Control of the proteolytic events by the Myostatin in the post-mortem skeletal muscle

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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. The study of these events and their regulation is of particular interest, in order to improve the quality of meat in agronomic field *(Ouali et al., 2006 Meat Sci)* and to understand their effect on muscle homeostasis in fundamental area.

Figure 1: *Post-mortem* maturation

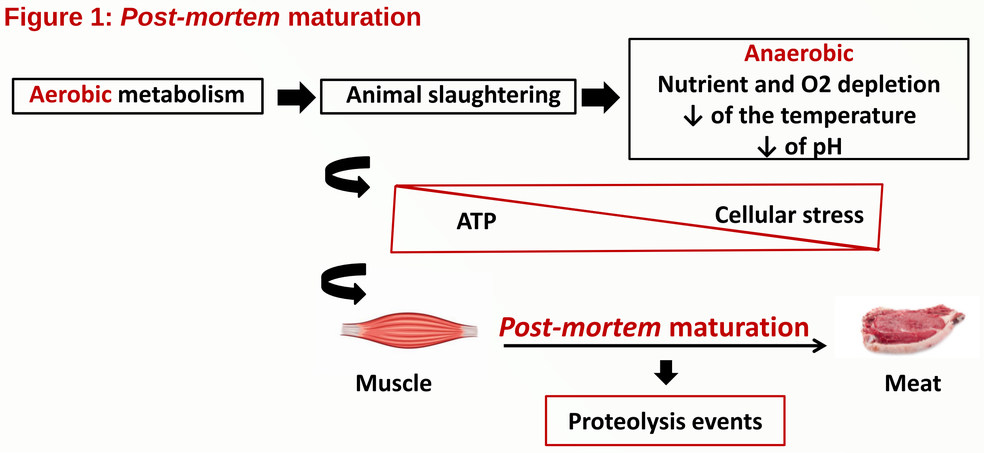


Figure 2: Proteolysis events

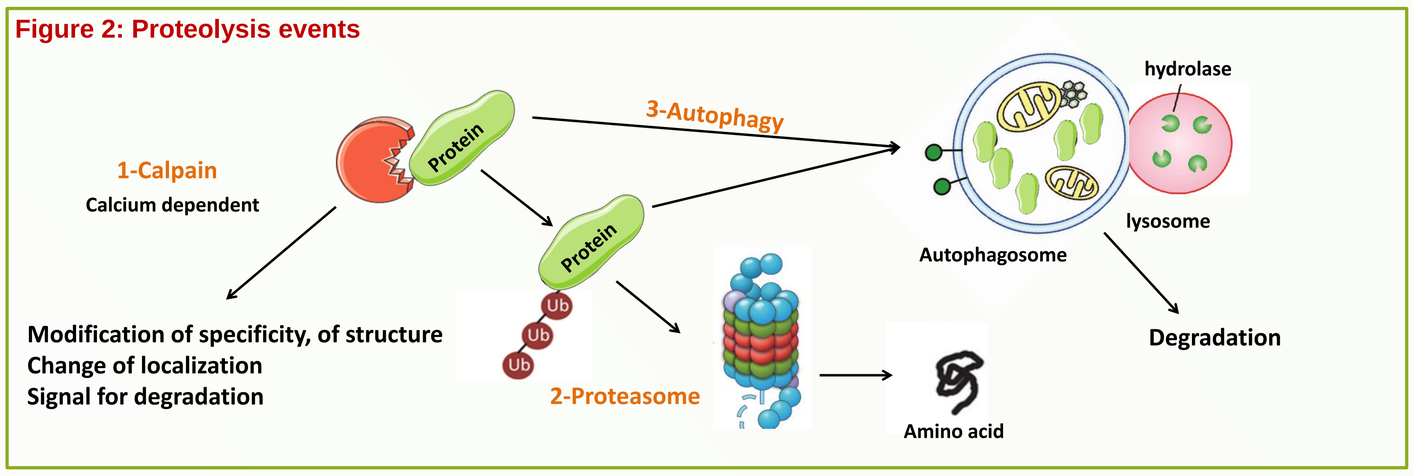
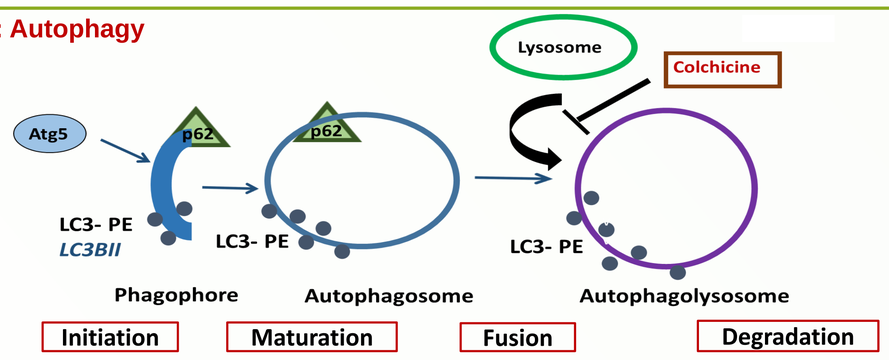


