



# Evidence for autophagy attenuation during post-mortem maturation of hypertrophied muscle in myostatin deficient mice

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## Introduction

The conversion of skeletal muscle into meat, i.e. maturation, is a complex process where muscle undergoes different biochemical and physiological changes (Ouali et al, 2006). In agronomic field, the study of these events is of particular interest, in order to improve the quality of the final product put on the market. If the characterization of the proteolytic mechanisms involved in skeletal muscle maturation is still ongoing, the participation of autophagy in this process is still under debate. The aim of the study was therefore to assess the involvement of autophagy during skeletal muscle maturation and to study the interaction between autophagy and myostatin, a negative regulator of skeletal muscle mass (Mc Pherron et al, 1997), within a 72h postmortem (PM) time frame in mice.

## Methods and model validation

### Animal model

Healthy 6 month-old *Mstn*<sup>+/+</sup> (WT) and *Mstn*<sup>-/-</sup> (*Mstn* KO; Grobet et al, 2003) male mice (n=72 for each genotype) were used in this study.



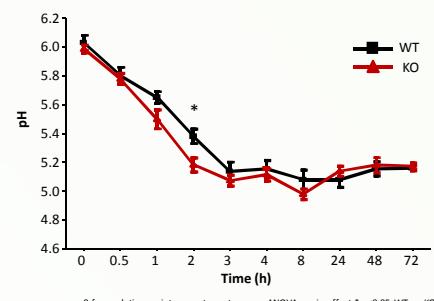
### Muscle sampling

Mice were sacrificed using cervical dislocation. After decapitation and bleeding, mice were stored at room temperature (22±2°C) during 1h and then at 4°C until the dissection time.



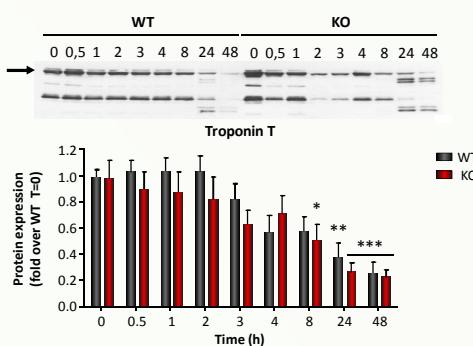
Longissimus dorsi and gastrocnemius muscles were harvested and used for pH and western-blotting analyses respectively.

### 1) pH evolution in the Longissimus muscle



Postmortem muscle pH decreased faster in *Mstn* KO mice compared to WT mice.

### 2) Myofibrillar protein degradation

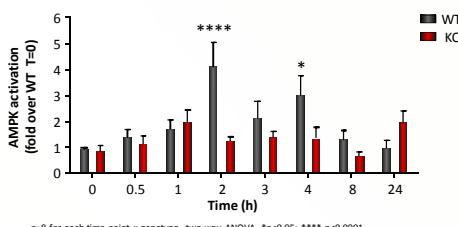
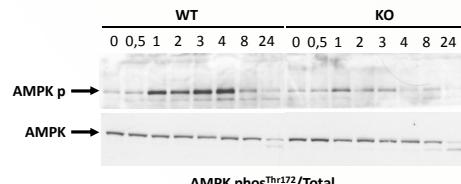


Myofibrillar proteins (e.g. Troponin T) showed a significant and progressive degradation over the 48h PM period and is more pronounced in gastrocnemius muscle of *Mstn* KO mice compared to WT mice.

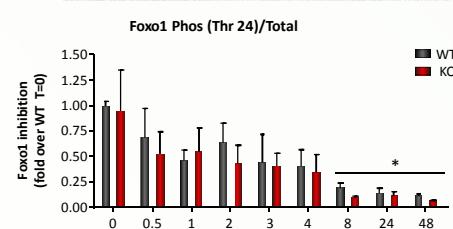
=> 3) Following PM, autophagy was assessed in skeletal muscle from the two genotypes using signaling pathways and autophagic flux analyses.

## Results

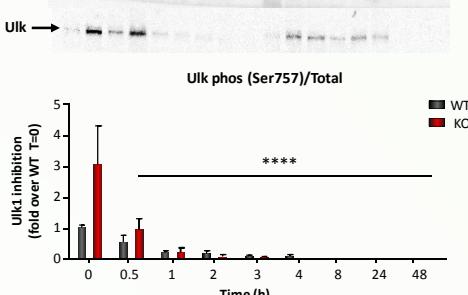
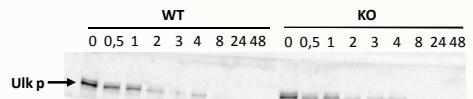
### 1) Phosphorylation state of proteins involved in autophagic signaling pathway (AMPK, FOXO and ULK)



Activation of AMPK is greater in WT mice compared to *Mstn* KO mice  
Energetic stress or/and Autophagy ?

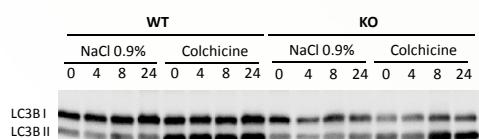


Inhibition of Foxo1 is relieved in the late PM interval (8h PM) in both genotypes => Activation of autophagy and Ub proteasome system

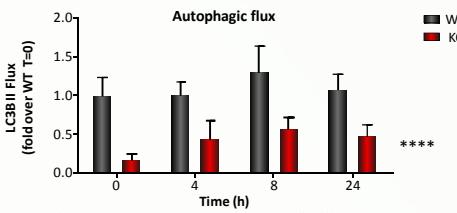


The decrease in ULK1 (Ser757) phosphorylation in *Mstn* KO mice suggests an early activation (1h PM) of autophagy

### 2) Autophagy flux measurement



Colchicine administration resulted in LC3BII accumulation  
(NaCl 0.9% vs. colchicine)



Basal and postmortem autophagic fluxes are greater in WT versus *Mstn* KO mice.

## Conclusion

In conclusion, our data showed that autophagy is preserved during skeletal muscle PM maturation, but to a lower extent in *Mstn*-deficient mice, suggesting a relationship between myostatin and autophagy. This work will be completed with microscopic analyses of skeletal muscle tissue sections to visualize *in situ* autophagic events.