



# Post-mortem proteolysis: Emerging link between Myostatin, Oxidative stress and Autophagy

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Université Libanaise

Ecole Doctorale  
Sciences et Technologie



# ***Post-mortem proteolysis: Emerging link between Myostatin, Oxidative stress and Autophagy***

Presented by  
**Rim Nassar**



National Council for Scientific Research

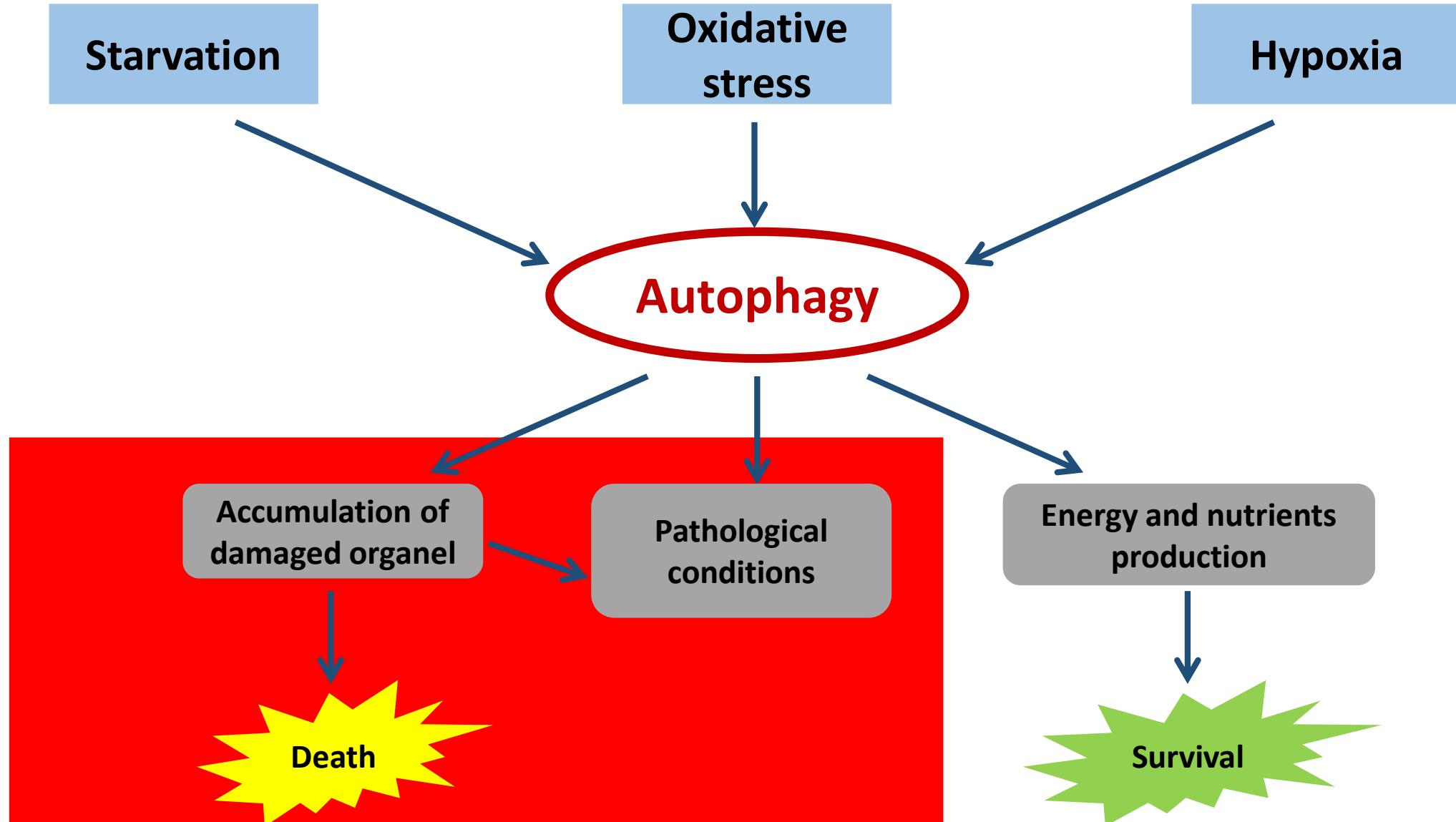
**DMeM**  
Dynamique Musculaire et Métabolisme

**LIT**

Laboratoire d'Innovation Thérapeutique

# *Role of autophagy*

Crucial process that is involved in the degradation and recycling of damaged components within the cell



# *Autophagy is required to maintain muscle mass and function*

➤ *Constitutive conditions* *Masiero et al 2009:*

The inhibition of autophagy



1. muscle atrophy
2. loss of force production
3. muscle weakness

➤ *Pathological muscle conditions associated to autophagy dysregulation*

Pompe disease *(C. Nascimbeni et al 2012)*

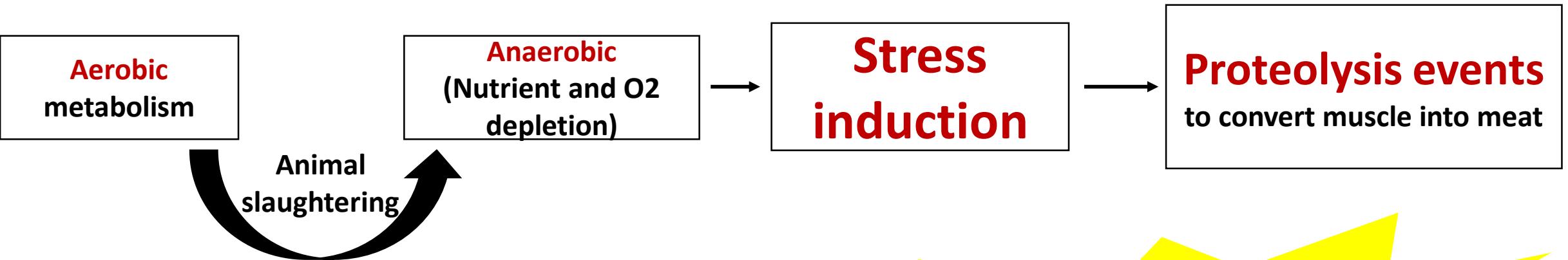
Vici syndrome *(Cullupe et al 2013)*

Duchenne Muscular Dystrophy *(De Plame et al 2012)*



Down-regulation of autophagy  
(accumulation of damaged  
organelles)

