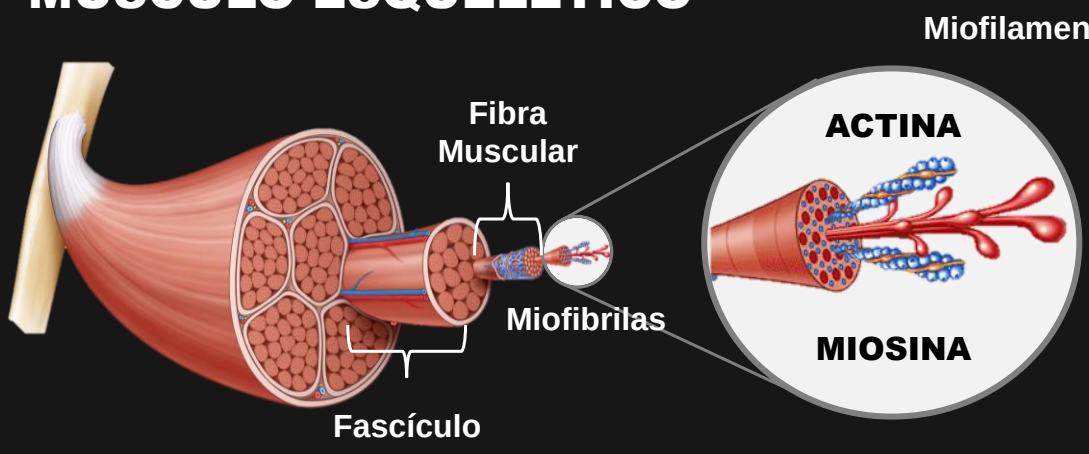
USP EEFERP
ESCOLA DE EDUCAÇÃO FÍSICA E ESPORTE
DE RIBEIRÃO PRETO

Estresse do Retículo Endoplasmático induzido por Exercício Físico no Músculo Esquelético

Discente:
Bruno Brieda Marafon
Orientador:
Adelino Sanchez Ramos da Silva

1

MÚSCULO ESQUELÉTICO



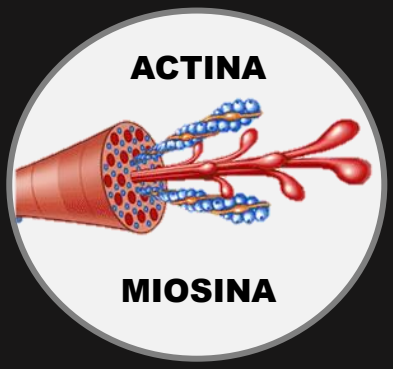
Mcardle; Katch; Katch, 2011
(Fisiologia do Exercício, 7° ed.)

2

MÚSCULO ESQUELÉTICO

Várias reações

ACTINA



MIOSINA

ADP

P_i

Energia Mecânica

Produção de Calor

3

MÚSCULO ESQUELÉTICO

Essencial para a locomoção, postura, termorregulação e metabolismo.

4

MÚSCULO ESQUELÉTICO

- Aproximadamente **40%** e **30%** do peso corporal total de homens e mulheres, respectivamente;

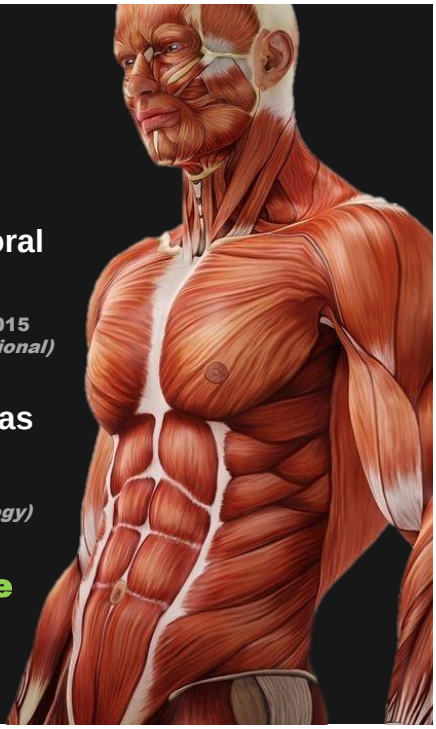
  Frontera and Ochala, 2015
  (Calcified Tissue International)

- O músculo esquelético contém **50-75%** de todas as proteínas em todo o corpo;

  Janssen et al., 2000
  (Journal of Applied Physiology)

- Utilizar caminhos que realizam a **regulação de conteúdos proteicos**.

