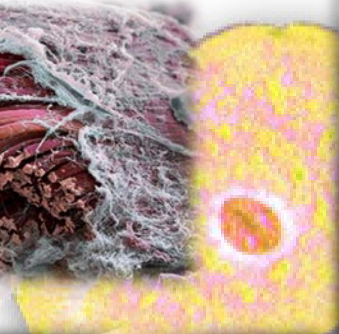
“Understanding training? Posttranscriptional regulation of training adaptation”

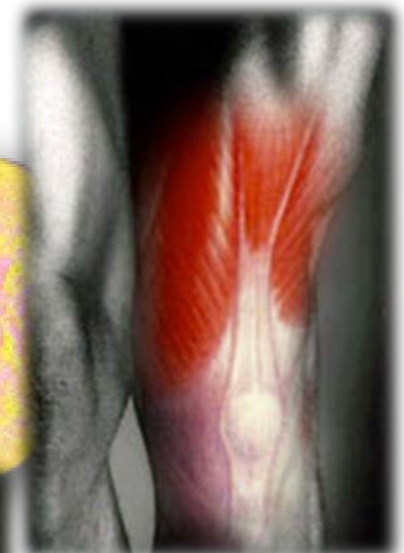
Wilhelm Bloch

Berlin, 21.11.2018

Goal of training is performance enhancement