# *Muscle post-mortem maturation*



Autophagy 10:1, 137–143; January 2014; © 2014 Landes Bioscience

## Autophagy during beef aging

Marina García-Macia,<sup>1,†</sup> Verónica Sierra,<sup>1,2,†</sup> Ana Palanca,<sup>1</sup> Ignacio Vega-Naredo,<sup>1</sup> David de Gonzalo-Calvo,<sup>1</sup> Susana Rodríguez-González,<sup>1</sup> Mamen Oliván,<sup>2</sup> and Ana Coto-Montes<sup>1,\*</sup>

**Quid of Autophagy regulation in PM ?**

**PM maturation depends on:**

- Biochemical factors: stress, pH, pathway signaling
- Physical factors: animal breeding and slaughtering
- **Genetic factors**

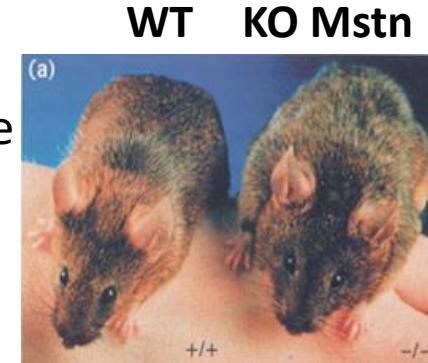
# *Myostatin: Negative regulator of muscle mass*

=> *Protein synthesis/degradation balance*

- **Absence** (KO Mstn) => Hypertrophy => increase of the muscle fiber number and size
- **Conserved function** among species



*Grobet et al 1997*



=> *Redox balance*

- **Absence** (*Ploquin et al 2012*) => **Antioxidant status enhancement**
- (*Sriram et al 2011*) => Addition of Mstn => increase the ROS production

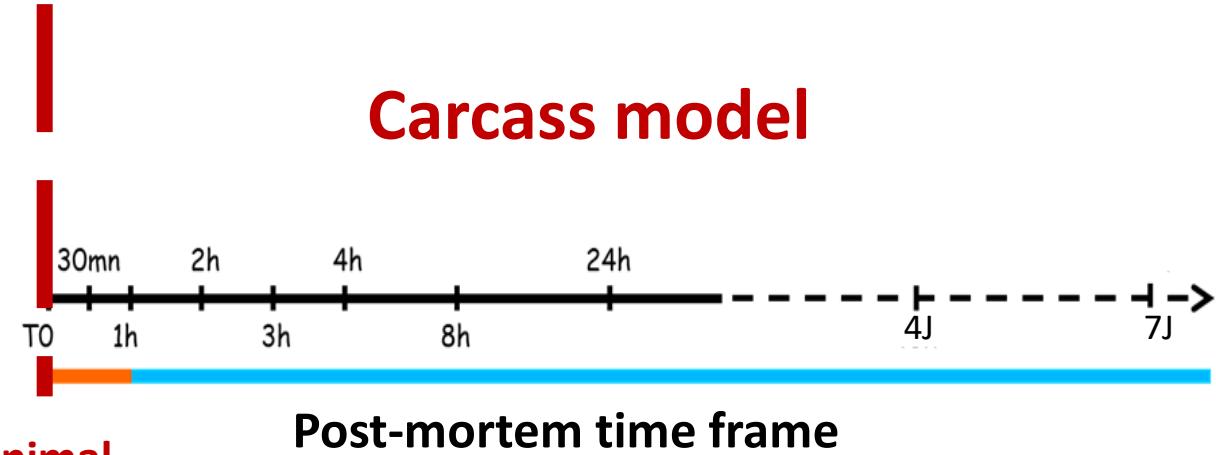
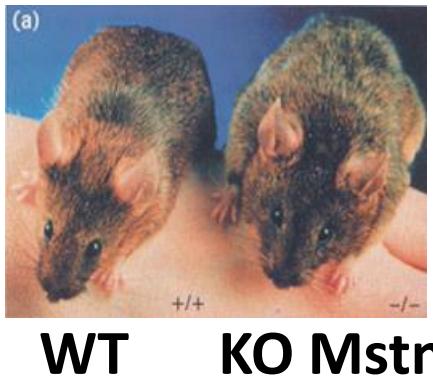




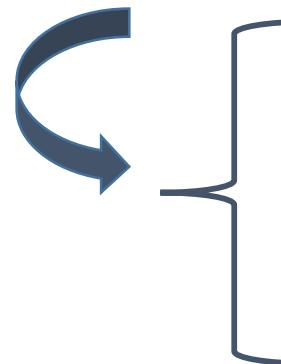
**Is the autophagic process involved in the post-mortem maturation of muscle into meat??**

**How this mechanism is regulated??**

# *Experimental design: Pilot study*



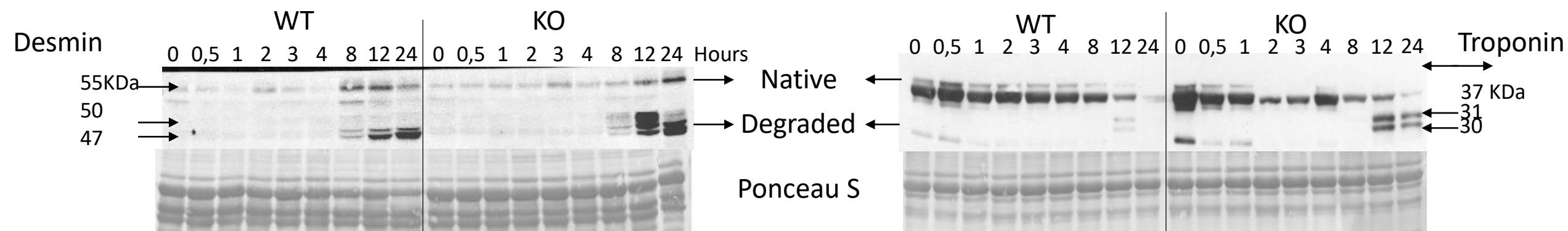
**Animal  
slaughtering**  
By cervical  
dislocation



