

# CONCEITOS BÁSICOS DA AUTOFAGIA

ANA PAULA PINTO

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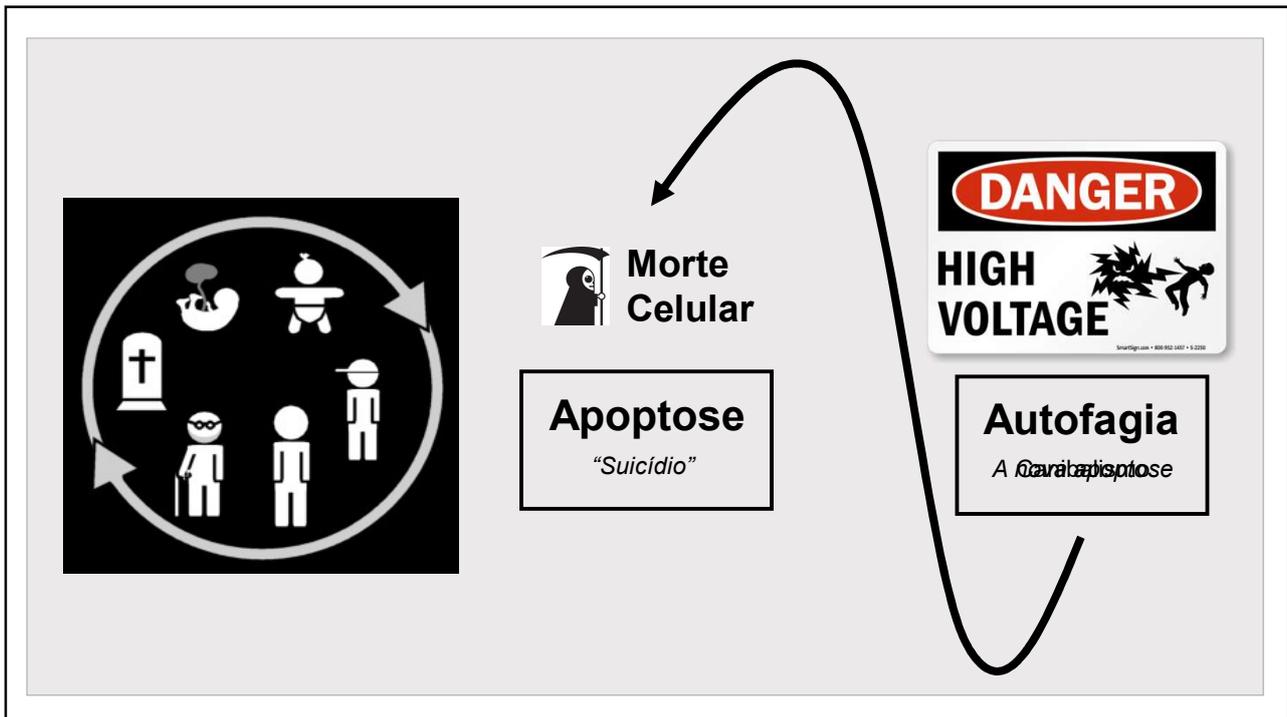
## AUTOFAGIA

Do grego:

- **Auto**: a si mesmo;
- **Phagy**: comer.

- A autofagia é o único mecanismo para **degradar grandes estruturas**, como organelas e proteínas.
- No seu estado basal fornece um serviço de "**eliminação de lixo**" para células, removendo componentes que poderiam tornar-se tóxicos.

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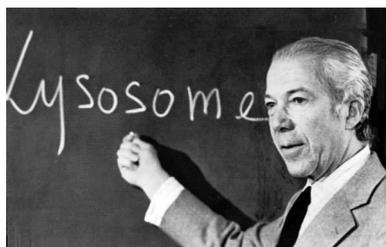


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## AUTOFAGIA

### • 1955 → Christian de Duve

- Lisossomos (1974 Premio Nobel)
- Organelas dentro de lisossomos



The cellular process through which intracellular materials are delivered to the lysosome or vacuole for degradation

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Descoberta dos mecanismos subjacentes à autofagia. Seu grupo isolou 15 mutantes de levedura levando à descoberta de vários genes relacionados à autofagia

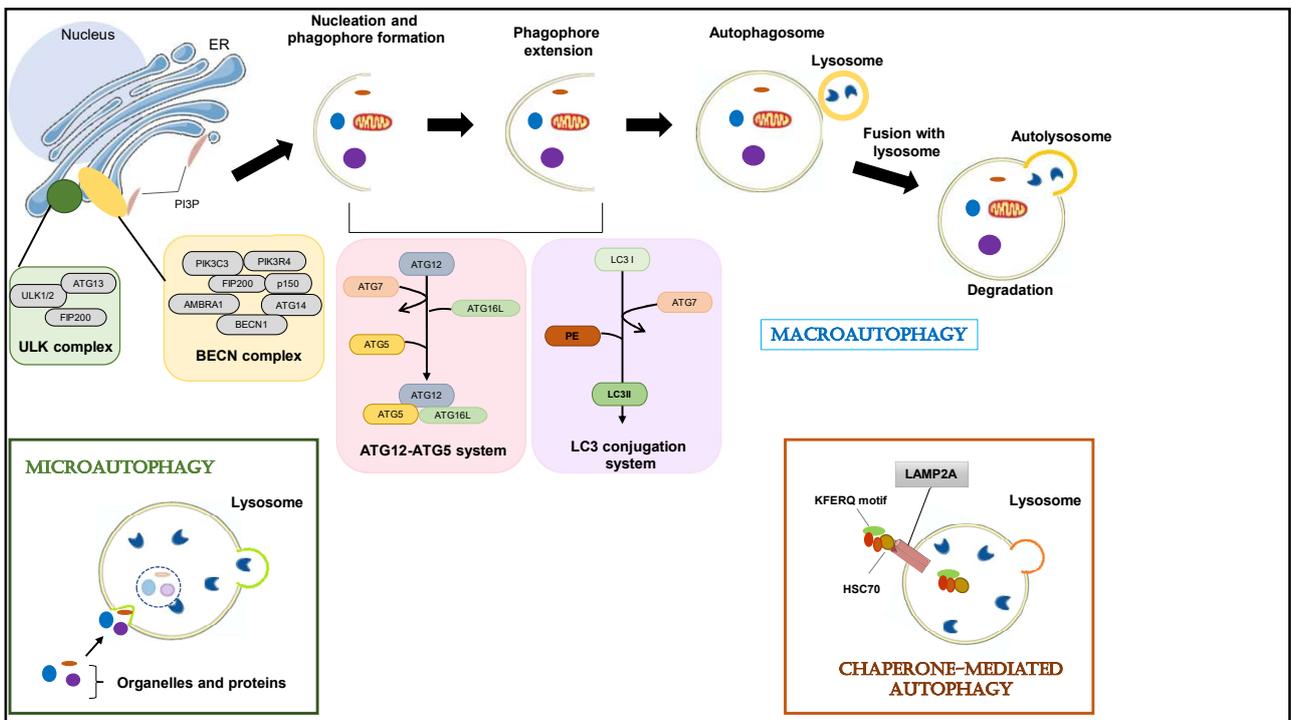
*The Nobel Assembly at Karolinska Institutet has today decided to award the*