Figure 3: Autophagy

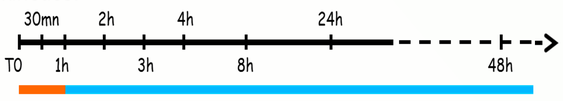


Aim & Design

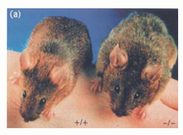
We designed a pilot study using mice to evaluate (1) the proteolytic mechanisms involvement within a 48h *post-mortem* time frame and (2) their interaction with myostatin, a negative regulator of skeletal muscle mass.

Model: Male mice Mstn +/+ (WT) and Mstn −/− (KO) 6 months old (n = 72 for each genotype).

After sacrifice, the different muscles (longissimus thoracis, tibialis anterior, gastrocnemius, and quadriceps) were taken according to the following *post-mortem* kinetics:



WT KO Mstn

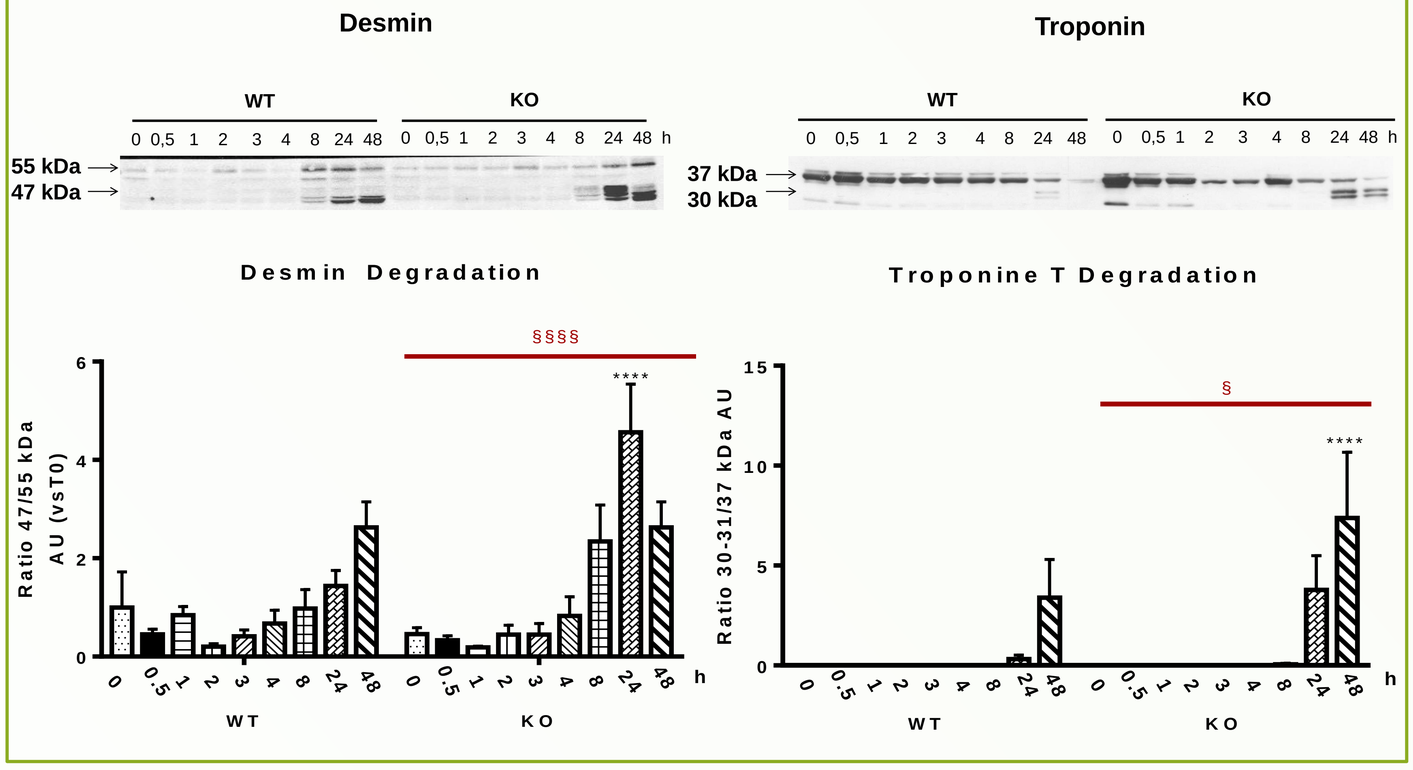


For each time point, pH was measured in longissimus thoracis. Myofibrillar and signaling pathway poteins expression in gastrocnemius was followed by Westen-blotting.

Autophagic flux was evaluated by injecting colchicine to mice every 12h for 48h, the different muscles were taken. The expression of the LC3 protein measured by Western-blotting allows the calculation of the flux.

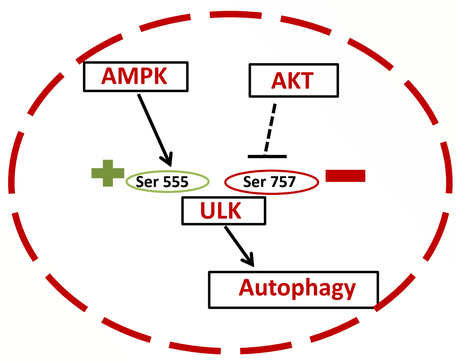
Results

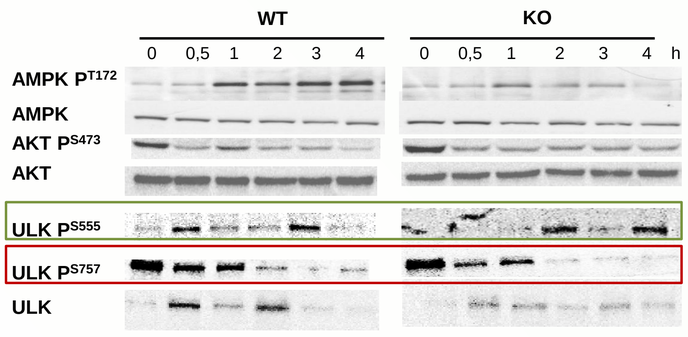
Figure 4: Myofibrillar protein degradation was significantly greater in KO Mstn mice over the 48h PM period.