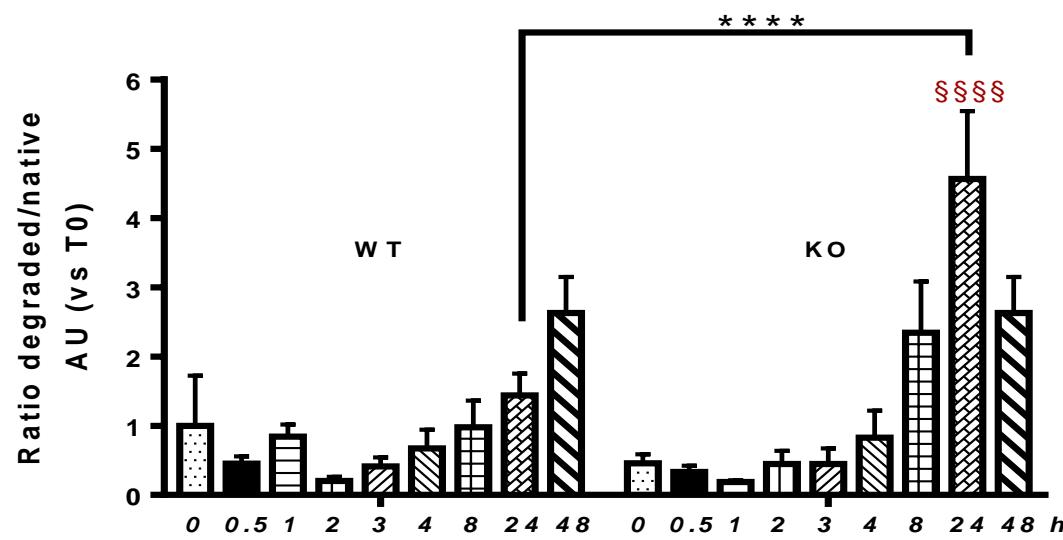
- Myofibrillar protein degradation (Troponin T- Filamin C - Desmin)
- Oxidative stress markers
- Autophagic flux



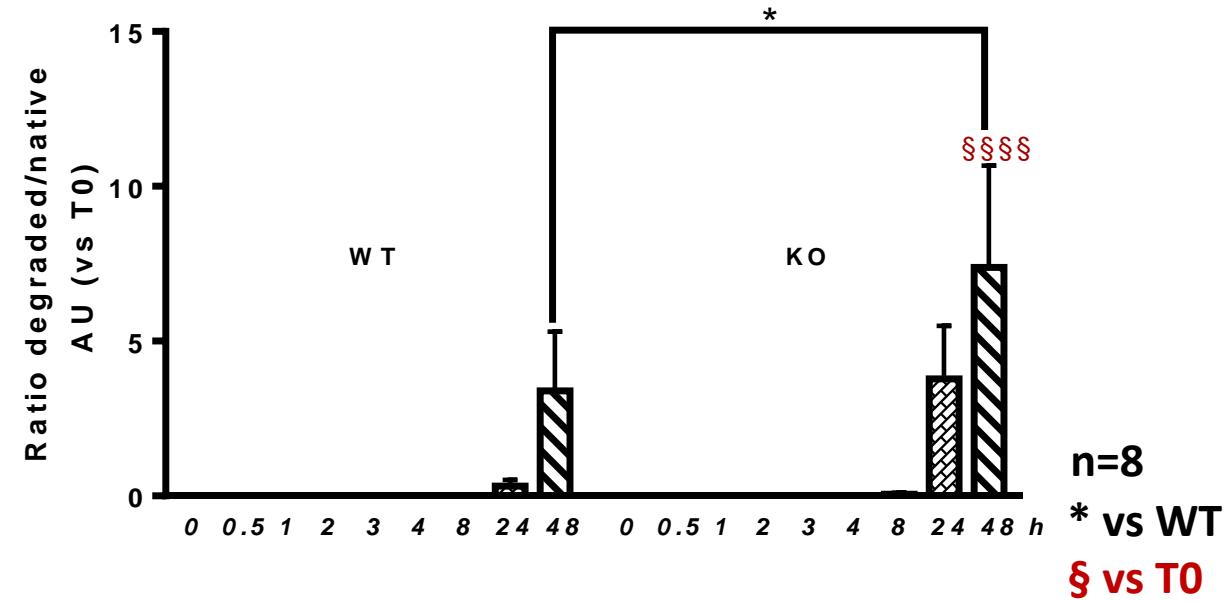
# Post-mortem myofibrillar protein degradation is more pronounced in KO Mstn