- **Functional Adaptation**

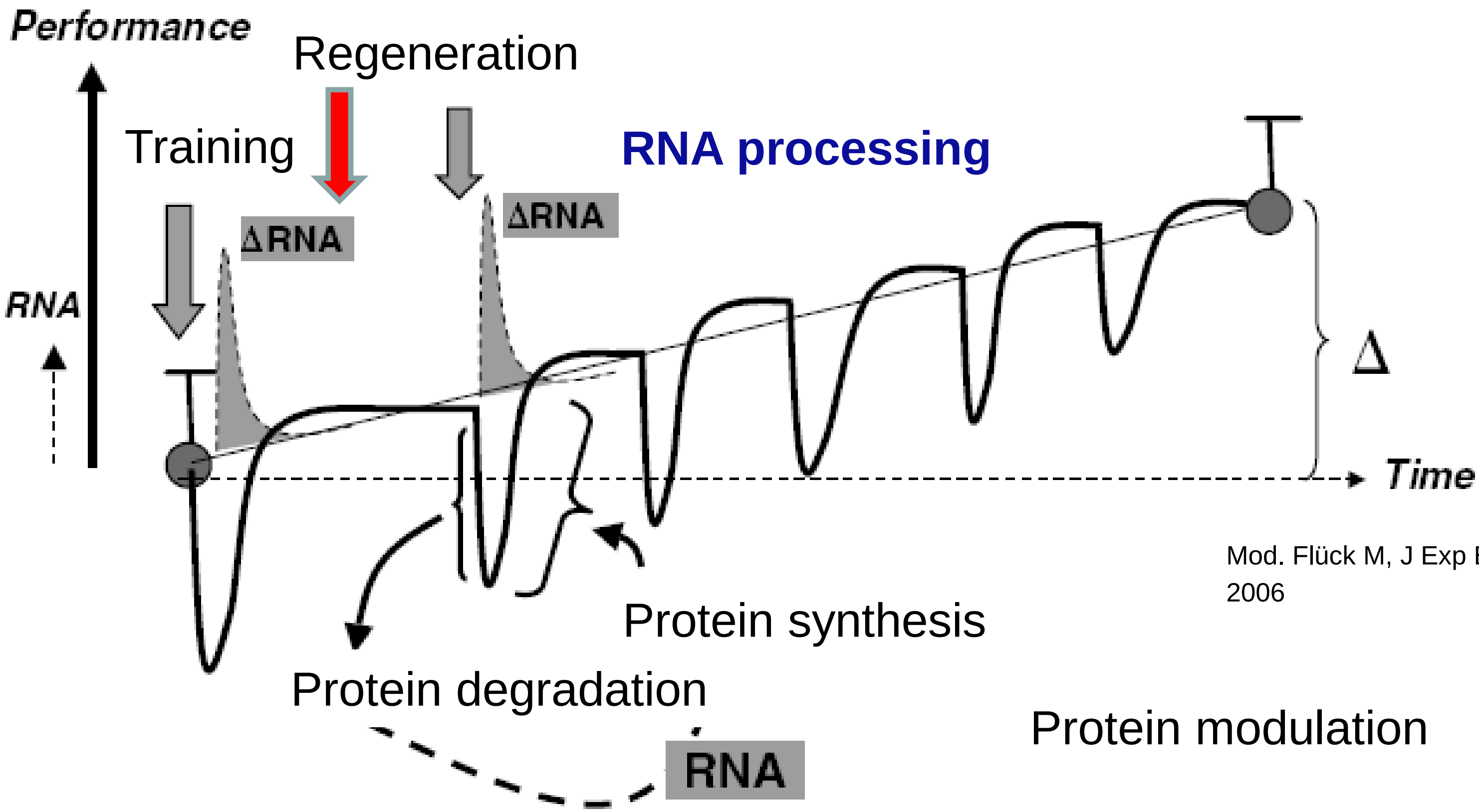




- **Structural Adaptation**

The muscle isn‘t only muscle fibers

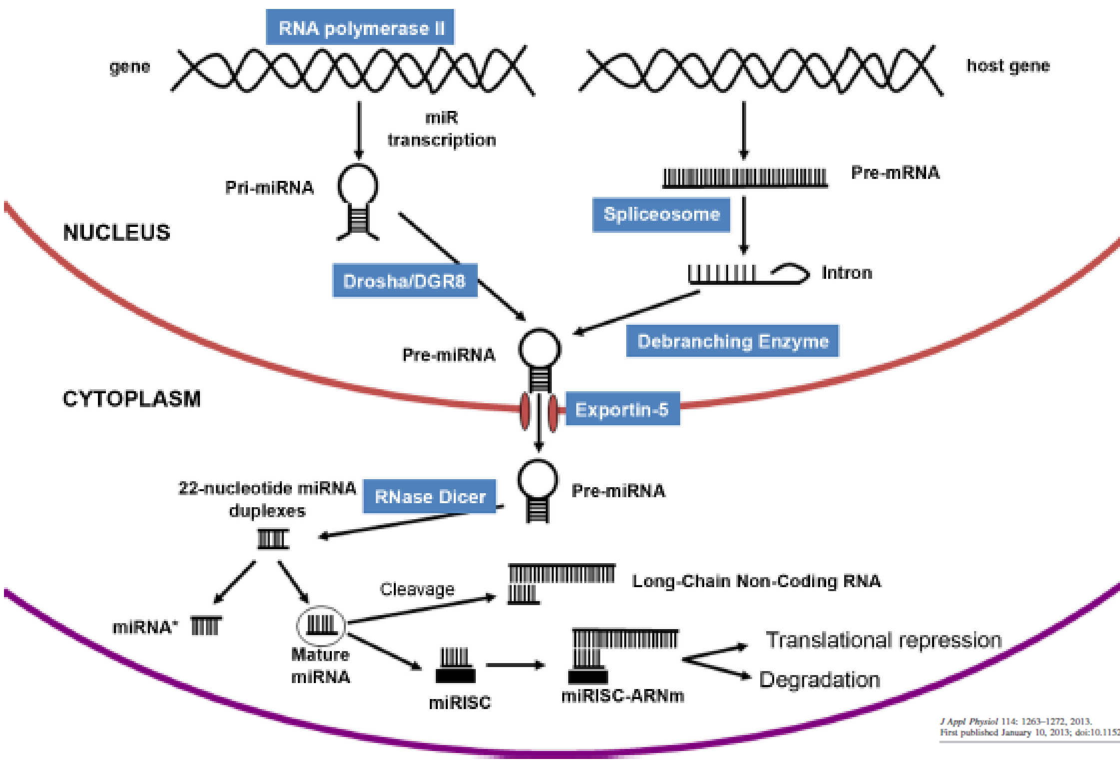
Posttranscriptional processes induced by physical training und regeneration