## 2016 NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE

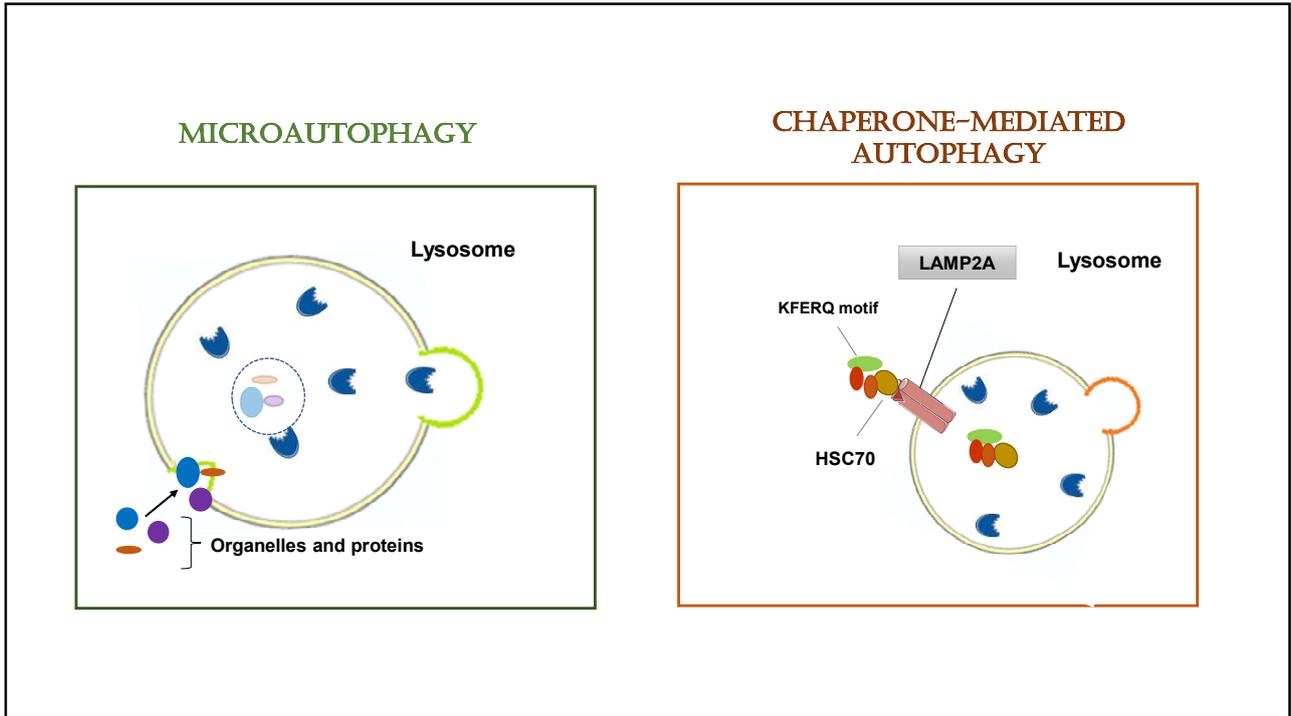


# Yoshinori Ohsumi

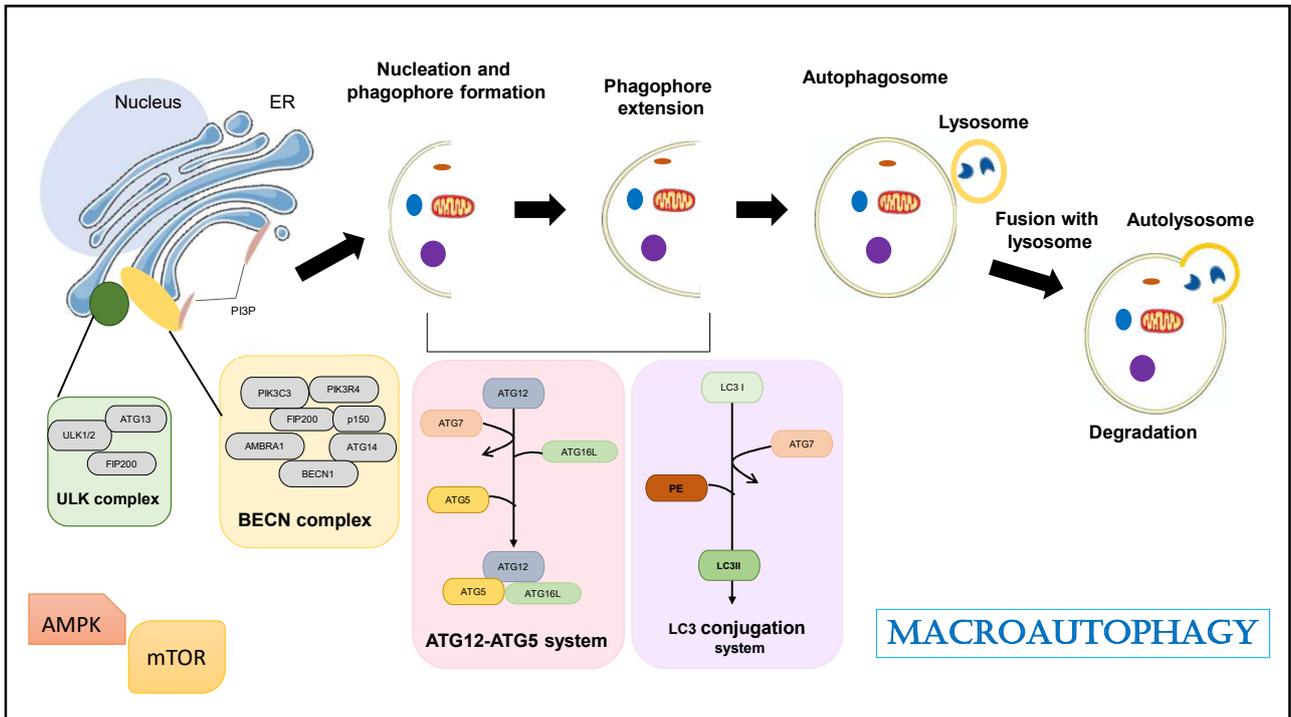
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REVIEWS

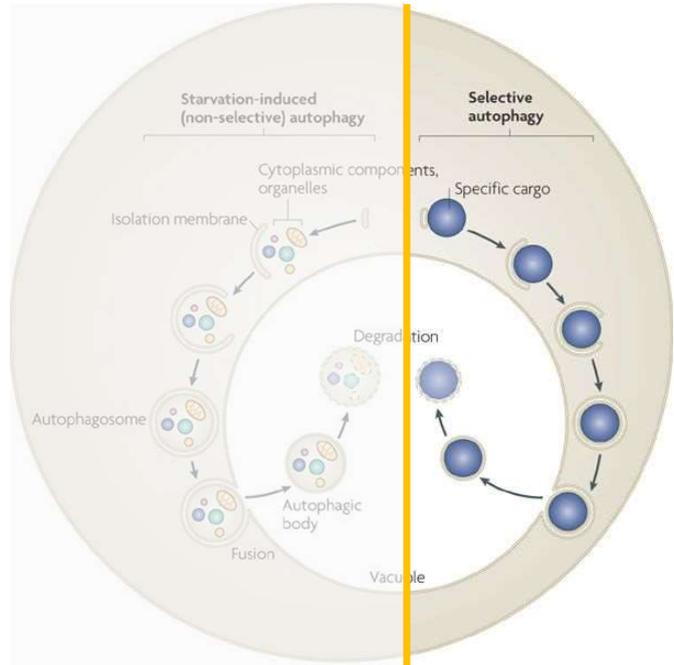
Dynamics and diversity in autophagy mechanisms: lessons from yeast