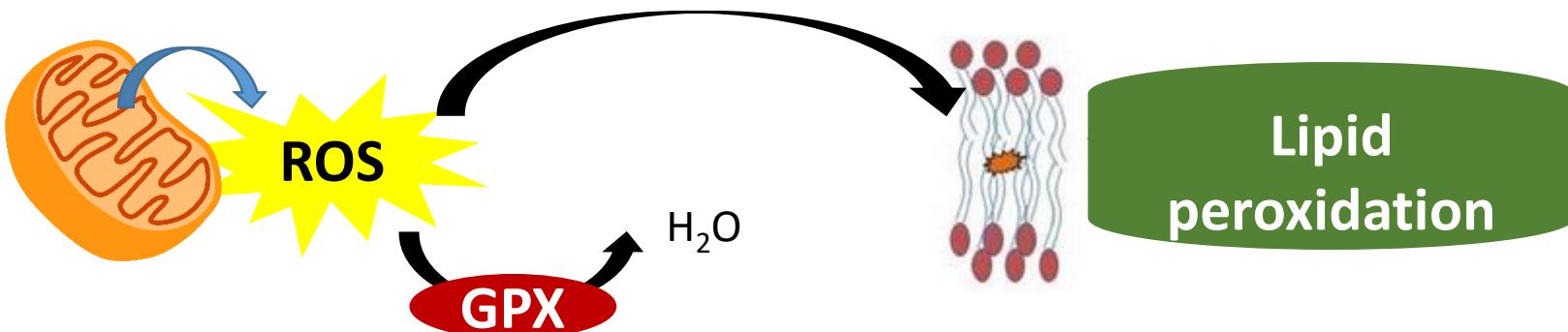
Desmin Degradation



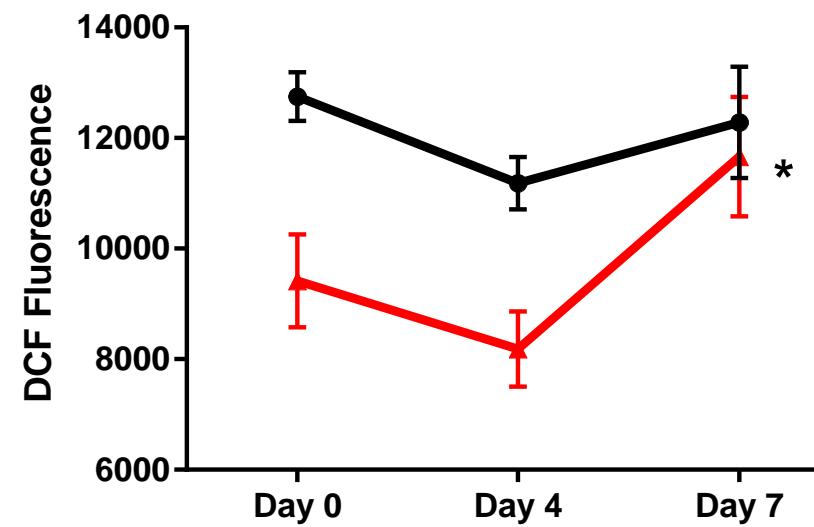
Troponin T Degradation



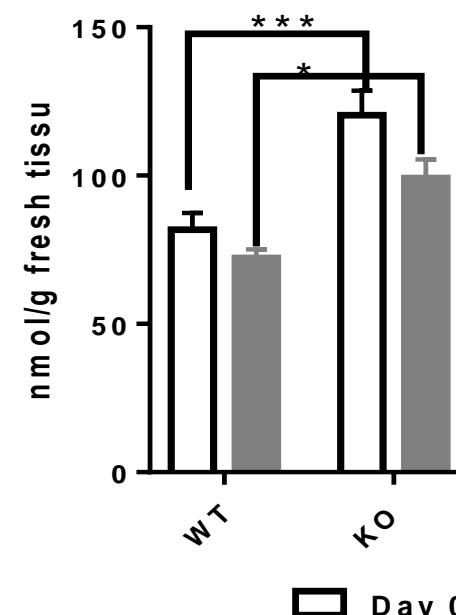
# The oxidative stress was not induced during the PM maturation in WT and KO Mstn mice



