Mechano-transduction to muscle protein synthesis is modulated by FAK
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Adjustments in muscle protein synthesis underlie the alterations of muscle mass to stimuli increasing and reducing mechanical loading. We examined the involvement of the integrin-associated focal adhesion kinase, FAK, in mechano-regulated myocellular signalling to protein synthesis. FAK signalling in mouse tibialis anterior muscle was modulated by somatic transgenesis and physiological modulation of muscle loading via hindlimb un- and reloading. Alterations in the induction of protein synthesis were monitored by assessing the activation status of phosphotransfer enzymes and downstream translation factors via measuring regulatory phosphorylation sites.

Gene electrottransfer with a constitutive-active expression plasmid of a FAK-homologue increased total FAK protein by 1.6-fold vs. empty-transfected contralateral muscle due to sarcolemma-targeted FAK overexpression. FAK overexpression was functionally important as shown by the enhancement of FAK auto-phosphorylation on Y397 between 1 and 6 hours of reloading. This FAK activation preceded the load-dependent activation of 70-kDa ribosomal S6 kinase (p70S6K) via T421/S424 phosphorylation within 24 hours of reloading. Factors residing up- or downstream of p70S6K, i.e. the kinase Akt and translation initiation factors 4E-BP1 and 2A, showed no FAK-modulated regulation.

Our findings identify FAK as a specific upstream element of the mechano-sensory pathway of p70S6K activation in striated muscle. The data support human physiological data that the mechanism underlying mechano-regulation of muscle mass is independent on the Akt-pathway commonly implicated in the regulation of muscle mass.