  Bonaldo and Sandri, 2013
  (Disease Models and Mechanisms)

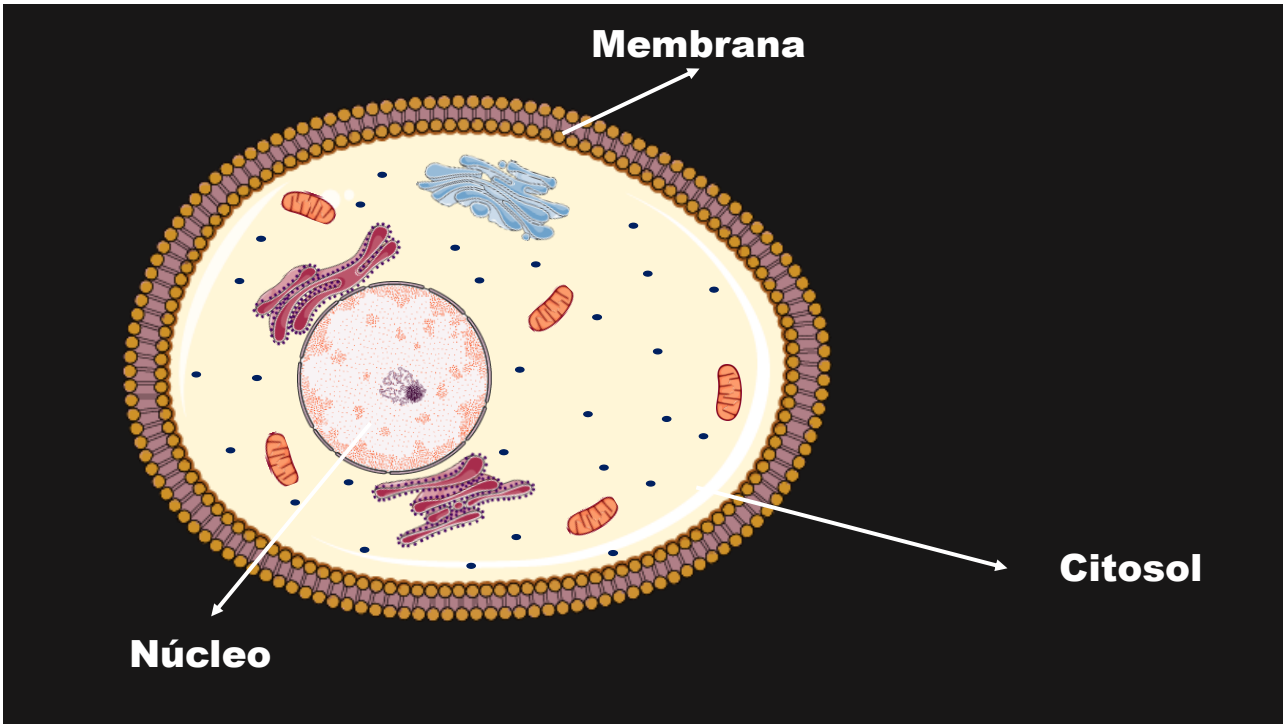


5

MÚSCULO ESQUELÉTICO

Uma organela responsável por esses eventos é o **retículo endoplasmático** (RE).