Hitoshi Nakatogawa\*, Kuninori Suzuki\*, Yoshiaki Kamada\* and Yoshinori Ohsumi\*

Abstract | Autophagy is a fundamental function of eukaryotic cells and is well conserved from yeast to humans. The most remarkable feature of autophagy is the synthesis of double membrane-bound compartments that sequester materials to be degraded in lytic compartments, a process that seems to be mechanistically distinct from conventional membrane traffic. The discovery of autophagy in yeast and the genetic tractability of this organism have allowed us to identify genes that are responsible for this process, which has led to the explosive growth of this research field seen today. Analyses of autophagy-related (Atg) proteins have unveiled dynamic and diverse aspects of mechanisms that underlie membrane formation during autophagy.

NATURE REVIEWS | MOLECULAR CELL BIOLOGY

- “Mitofagia”
- “Lipofagia”
- “Ribofagia”
- “Ferritinofagia”



Nature Reviews | Molecular Cell Biology

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REVIEWS

Dynamics and diversity in autophagy mechanisms: lessons from yeast

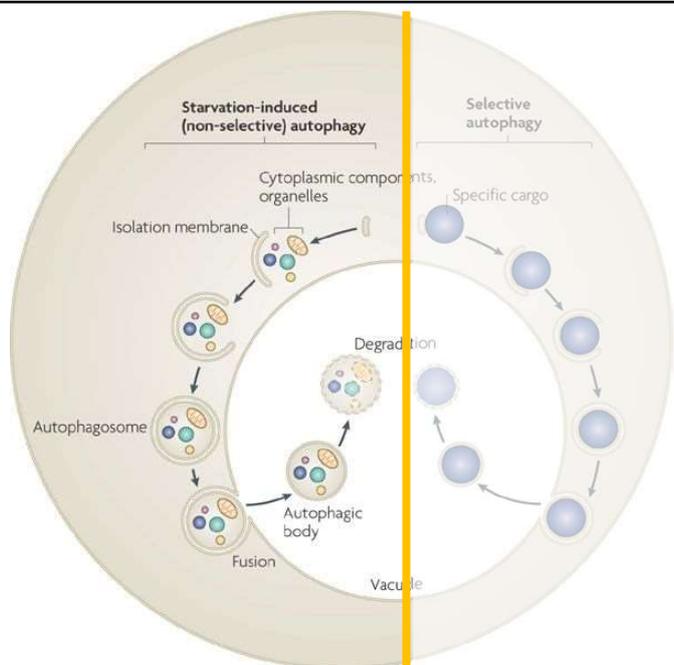
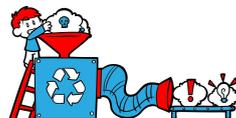
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NATURE REVIEWS | MOLECULAR CELL BIOLOGY

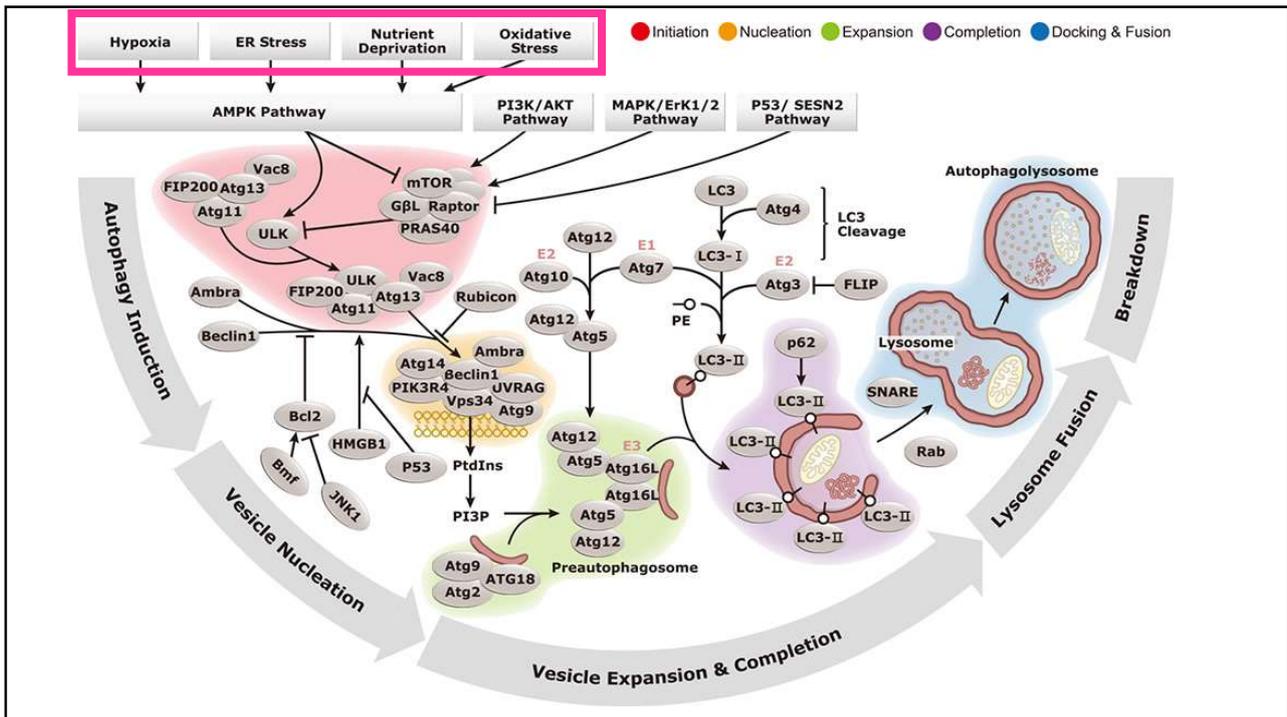
Degradação não-específica  
(em princípio)

Reciclagem e  
liberação de  
nutrientes



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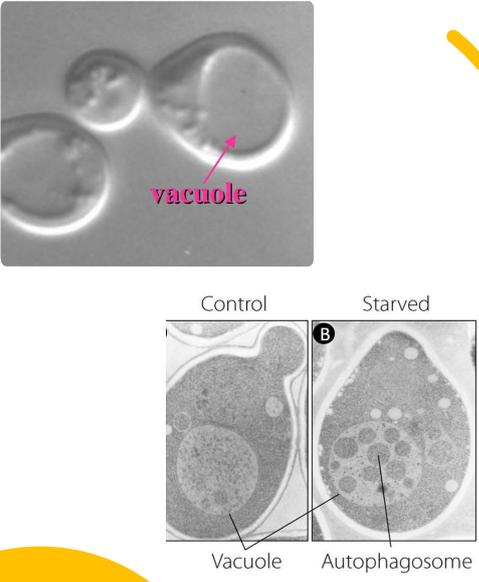
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# AUTOFAGIA

## ESSENCIAL:

- manutenção energética;
- resposta celular ao estresse;
- defesa contra patógenos;
- reprogramação celular.

