Lack of eukaryotic initiation factor 3f expression promotes disuse atrophy in mouse skeletal muscle

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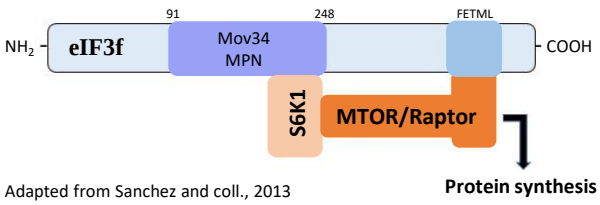
INTRODUCTION

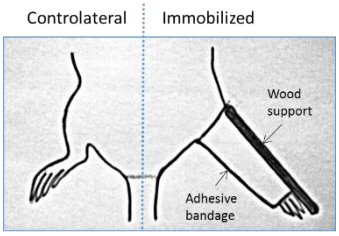
Muscle mass homeostasis is controlled by protein synthesis and degradation. The eukaryotic initiation factor 3f, a subunit of the eukaryotic initiation complex of translation eIF3, plays an important role in the atrophy/hypertrophy antagonism. eIF3f is a fundamental element of MTORC1 pathway, allowing the physical interaction between S6K1 and MTOR. While homozygous eIF3f knockout showed embryonic lethality, heterozygous knockout mice generated in our laboratory were viable and fertile. The aim of this study was to investigate *in vivo* the influence of eIF3f expression during skeletal muscle disuse. Wild-type and eIF3f $^{+/-}$ mice were subjected to hindlimb immobilization. Analysis of mass variations, cross-sectional areas, synthesis flows, S6K1 activity and eIF3f expression were conducted on quadriceps muscles.

MATERIAL & METHODS



Adapted from Sanchez and coll., 2013

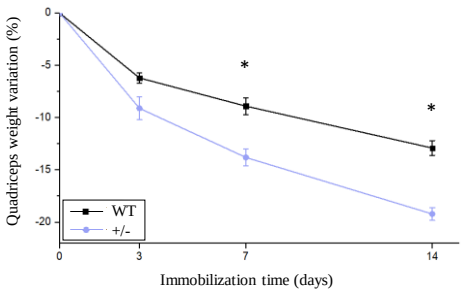
6/9-months-old C57BL/6 WT and eIF3f $^{+/-}$ males mice were submitted to unilateral immobilization for 3, 7 or 14 days. Mice were anesthetized by isoflurane inhalation to gently fix adhesive bandage. Opposed hindlimb was used as an internal control. A puromycin injection (0,04 µmol/g) was performed 15 minutes before cervical dislocation.



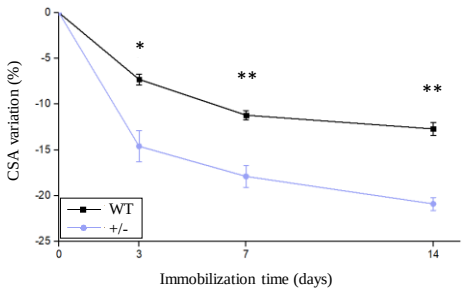
RESULTS

Values are mean ± SEM
*Significantly different at * : p <0.05 or ** : p < 0.01*

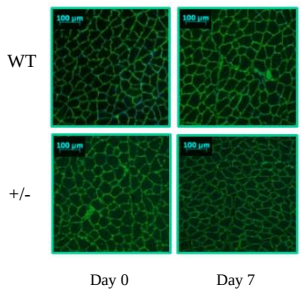
Larger decrease of muscle mass in eIF3f $^{+/-}$ mice during immobilization.



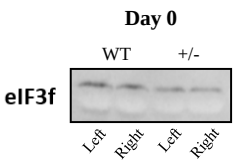
eIF3f $^{+/-}$ mice show faster and larger CSA reduction of quadriceps myofibers during immobilization.

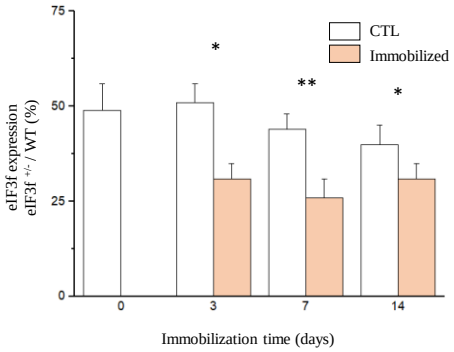


Laminin labelling

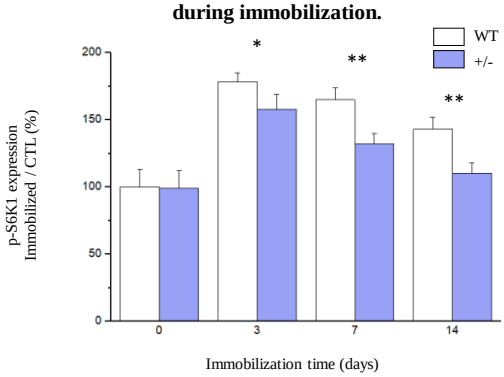


eIF3f expression level in eIF3f $^{+/-}$ mice is 50 % lower in non-immobilized hindlimb and shows larger decrease during immobilization.

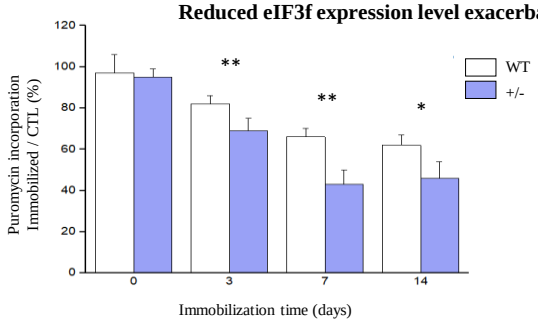


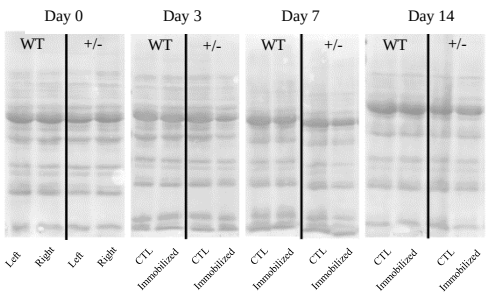


Less activity of S6K1 in eIF3f $^{+/-}$ mice during immobilization.



Reduced eIF3f expression level exacerbates protein synthesis reduction during immobilization.





CONCLUSION

Unilateral immobilization negatively impacts muscle mass, cross-sectional area of myofibers, rate of protein synthesis with an increase of MTOR activity. Activation of MTOR helps to alleviate the atrophic effect of muscle disuse. The reduction of eIF3f expression level in heterozygous mice results in a stronger atrophy, with a larger decrease in muscle mass and protein synthesis associated to a reduced MTOR activation. These results confirm *in vivo* the essential role of eIF3f in muscle mass homeostasis.