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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 (Mcp Herron et al, 1997), within a 72h postmortem (PM) time frame in mice.

Methods and model validation

Animal model

Healthy 6 month-old Mstn-/- (WT) and Mstn+/- (Mtn 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 (Mstn KO; Grobet et al, 2003) male mice (n= 72) and then at 4 °C until the dissection time.

Muscle sampling

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

Results

1) pH evolution in the Longissimus muscle

WT KO Mstn

2) Myofibrillar protein degradation

WT KO

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

AMPK

AMPK

AMPK

AMPK

AMPK

Foxo1 Phos (Thr 24)/Total

Foxo1 Phos (Thr 24)/Total

Foxo1 Phos (Thr 24)/Total

Foxo1 Phos (Thr 24)/Total

Foxo1 Phos (Thr 24)/Total

Ulk1 Phos (Ser 757)/Total

Ulk1 Phos (Ser 757)/Total

Ulk1 Phos (Ser 757)/Total

Ulk1 Phos (Ser 757)/Total

Ulk1 Phos (Ser 757)/Total

myostatin-deficient WT mice compared to WT mice.

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

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Foxo1 Phos (Thr 24)/Total

Foxo1 Phos (Thr 24)/Total

Ulk1 Phos (Ser 757)/Total

Ulk1 Phos (Ser 757)/Total

Ulk1 Phos (Ser 757)/Total

Ulk1 Phos (Ser 757)/Total

Ulk1 Phos (Ser 757)/Total

myostatin-deficient WT mice compared to WT mice.

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

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.