Mod. Flück M, J Exp Biol. 2006

RNA-processing, Protein synthesis, Protein degradation, Autophagy, Protein tunrover, Protein modulation – Optimizing structure and function

mRNA stability and availability is posttranscriptional regulated by miRNA



J Appl Physiol 114: 1263–1272, 2013.
First published January 10, 2013; doi:10.1152/japplphysiol.01027.2012.

HIGHLIGHTED TOPIC | *Muscle Dysfunction in COPD*

Epigenetic regulation of muscle phenotype and adaptation: a potential role in COPD muscle dysfunction

Esther Barreiro[1,2] and Jacob I. Sznajder[3]

Free Radic Biol Med. 2013 September ; 64: 95–105. doi:10.1016/j.freeradbiomed.2013.07.004.

MicroRNAs in skeletal muscle biology and exercise adaptation

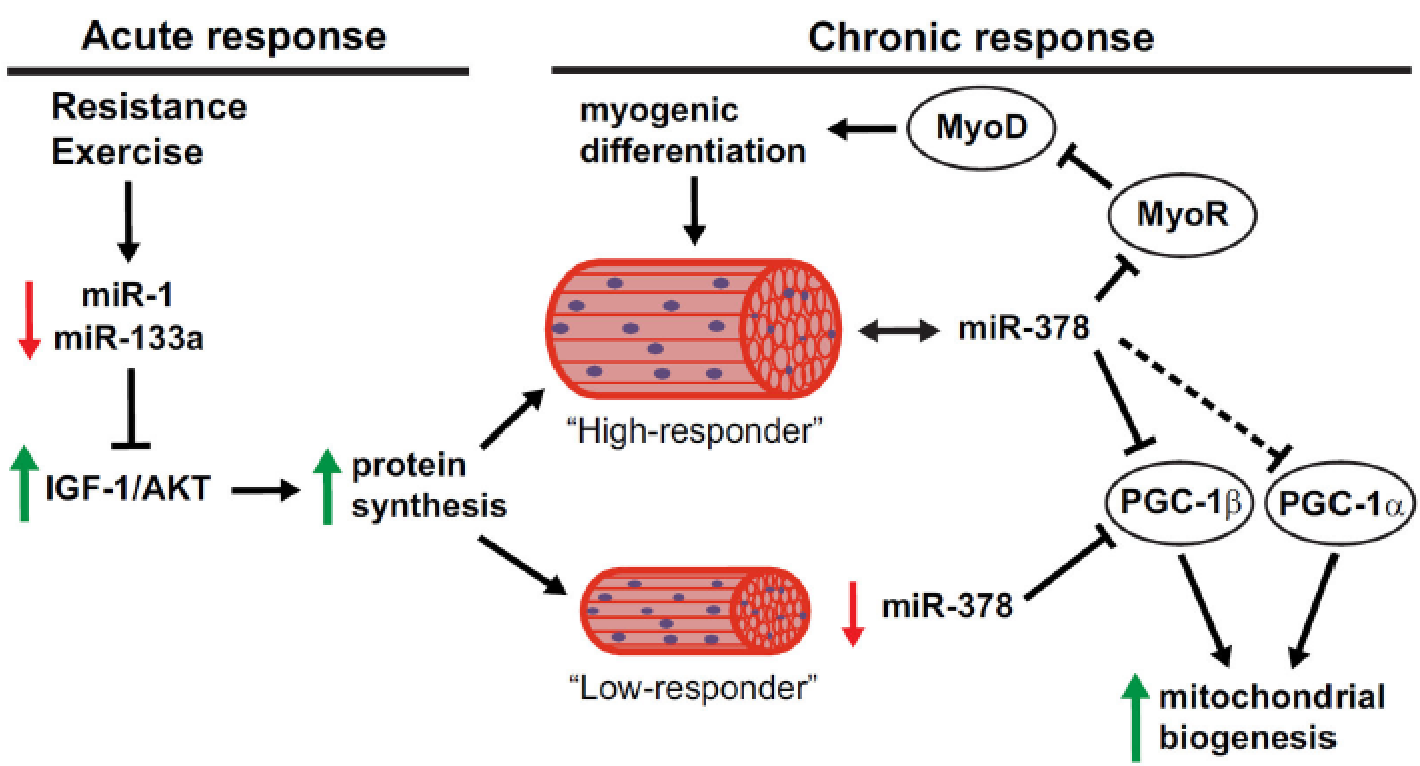


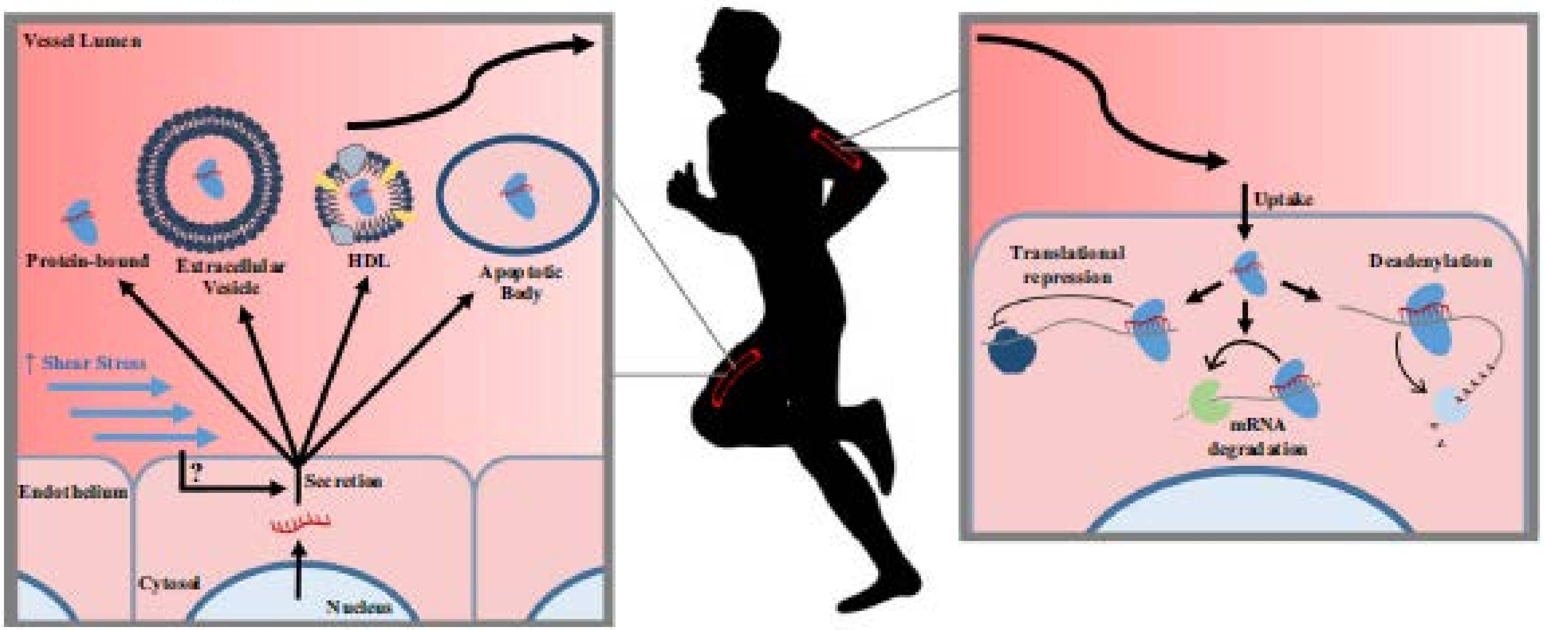
Figure 1. MicroRNA regulation of resistance exercise adaptations

J Appl Physiol 122: 702–717, 2017.
First published December 29, 2016; doi:10.1152/japplphysiol.00982.2016.