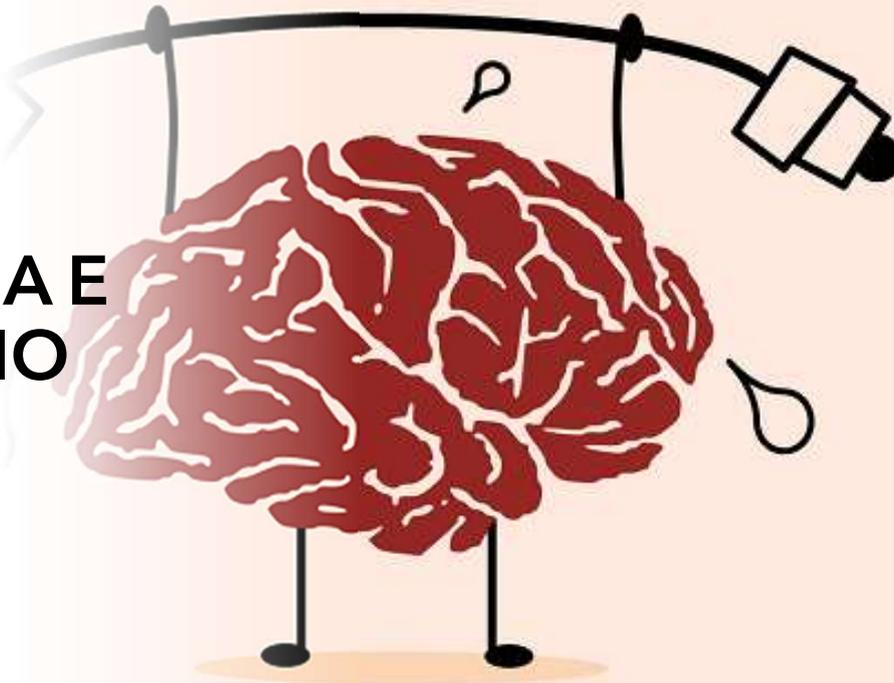
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# AUTOFAGIA

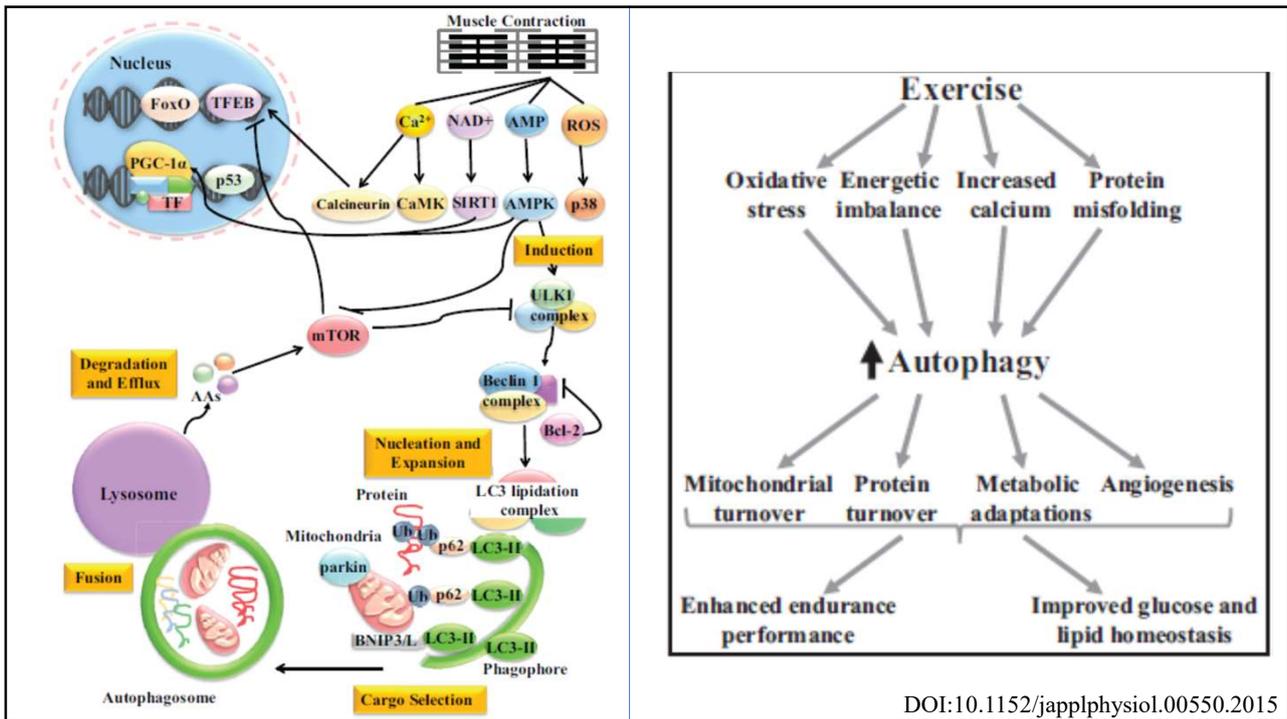
- **Descobertas importantes:**
  - Glucagon → induz autofagia no fígado
  - Insulina → reprime autofagia
  - Privação nutricional → induz autofagia
  - Ritmos circadianos → modulam a autofagia
  - Aminoácidos individuais (Leu, Tyr, Phe, Gln, Pro, His, Trp e Met) → reprime autofagia
  - > pH do lisossomo → reprime autofagia (cloroquina).

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## AUTOFAGIA E EXERCÍCIO FÍSICO