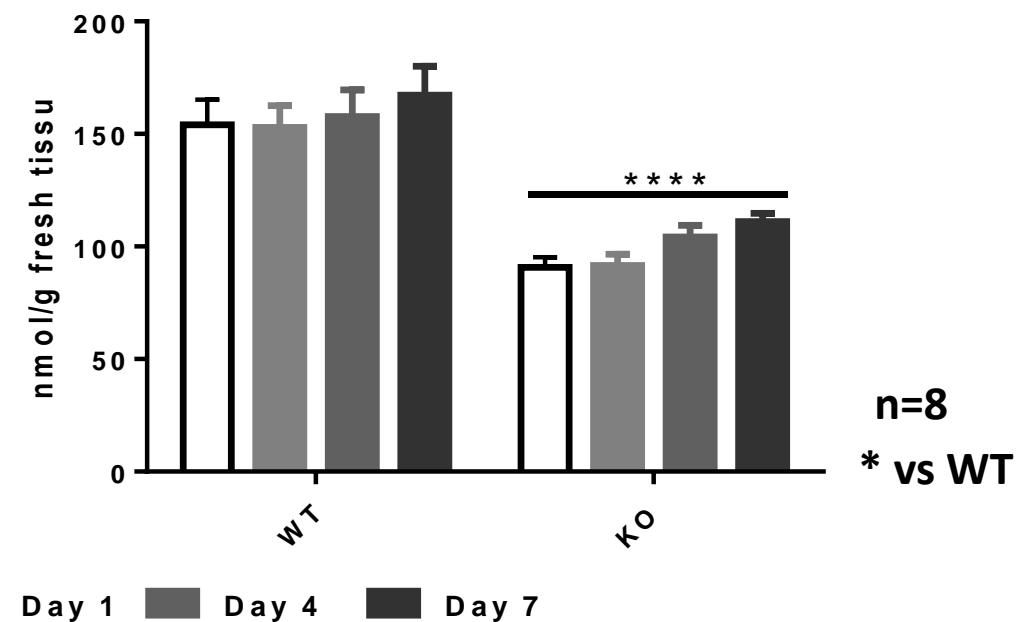
ROS measurement



GPx activity



Lipid peroxidation



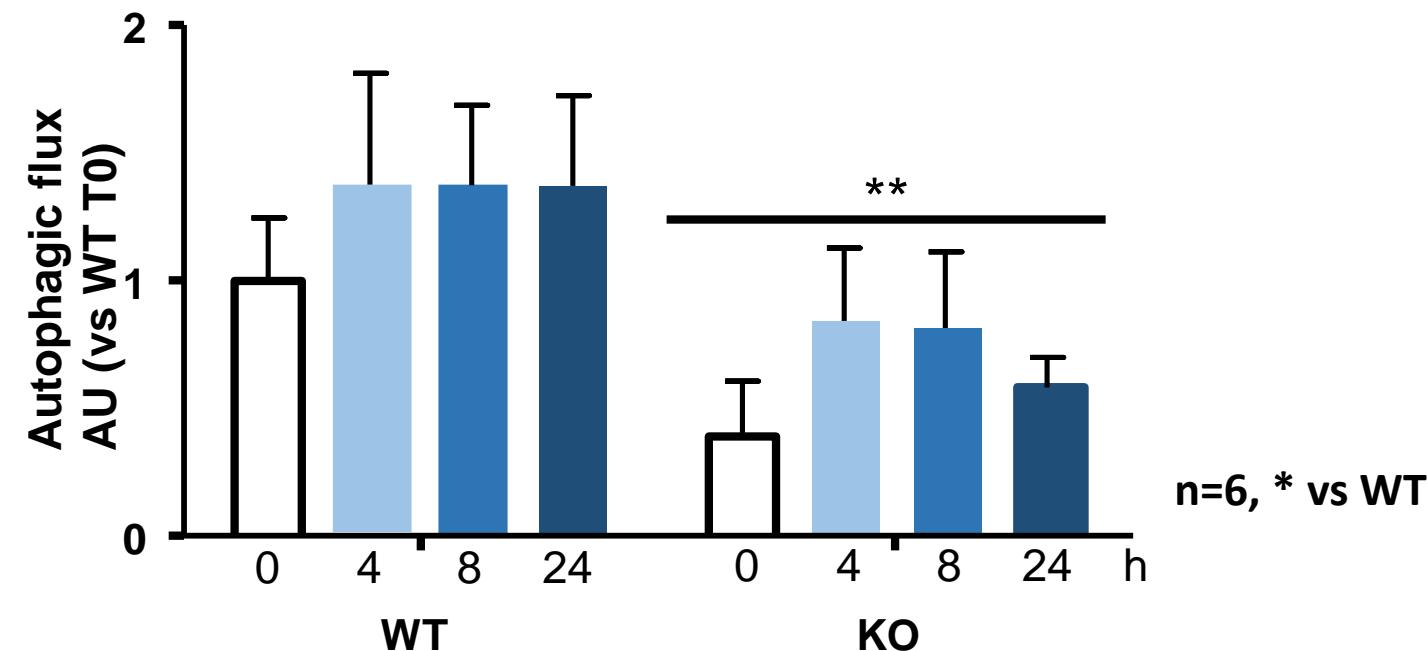
n=8

\* vs WT

# The autophagy was not induced during the PM maturation in WT and KO Mstn mice



Autophagic flux (LC3BII coL – LC3BII SP)



In our PM model (muscle on carcass):

*Absence of ROS production  
alteration*

*Absence of autophagy induction*

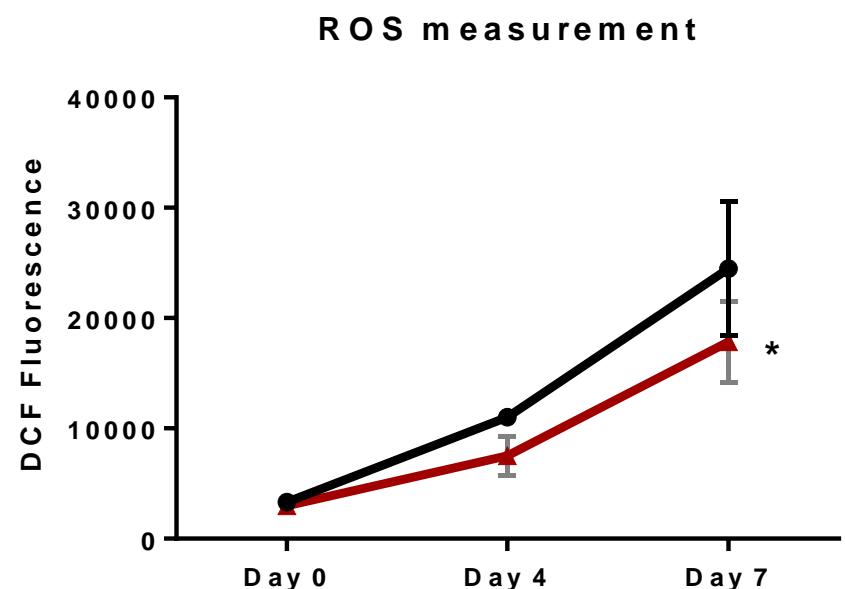
**Is the model carcass representative of livestock  
slaughtering condition?**