6



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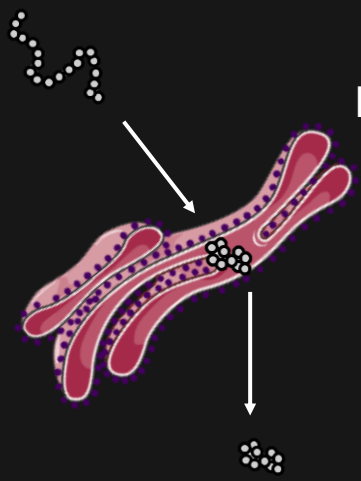
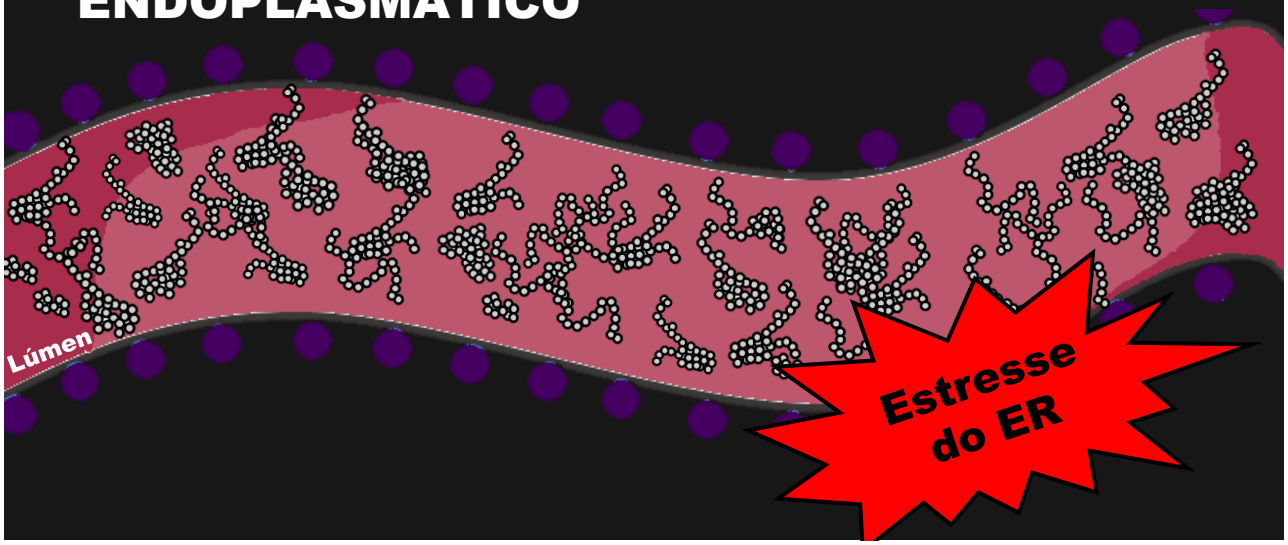


RETÍCULO ENDOPLASMÁTICO

- **Organela essencial para o organismo;**
- **Extrema importância para a sobrevivência da célula:**
  - ✓ **Dobramento de proteínas;**
  - ✓ **Modificações de proteínas;**
  - ✓ **Formação de complexos proteicos.**