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# Physiological Reports

Open Access

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ORIGINAL RESEARCH

## Exercise and exercise training-induced increase in autophagy markers in human skeletal muscle

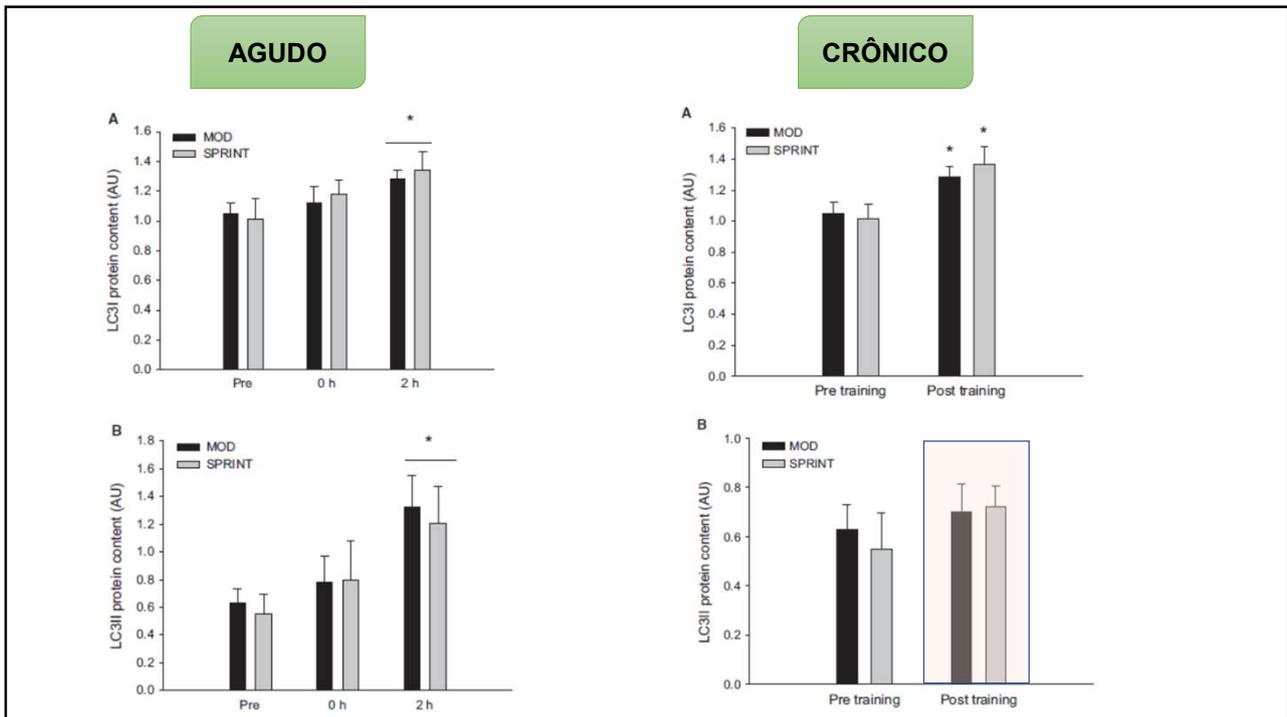
Nina Brandt<sup>1</sup>, Thomas P. Gunnarsson<sup>2</sup>, Jens Bangsbo<sup>2</sup> & Henriette Pilegaard<sup>1</sup>

1 Section for Cell Biology and Physiology, Department of Biology, University of Copenhagen, Copenhagen, Denmark  
 2 Section of Integrated Physiology, Department of Nutrition, Exercise and Sports, University of Copenhagen, Copenhagen, Denmark

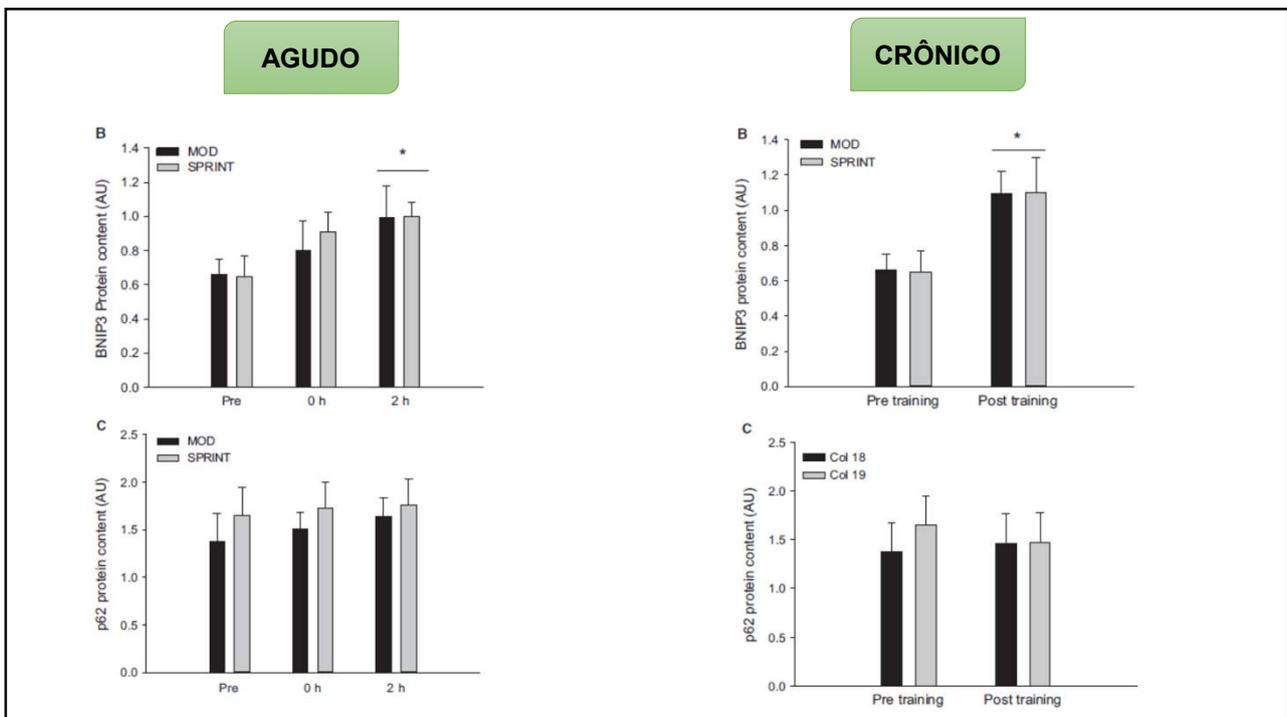
**A**

**B**

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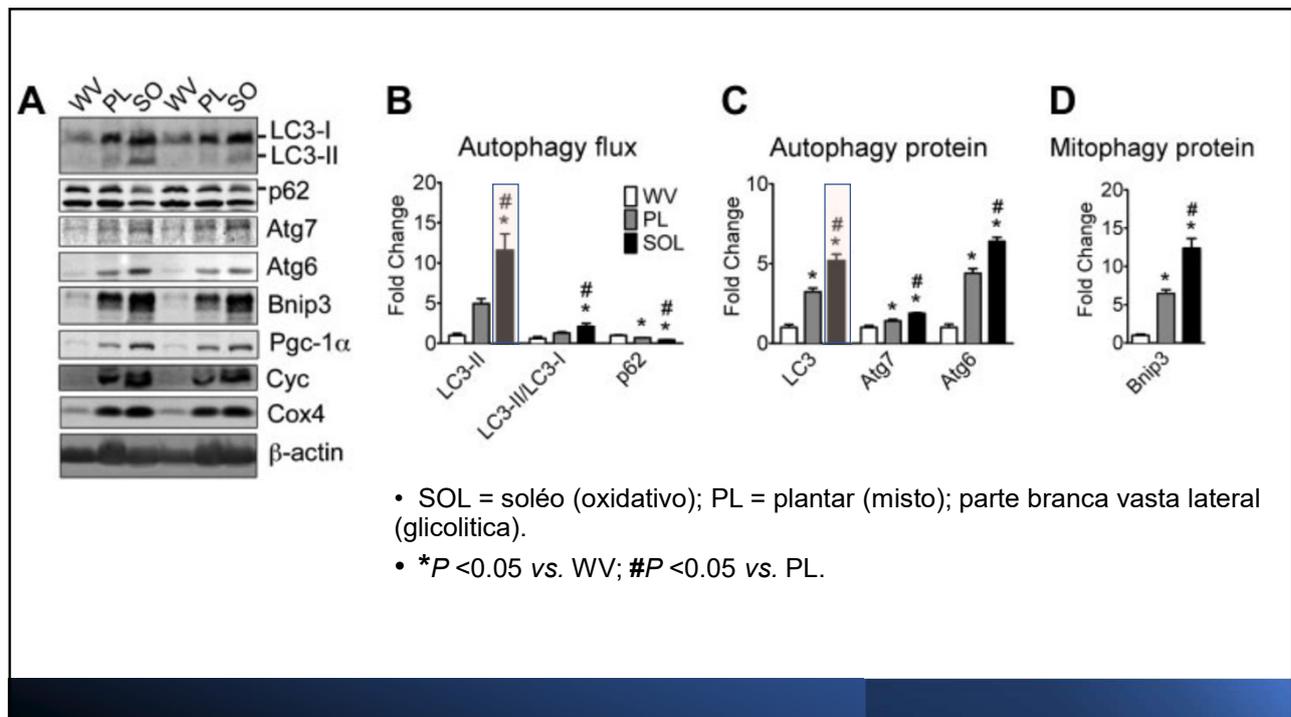
## Autophagy is required for exercise training-induced skeletal muscle adaptation and improvement of physical performance