Carcass model Vs isolated muscle

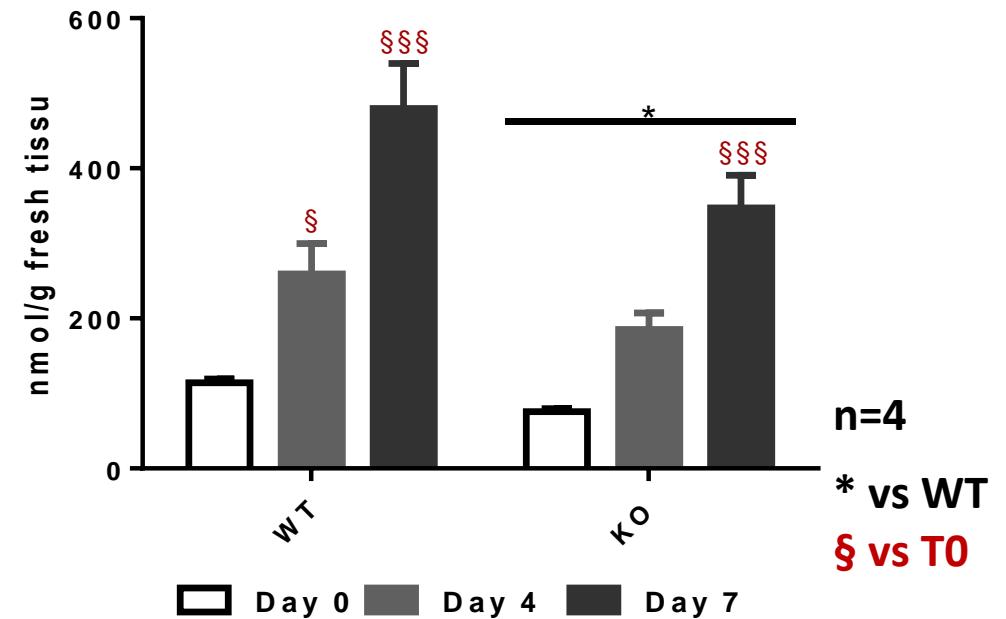


# *The oxidative stress markers were increased during the PM maturation*

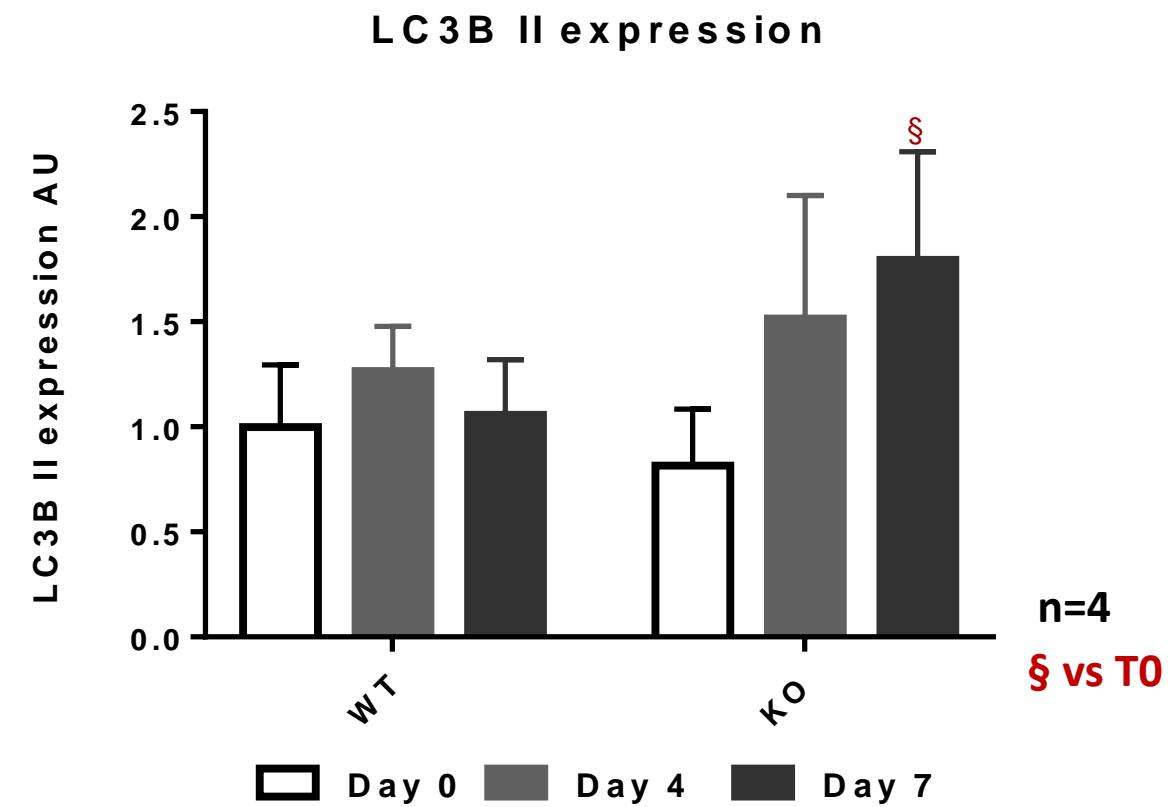
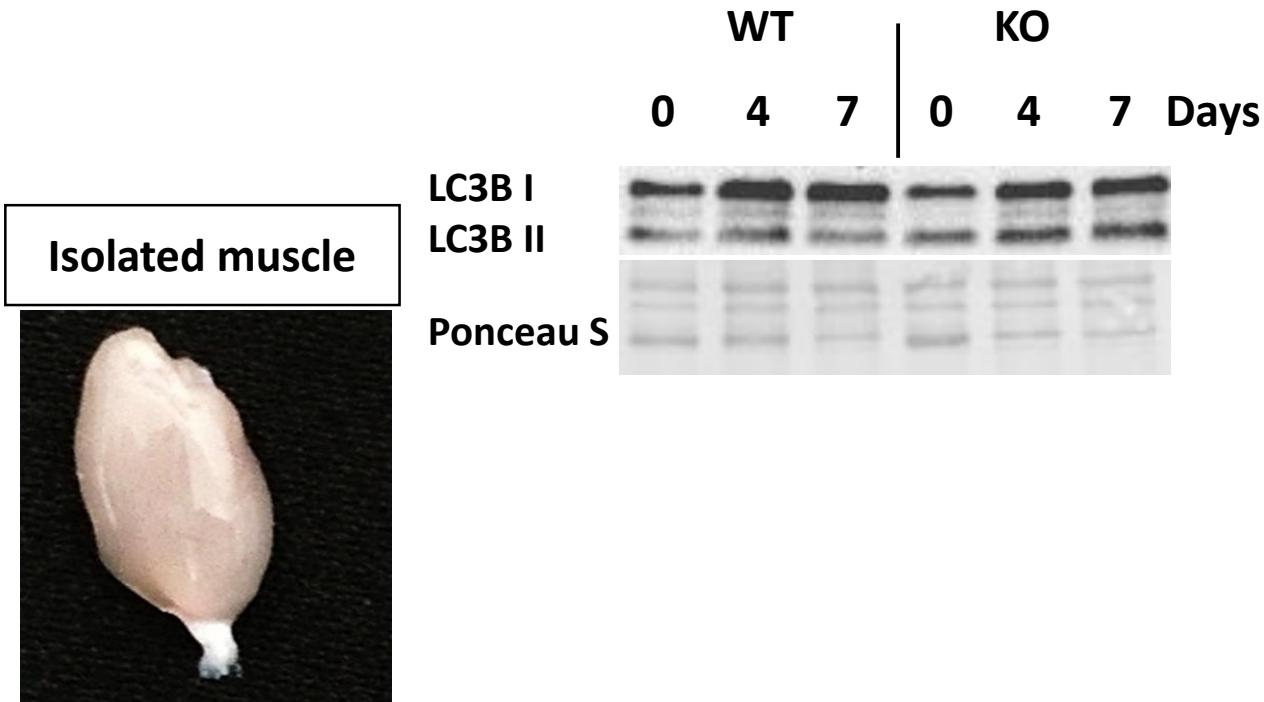
Isolated muscle



Lipid peroxidation



# *Increasing of LC3 expression during PM in the absence of myostatin*



# Conclusion



***Our pilot model on isolated muscle suggested:***

1. The involvement of autophagic process in PM
2. The PM autophagy could be correlated to an oxidative stress and may depend on genotype
  - Increasing the « n » number of animal
  - Measurement of the autophagic flux



