eIF3f depletion impedes mouse embryonic development, reduces adult skeletal muscle mass and amplifies muscle loss during disuse

Aurélie Docquier, Laura Pavlin, Audrey Raibon, Christelle Bertrand, Chamroeun Sar, Serge S. Leibovitch, Robin Candau, Florence Sabatier, Henri Bernardi

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**INTRODUCTION**

Embryonic death suggests an essential role of eukaryotic Initiation Factor 3f for mice development. Whole body partial depletion allows normal growth despite a body mass reduction without change in body size. Mass lowering concerns only lean mass, skeletal muscles of heterozygous mice displaying a smaller fiber size. elf3f mRNA and protein expressions are reduced in muscles of elf3f+/- mice, as well as protein synthesis and MTORC1 pathway activity. During immobilization, reduction of elf3f induction results in a stronger atrophy, with a larger decrease in muscle mass and CSA in elf3f+/- mice. Protein synthesis is also reduced and associated with a lower MTORC1 pathway activity in elf3f+/- mice. These results confirm in vivo the essential role of elf3f in development, muscular growth and muscle mass homeostasis.

**MATERIAL & METHODS**

Whole body partial depletion was obtained using elf3f allele coding sequence was substituted by lacZ reporter gene to generate heterozygous mice (elf3f +/-). elf3f+/- mice intercrosses were done to generate homozygous elf3f knockout. Genotyping using elf3f and lacZ primers allowed to identify newborn mutants. elf3f mRNA and protein expression were analyzed in skeletal muscles of elf3f+/- and wild-type (WT) mice. These, 6/9-months-old C57Bl/6 WT and elf3f+/- males mice were submitted to unilateral immobilization for 3, 7 or 14 days. Mice were anesthetized by isoflurane inhalation to gently fix adhesive bandage. A puromycin injection was performed 15 minutes before cervical dislocation. Analysis of mass, cross-sectional areas (CSA), synthesis flows and MTORC1 pathway activity were all conducted on quadriceps muscle. Opposed hindlimb was used as an internal control.

**HINDLIMB IMMOBILIZATION STUDY**

Significantly different at *: p<0.05, **: p<0.01 or ***: p<0.001

Embryonic death occurs at early stage of development

Embryonic death occurs at early stage of development

Values are mean ± SEM

**CONCLUSION**

Embryonic death suggests an essential role of eukaryotic Initiation Factor 3f for mice development. Whole body partial depletion allows normal growth despite a body mass reduction without change in body size. Mass lowering concerns only lean mass, skeletal muscles of heterozygous mice displaying a smaller fiber size. elf3f mRNA and protein expressions are reduced in muscles of elf3f+/- mice, as well as protein synthesis and MTORC1 pathway activity. During immobilization, reduction of elf3f induction results in a stronger atrophy, with a larger decrease in muscle mass and CSA in elf3f+/- mice. Protein synthesis is also reduced and associated with a lower MTORC1 pathway activity in elf3f+/- mice. These results confirm in vivo the essential role of elf3f in development, muscular growth and muscle mass homeostasis.

**REFERENCE**

Aurélie Docquier, Laura Pavlin, Audrey Raibon, Christelle Bertrand-Gaday, Chamroen Sari, Serge Leibovitch, Robin Candau, Florence Sabatier, Henri Bernardi

*INRA – UMR 604 – Dynamique Musculaire & Métabolisme – 2 Pavre Pierre Viala, 34 060 Montpellier

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