actin where, in part collaboration with RhoA, stimulates the binding of free G-actin to F-actin filaments, resulting in enhanced actin polymerization and/or stabilization. The reduction in the pool of free G-actin removes its inhibition of the transcriptional co-activator myocardin-related transcription factor-A (MRTF-A) (Sotiropoulos *et al.*, 1999); the latter a positive regulator of serum response factor (SRF) transcriptional activity (Miralles *et al.*, 2003). Actin polymerization is also associated with increased skeletal muscle glucose uptake (Kanzaki, 2006). High levels of palmitic acid (PA) can cause apoptosis and attenuate glucose uptake (Turpin *et al.*, 2006), however whether this is associated with a reduction of STARS and actin polymerization is unknown.

Methods. Differentiated L6 muscle cells were treated with or without 0.75mM PA for 24 hours, followed by stimulation with or without 10 nM insulin for 30 minutes. Glucose uptake was determined by measuring the uptake of C^{14}-2-Deoxy-D-glucose (2-DG). STARS mRNA was measured using qPCR. Statistical analyses were performed using a one-way ANOVA.

Results. As shown in the figure PA reduced both basal and insulin stimulated 2-DG uptake ($p<0.05$) with a concomitant reduction in STARS mRNA ($p<0.01$).



Conclusions. PA-induced reduction in 2-DG uptake is associated with a decrease in STARS mRNA in L6 muscle cells. By analogy, the reduced level of STARS indicates a decrease in actin polymerization, MRTF translocation and SRF transcription. These results suggest that STARS signalling might play a role in basal and insulin stimulated glucose uptake. Future studies are required to establish if the down regulation of STARS has a causal influence on glucose uptake and insulin sensitivity in skeletal muscle.

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