**Via which mechanism the myostatin could regulates proteolysis??**

# Acknowledgment

## Participants

### UMR DMeM INRA- Montpellier

Anne Bonnieu  
Béatrice Chabi  
Arnaud Chatonnêt  
Barbara Vernus  
François Casas  
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**BIOZENTRUM**

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The Center for Molecular Life Sciences

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Romain Godoye  
Mélanie Macart

### Laboratoire d’Innovation Thérapeutique Beyrouth

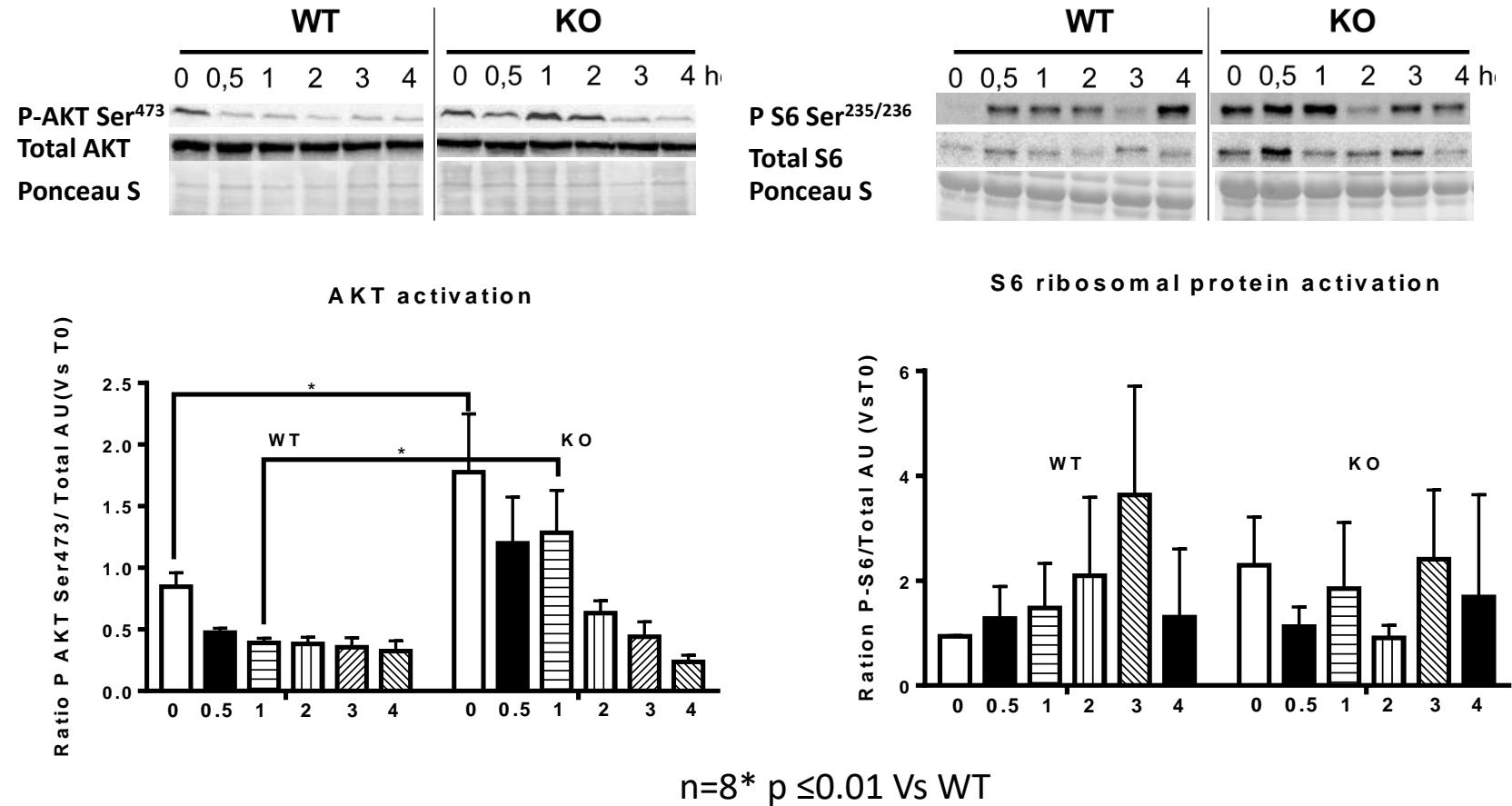
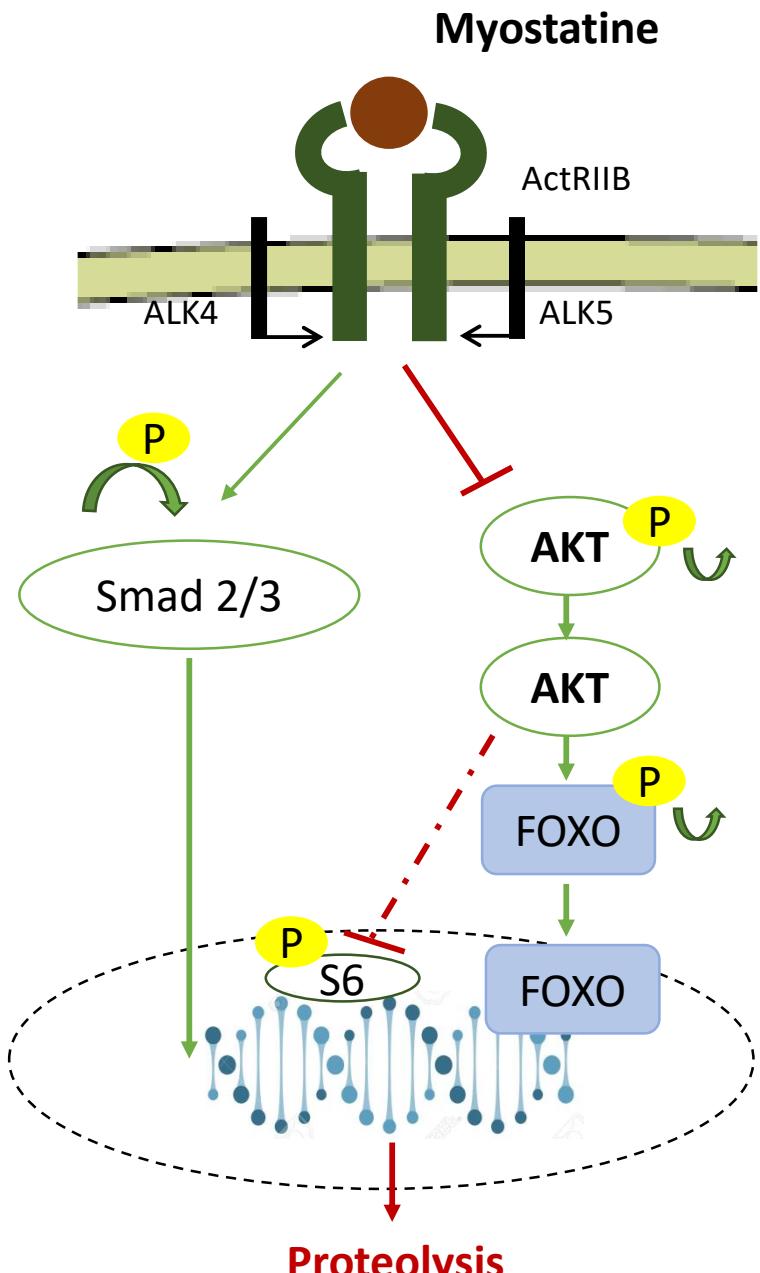
Fadia Najjar  
Aline Hamade