Vitor A. Lira,<sup>\*,§</sup> Mitsuharu Okutsu,<sup>\*,§</sup> Mei Zhang,<sup>\*,§</sup> Nicholas P. Greene,<sup>\*,§</sup>  
Rhianna C. Laker,<sup>\*,§</sup> David S. Breen,<sup>†</sup> Kyle L. Hoehn,<sup>†</sup> and Zhen Yan<sup>\*,†,‡,§,1</sup>

<sup>\*</sup>Department of Medicine, <sup>†</sup>Department of Pharmacology, <sup>‡</sup>Department of Molecular Physiology and Biological Physics, and <sup>§</sup>Center for Skeletal Muscle Research, Robert M. Berne Cardiovascular Research Center, University of Virginia, Charlottesville, Virginia, USA

- 1. Comparação:** Autofagia basal entre músculos de diferentes capacidades oxidativas.
- Camundongos haplodeficientes para o gene relacionado à autofagia 6 (Atg6/Beclin1), que é essencial para a formação do autofagossomo, submetidos a corrida voluntária de longa duração → as adaptações fenotípicas no músculo esquelético, bem como o desempenho físico.

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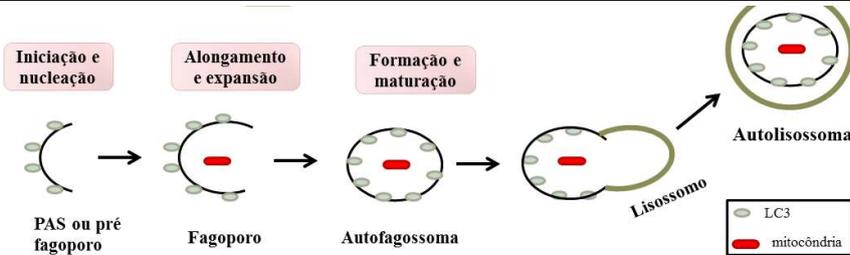


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# FLUXO AUTOFÁGICO

Inibidor de  
degradação  
lisossomal

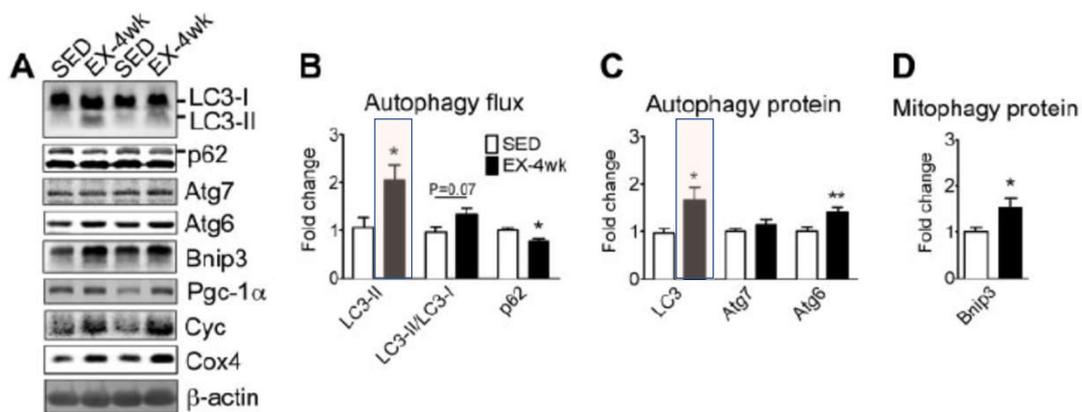
Frequentemente definido como uma medida da atividade de degradação autofágica. Refere-se a todo o processo autofágico



**Sem o inibidor de degradação autofágico** –  $\uparrow$ LC3 II também pode indicar bloqueio na maturação do autofagossoma.

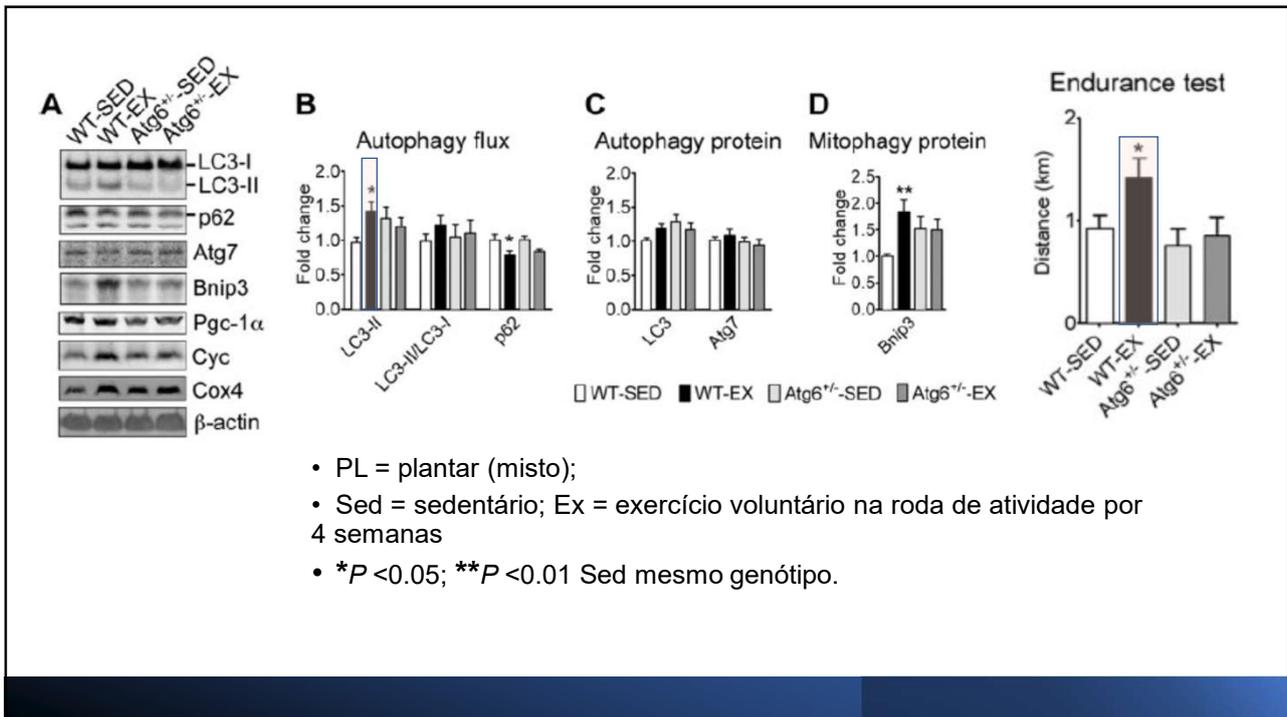
**Com o inibidor de degradação autofágico** –  $\uparrow$ LC3 II indicam que o fluxo autofágico está acontecendo, pois o trânsito de LC3 II através da via será bloqueado.