8

ESTRESSE DO RETÍCULO ENDOPLASMÁTICO



9

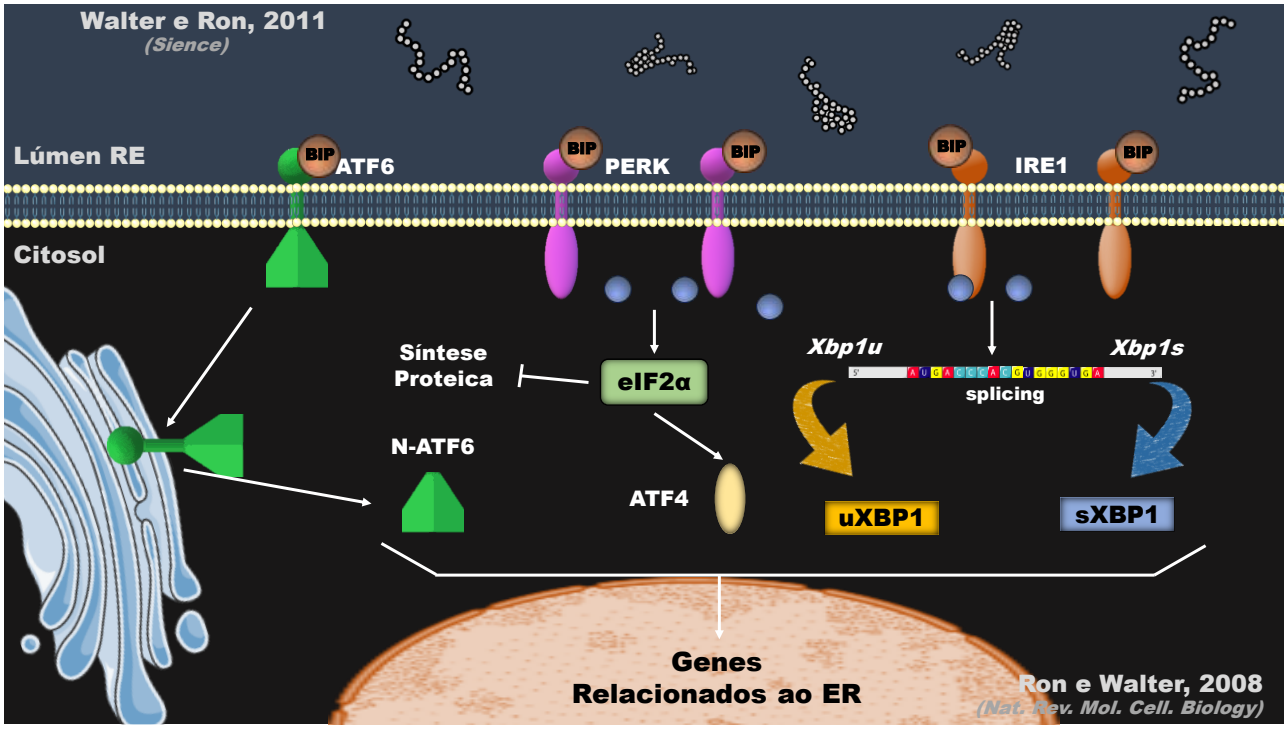
UNFOLDED PROTEIN RESPONSE

a) REDUÇÃO DE PROTEÍNAS QUE ENTRAM NO ER;

b) AUMENTO DA CAPACIDADE DE DOBRAR PROTEÍNAS;

c) MORTE CELULAR

10



11

Walter e Ron, 2011
(Sience)

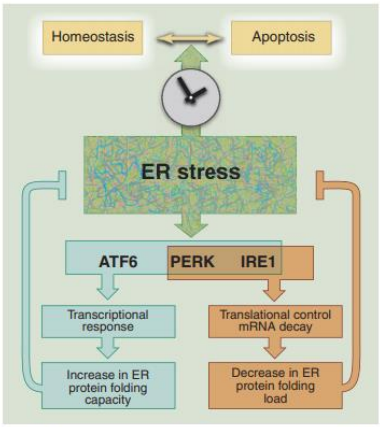


Fig. 1. A simplified wiring diagram of the core elements of the UPR signaling network. ER stress activates the stress sensors ATF6, IRE1, and PERK, representing the three branches of the UPR. Activation of each sensor produces a transcription factor [ATF6(N), XBP1, and ATF4, respectively] that activates genes to increase the protein-folding capacity in the ER. IRE1 (via RIDD) and PERK (via eIF2α phosphorylation) also decrease the load of proteins entering the ER. Both outcomes work as feedback loops that mitigate ER stress. If cells cannot reestablish homeostasis but continue to experience prolonged and unmitigated ER stress (depicted by the timer), they apoptose.

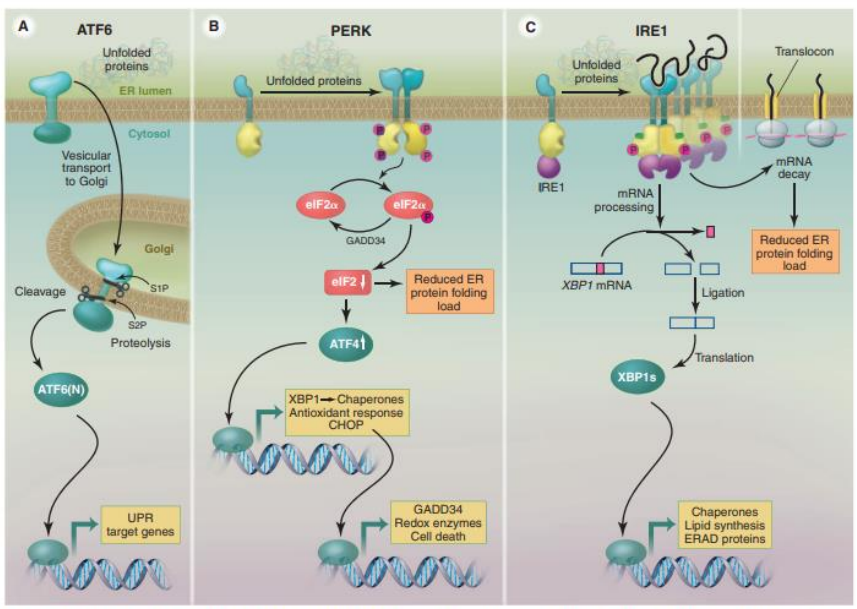
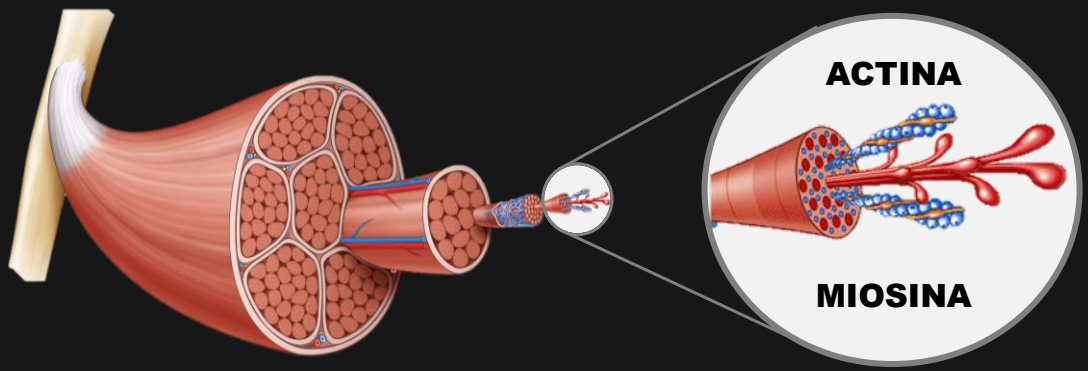