## Collaborations

UMRH Theix  
Brigitte Picard  
Isabelle Cassar-Malek

INSERM, ERI25-Muscles et Pathologies, Montpellier  
Gilles Carnac

# Ongoing work

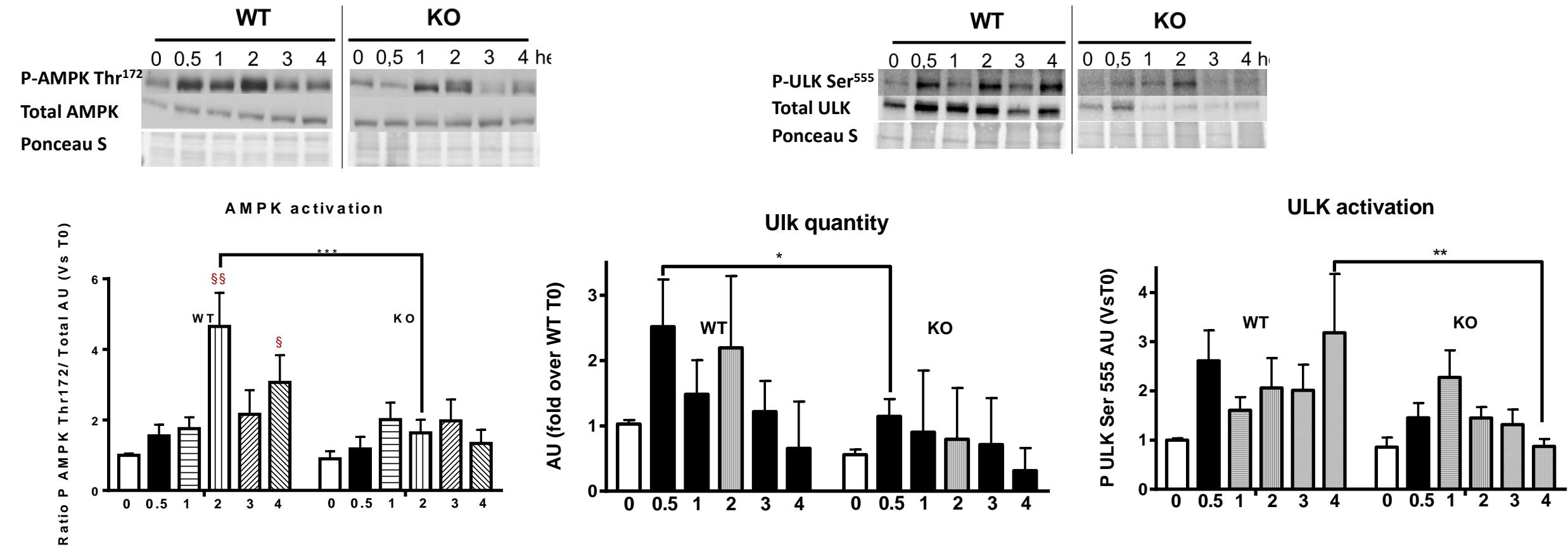


**KO Mstn enhances the activation of AKT correlated with S6 activation at basal level**

# Ongoing work



n=8\* p ≤0.01 Vs WT, § p ≤0.01 Vs T0



**KO Mstn reduces AMPK activation and total ULK synthesis => reduced ULK activation during PM maturation**

# Stress induction at 7 days post-mortem in an isolated muscle correlated with autophagic induction

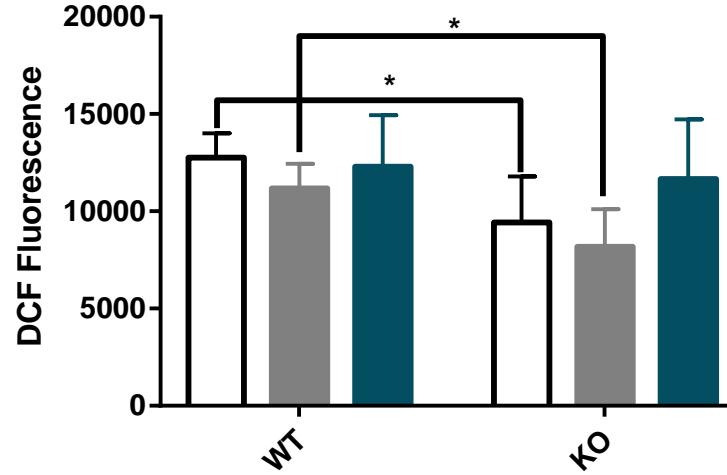
## Isolated muscle



## Carcasse



### ROS measurement



### LC3 II expression