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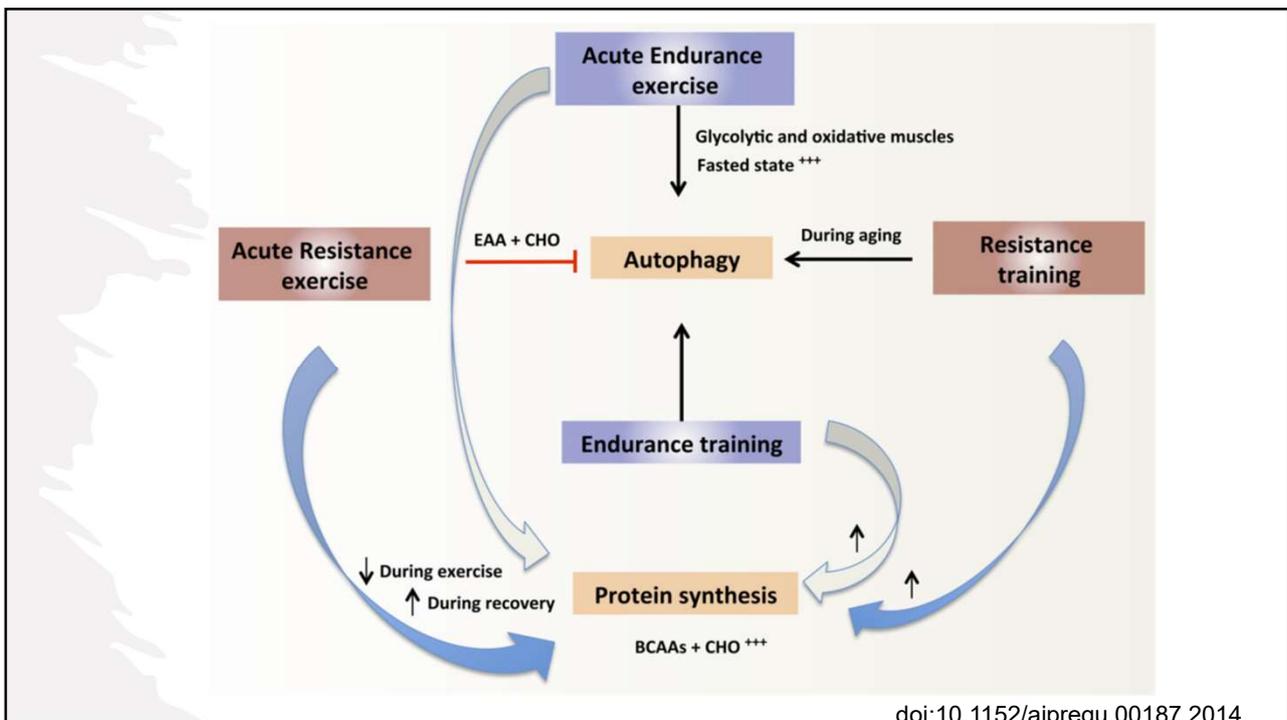


- PL = plantar (misto);
- Sed = sedentário; Ex = exercício voluntário na roda de atividade por 4 semanas
- \* $P < 0.05$ ; \*\* $P < 0.01$