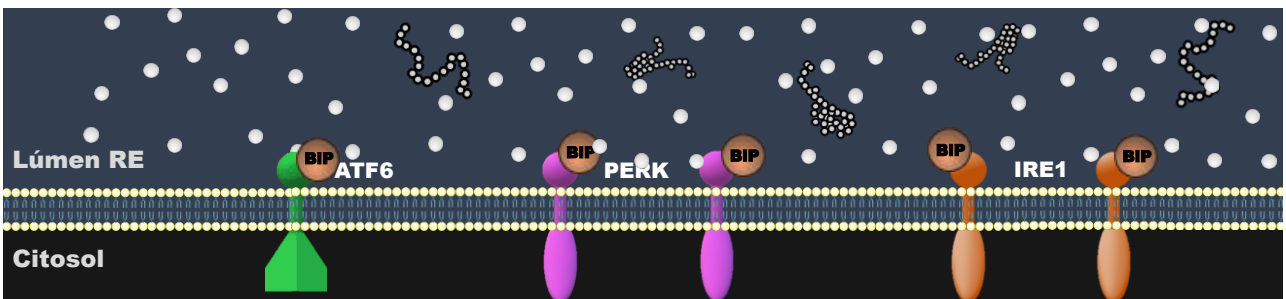
Fig. 2. (**A** to **C**) The three branches of the UPR. Three families of signal transducers (ATF6, PERK, and IRE1) sense the protein-folding conditions in the ER lumen and transmit that information, resulting in production of bZIP transcription regulators that enter the nucleus to drive transcription of UPR target genes. Each pathway uses a different mechanism of signal transduction: ATF6 by regulated proteolysis, PERK by translational control, and IRE1 by nonconventional mRNA splicing. In addition to the transcriptional responses that largely serve to increase the protein-folding capacity in the ER, both PERK and IRE1 reduce the ER folding load by down-tuning translation and degrading ER-bound mRNAs, respectively.

12

ESTRESSE DO RE E EXERCÍCIO FÍSICO



13



- Associação entre BiP e proteínas malformadas é estabilizada por **altas concentrações de Ca^{2+}** ;

Krebs et al., 2015
(Bioch. and Bioph. Res. Communications)

- A depleção de Ca^{2+} pode **prejudicar o trabalho das chaperonas** no dobramento de proteínas mal dobradas e levar ao estresse do RE

Krebs et al., 2015
(Bioch. and Bioph. Res. Communications)

14

ESTRESSE DO RE E EXERCÍCIO FÍSICO

15

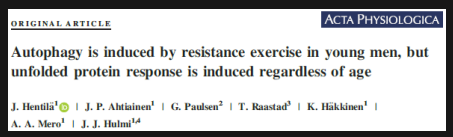
EXERCÍCIO FÍSICO AGUDO (Força)

The unfolded protein response is triggered following a single, unaccustomed resistance-exercise bout

Daniel L Ogborn,[1] Bryon R. McKay,[1] Justin D. Crane,[2] Gianni Parise,[2] and Mark A. Tarnopolsky[3]

[1]Department of Medical Sciences, McMaster University, Hamilton, Ontario, Canada; [2]Department of Kinesiology, McMaster University, Hamilton, Ontario, Canada; and [3]Department of Pediatrics and Medicine, McMaster University, Hamilton, Ontario, Canada

Submitted 19 November 2013; accepted in final form 7 July 2014



ORIGINAL ARTICLE

ACTA PHYSIOLOGICA

Autophagy is induced by resistance exercise in young men, but unfolded protein response is induced regardless of age

