Regeneration of the rat tibialis anterior muscle is impaired despite induction of the SPARC-b-catenin pathway during post-immobilization recovery

Lamia Slimani, Emilie Vazeille, Christiane Deval, Julien Amat, Cécile Polge, Daniel D. Bechet, Daniel Taillandier, Dominique Dardevet, Anne Listrat, Didier Attaix, et al.

Abstract pour 7th Cachexia conferences, Kobe, Japan

Regeneration of the rat tibialis anterior muscle is impaired despite induction of the SPARC-β-catenin pathway during post-immobilization recovery

Slimani Lamia[1,2], Vazeille Emilie[3], Deval Christiane[1,2], Amat Julien[1,2], Polge Cécile[1,2], Béchet Daniel[1,2], Taillandier Daniel[1,2], Dardevet Dominique[1,2], Combaret Lydie[1,2], Attaix Didier[1,2]

[1]INRA, Unité de Nutrition Humaine (UNH, UMR 1019), CRNH Auvergne, F-63000 CLERMONT-FERRAND, France
[2]Clermont Université, Université d'Auvergne, F-63000 CLERMONT-FERRAND, France
[3]Centre Hospitalier Universitaire, 63000 Clermont-Ferrand, France.

Background and aims

The immobilization-induced tibialis anterior (TA) muscle atrophy worsens after cast removal concomitantly with changes in the extracellular matrix composition. SPARC is a matricellular glycoprotein involved in tissue response to injury and in stabilization of β-catenin, which induces muscle regulatory factors (MRFs) controlling muscle regeneration. We hypothesized that SPARC expression changed upon immobilization and could be involved in the worsening of TA muscle atrophy by altering muscle regeneration processes pending cast removal.

Methods

Wistar rats were subjected to hindlimb immobilization for 8 days (I8) or not (I0), and allowed to recover for 1 to 10 days (R1-10). Expression of SPARC, β-catenin, and proliferative (i.e. MyoD and MyF5) or differentiation (i.e. myogenin) MRFs were assessed by Western blots and/or RT-qPCR in previously immobilized TA during recovery.

Results

SPARC mRNA levels increased only during recovery at R1 (+161%) and R10 (+200%), compared to I8 and I0. β-catenin mRNA levels increased at I8 (+80%) and R10 (+190%), while protein levels accumulated from R1 to R10 (+350 to 400%) in immobilized TA vs. I0. MyoD and MyF5 mRNA levels increased by 2-3 fold only at I8 and R1 in immobilized TA vs. I0. By contrast, myogenin mRNA levels decreased at I8 (-60%) and R1 (-90%), and increased at R10 (+100%).

Conclusions

We report an induction of the SPARC-β-catenin pathway associated with increased mRNAs of the proliferative MRFs (Myf5 and MyoD) in the recovering TA early after cast removal. The differentiation MRF myogenin was first largely repressed, but increased later on, when TA started to recover. Altogether, the data suggest that the TA tended to preserve muscle regeneration potential through induction of proliferative MRFs. However this process was poorly efficient presumably because of an alteration in satellite cell differentiation.