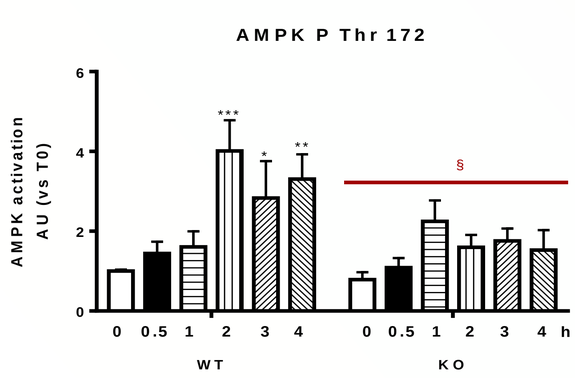


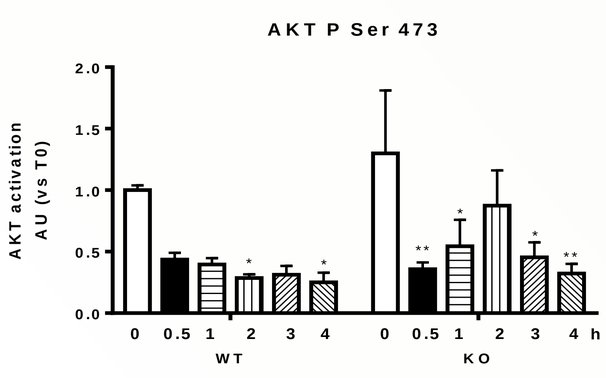
Results

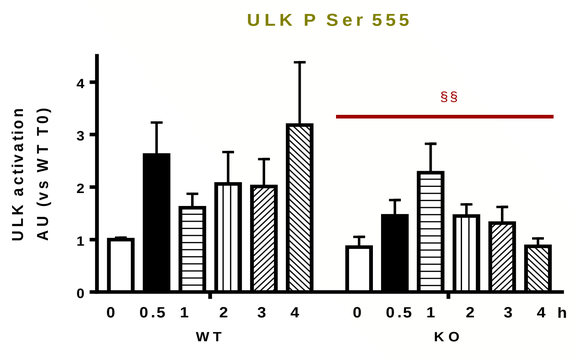
Figure 5: AMPK activation was attenuated in Mstn KO mice and was associated to a lower activation of the protein kinase ULK (inducer of autophagy) which suggests a reduced autophagy in Mstn KO mice.

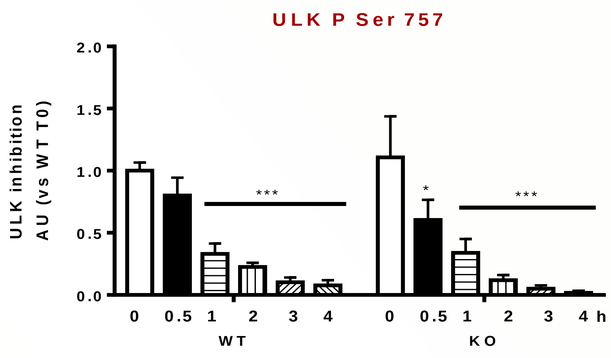






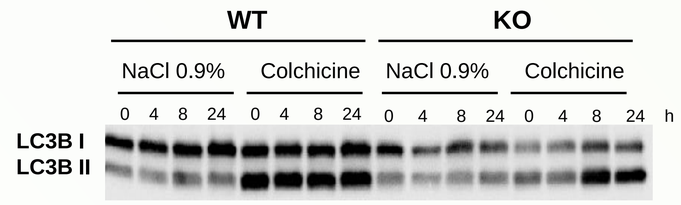




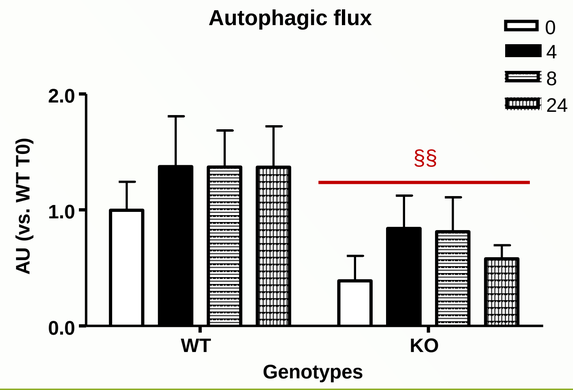


Results

Figure 6: Mstn KO muscle presents a reduced basal autophagic flux that remained low within the *postmortem* time frame.



$LC3BII_{colchicine} - LC3BII_{NaCl\ 0.9\%}$ *(Jeong-Sun Jun et al, 2010)*



Conclusions

- ✓ **Our results showed a difference in the proteolytic profile between the two genotypes during the post-mortem maturation of skeletal muscle.**
- ✓ **The absence of myostatin promotes a faster degradation of myofibrillar proteins associated to a reduced level of autophagy.**

What are the mechanisms responsible for this difference? Relationship with *post-mortem* oxidative stress?
What is the impact of autophagic inhibition on other proteolysis events?

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