J. Hentilä[1] | J. P. Ahtiainen[1] | G. Paulsen[2] | T. Raastad[3] | K. Häkkinen[1] | A. A. Mero[1] | J. J. Hulmi[1,4]

Normal Ribosomal Biogenesis but Shortened Protein Synthetic Response to Acute Eccentric Resistance Exercise in Old Skeletal Muscle

Daniel W. D. West[1], George R. Marcotte[2], Courtney M. Chason[2], Natalie Jusi[2], Leslie M. Baehr[1], Sue C. Bodine[1,2,3] and Keith Baar[1,2,3]*

- Leg Press
- Extensora
  - ✓ 4 Séries
  - ✓ 10 repetições

- Leg Press
  - ✓ 5 Séries
  - ✓ 10 repetições

- Estimulação elétrica
- Animais

16

EXERCÍCIO FÍSICO AGUDO (Força)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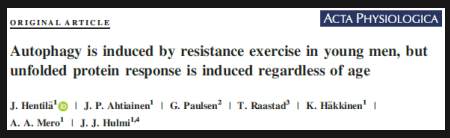
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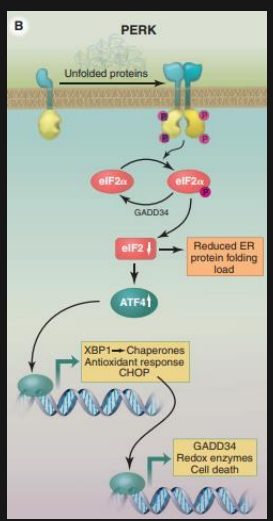
↑ BiP
PERK
IRE1 ↔ peIF2α
Atf4
Ddit3

↑ BiP
PERK
ATF4 ↔ *Ddit3*
Xbp1s
Xbp1u

↑ peIF2α
BiP
↔ CHOP

17

EXERCÍCIO FÍSICO AGUDO (Força)



Apesar do aumento da **PERK**, **peIF2α** e **ATF4**, o exercício de **FORÇA** agudo não aumenta os níveis de **CHOP** e ***Ddit3***.

Provavelmente, esse tipo de exercício **não induz** a sinalização de apoptose celular.

18

EXERCÍCIO FÍSICO AGUDO (Endurance)

Published in final edited form as:
Cell Metab. 2011 February 2; 13(2): 160–169. doi:10.1016/j.cmet.2011.01.003.

The unfolded protein response mediates adaptation to exercise in skeletal muscle through a PGC-1α /ATF6α complex

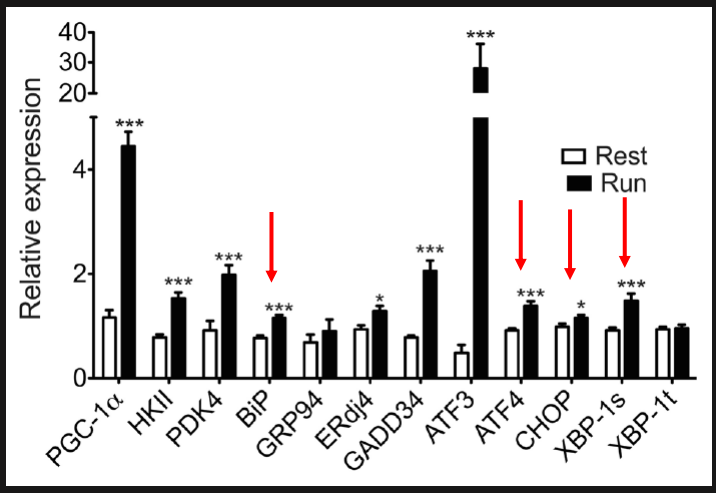
Jun Wu[1], Jorge L. Ruas[1], Jennifer L. Estall[1], Kyle A. Rasbach[1], Jang Hyun Choi[1], Li Ye[1], Pontus Boström[1], Heather M. Tyra[3], Robert W. Crawford[4], Kevin P. Campbell[4], D. Thomas Rutkowski[3], Randal J. Kaufman[2], and Bruce M. Spiegelman[1,*]

[1] Dana-Farber Cancer Institute and Department of Cell Biology, Harvard Medical School, Boston, MA 02115, USA

[2] Departments of Biological Chemistry and Internal Medicine, University of Michigan Medical Center, Ann Arbor, MI 48109, USA

[3] Department of Anatomy and Cell Biology, University of Iowa, Iowa City, IA 52242, USA

[4] Howard Hughes Medical Institute, Department of Molecular Physiology and Biophysics, Department of Neurology, and Department of Internal Medicine, Carver College of Medicine, The University of Iowa, Iowa City, IA 52242, USA