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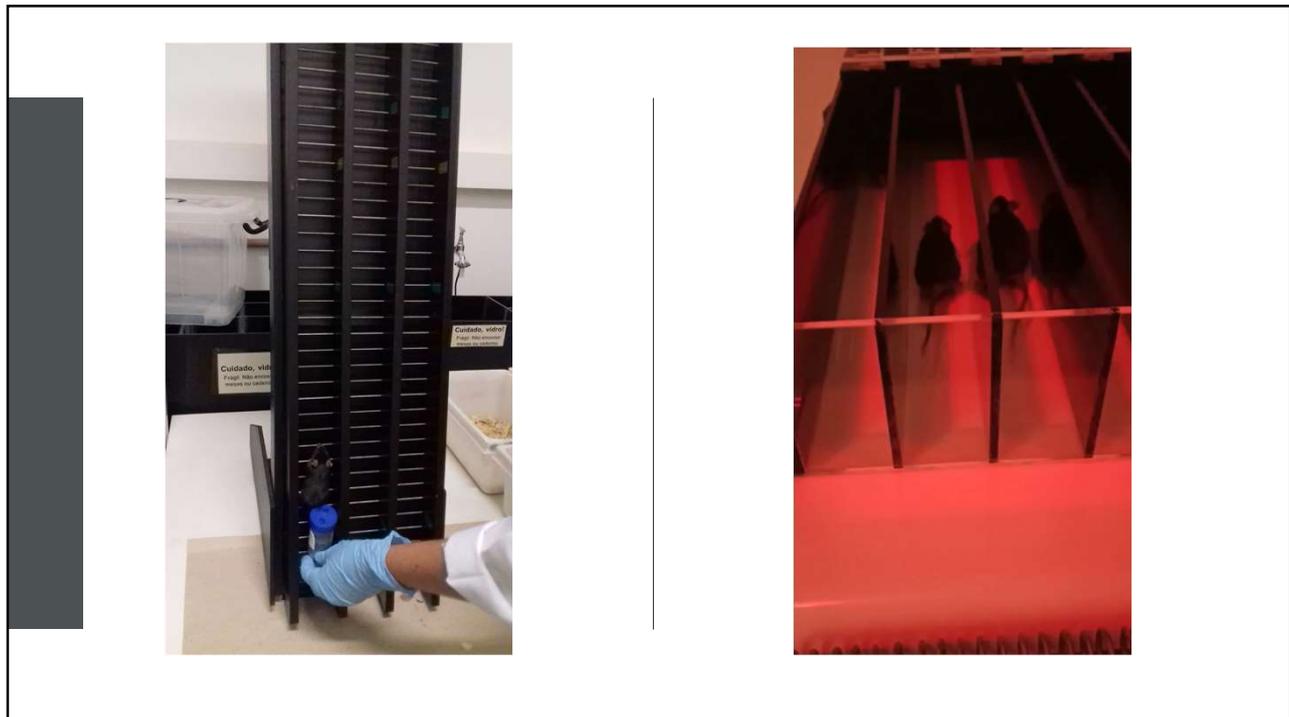
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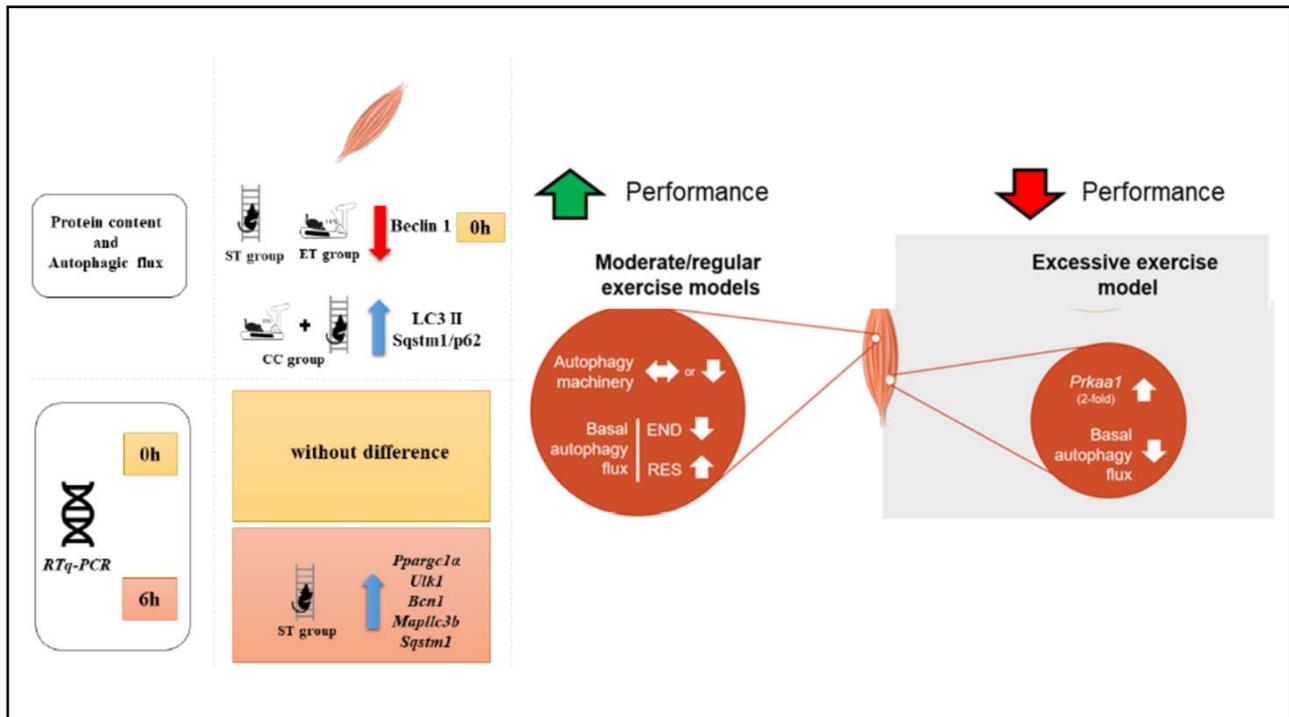
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## Conclusões

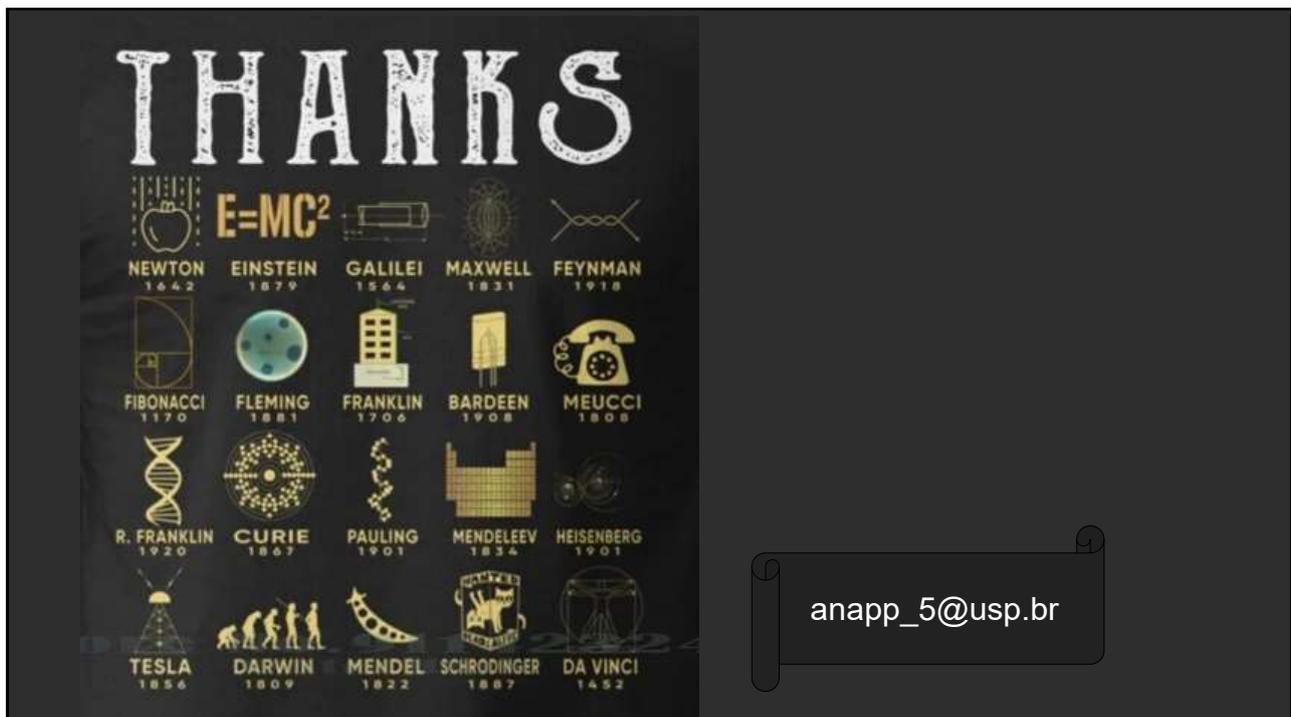
- Autofagia é um dos principais contribuintes para o metabolismo celular.
- Fornece nutrientes internos quando os externos não estão disponíveis.
- Fornece um meio essencial de renovação e remodelação de células.
- É necessário para o desenvolvimento normal, incluindo o dos tecidos metabólicos.

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## Conclusões

- Autofagia basal é diferente para cada tipo de músculo.
- Ausência de algum gene da via da autofagia diminui performance.
- Exercício de endurance agudo e/ou crônico aumenta a autofagia.
- São necessários mais estudos com outros modelos de exercício físico.

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