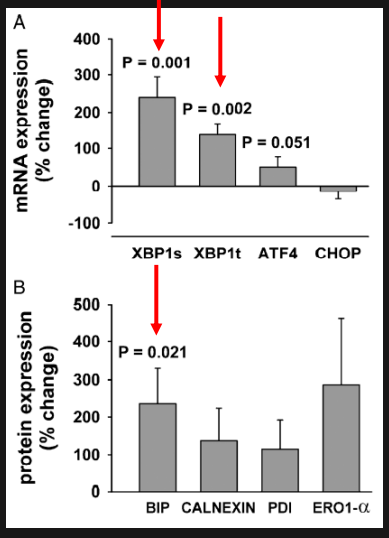
19

EXERCÍCIO FÍSICO AGUDO (Endurance)

Endoplasmic Reticulum Stress Markers and Ubiquitin–Proteasome Pathway Activity in Response to a 200-km Run

HYO JEONG KIM[1], CÉCILE JAMART[2], LOUISE DELDICQUE[2], GANG-LI AN[2], YOON HEE LEE[1], CHANG KEUN KIM[1], JEAN-MARC RAYMACKERS[2], and MARC FRANCAUX[2]

[1]Human Physiology, Korea National Sport University, Seoul, SOUTH KOREA; and [2]Institute of Neuroscience, Université Catholique de Louvain, Louvain-la-Neuve, BELGIUM



20

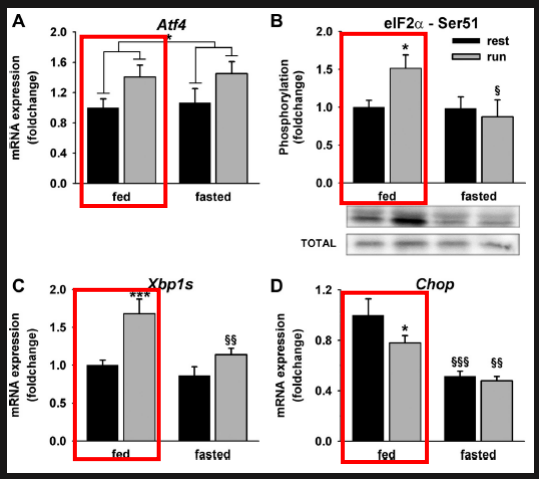
EXERCÍCIO FÍSICO AGUDO (Endurance)

Am J Physiol Endocrinol Metab 305: E964–E974, 2013.
First published August 20, 2013; doi:10.1152/ajpendo.00270.2013.

Higher activation of autophagy in skeletal muscle of mice during endurance exercise in the fasted state

Cécile Jamart, Damien Naslain, Hélène Gilson, and Marc Francaux
Institute of Neuroscience, Université catholique de Louvain, Louvain-la-Neuve, Belgium

Submitted 16 May 2013; accepted in final form 14 August 2013



21

EXERCÍCIO FÍSICO CRÔNICO

Research Article

Long-Term Exercise Protects against Cellular Stresses in Aged Mice

Irina Belaya, Masataka Suwa, Tao Chen, Rashid Giniatullin, Katja M. Kanninen, Mustafa Atalay, and Shuzo Kumagai

Korean J Physiol Pharmacol
Vol 18: 211 – 216, June, 2014
http://dx.doi.org/10.4196/kjpp.2014.18.3.211

Effect of Exercise Intensity on Unfolded Protein Response in Skeletal Muscle of Rat

Kihoon Kim, Yun-Hye Kim, Sung-Hye Lee, Man-Joong Jeon, So-Young Park, and Kyung-Oh Doh

Am J Physiol Cell Physiol 310: C1024–C1036, 2016.
First published April 27, 2016; doi:10.1152/ajpcell.00009.2016.

The unfolded protein response mediates adaptation to exercise in skeletal muscle through a PGC-1α /ATF6α complex

Jun Wu, Jorge L. Ruas, Jennifer L. Estall, Kyle A. Rasbach, Jang Hyun Choi, Li Ye, Pontus Boström, Heather M. Tyra, Robert W. Crawford, Kevin P. Campbell, D. Thomas Rutkowski, Randal J. Kaufman, and Bruce M. Spiegelman

Chronology of UPR activation in skeletal muscle adaptations to chronic contractile activity

Jonathan M. Memme, Ashley N. Oliveira, and David A. Hood
Muscle Health Research Centre, School of Kinesiology and Health Science, York University, Toronto, Ontario, Canada

Submitted 8 January 2016; accepted in final form 27 April 2016

ORIGINAL RESEARCH

Swimming Differentially Affects T2DM-Induced Skeletal Muscle ER Stress and Mitochondrial Dysfunction Related to MAM

Zhe Zhang, Di Cui, Tan Zhang, Yi Sun, Shuzhe Ding

This article was published in the following Dove Press journal:
Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy

22

EXERCÍCIO FÍSICO CRÔNICO

↓ CHOP
pIRE1α
ATF6
Atf4
Ddit3
Xbp1s

⟷ BiP
PERK
CHOP
Xbp1u
Ddit3

23

EXERCÍCIO FÍSICO CRÔNICO

Contents lists available at ScienceDirect

Life Sciences

journal homepage: www.elsevier.com/locate/lifescie

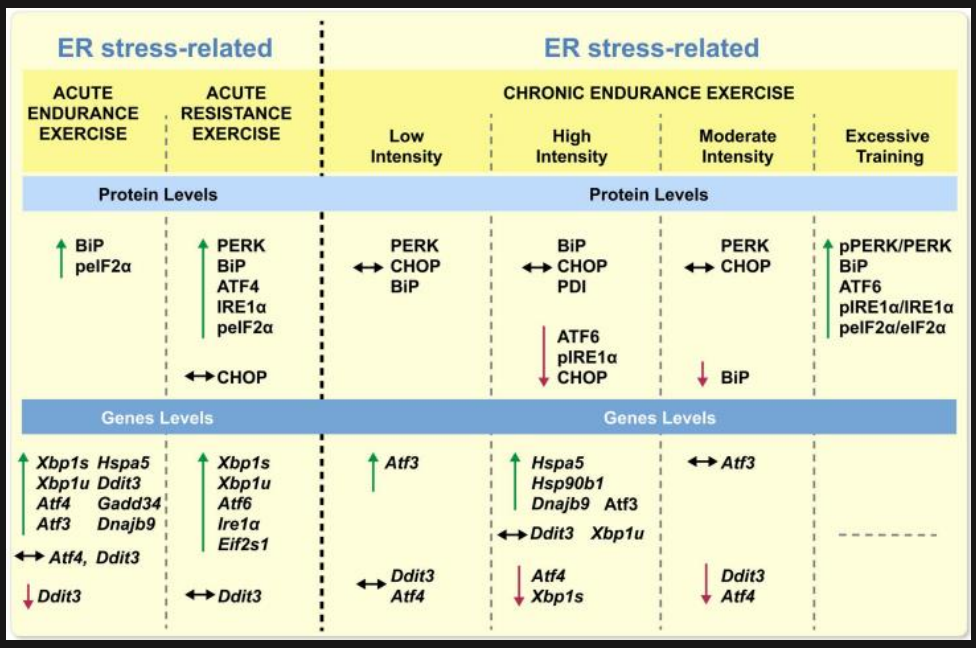
Excessive eccentric exercise-induced overtraining model leads to endoplasmic reticulum stress in mice skeletal muscles

Bruno C. Pereira [a,1], Alisson L. da Rocha [a,1], Ana P. Pinto [a], José R. Pauli [b], Claudio T. de Souza [c], Dennys E. Cintra [b], Eduardo R. Ropelle [b], Ellen C. de Freitas [d], Alessandro M. Zagatto [e], Adelino S.R. da Silva [a,d,*]

[a] Postgraduate Program in Rehabilitation and Functional Performance, Ribeirão Preto Medical School, USP, Ribeirão Preto, São Paulo, Brazil
[b] Sport Sciences Course, Faculty of Applied Sciences, State University of Campinas (UNICAMP), Limeira, São Paulo, Brazil
[c] Exercise Biochemistry and Physiology Laboratory Postgraduate Program in Health Sciences, Health Sciences Unit, University of Far Southern Santa Catarina, Criciúma, Santa Catarina, Brazil
[d] School of Physical Education and Sport of Ribeirão Preto, University of São Paulo (USP), Ribeirão Preto, São Paulo, Brazil
[e] Laboratory of Physiology and Sport Performance (LAFIDE), Faculty of Sciences, Univ Estadual Paulista – UNESP, Bauru, São Paulo, Brazil

↑ BiP
pIRE1α/IRE1α
pPERK/PERK
peIF2α/eIF2α
ATF6

24



Marafon et al., 2022
(Acta Physiologica)

25

Obrigado!

26