REVIEW | *Synthesis*

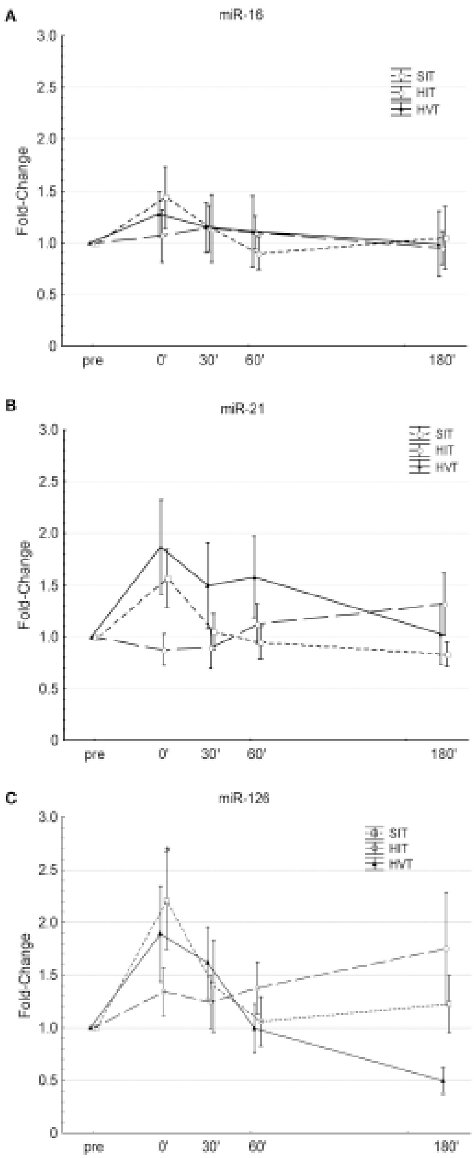
Circulating microRNAs in acute and chronic exercise: more than mere biomarkers

Ryan M. Sapp, Daniel D. Shill, Stephen M. Roth, and James M. Hagberg

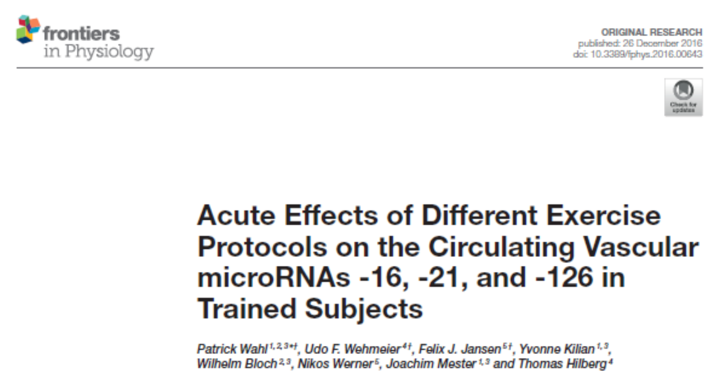


Information for posttranscriptional regulation can be shared over the body

Release of miRNA is dependent from trainings protocol



Origin from endothelial cells and transfer to vascular smooth muscle cells by microparticles


frontiers in Physiology

ORIGINAL RESEARCH
published: 26 December 2016
doi: 10.3389/fphys.2016.00643

Acute Effects of Different Exercise Protocols on the Circulating Vascular microRNAs -16, -21, and -126 in Trained Subjects

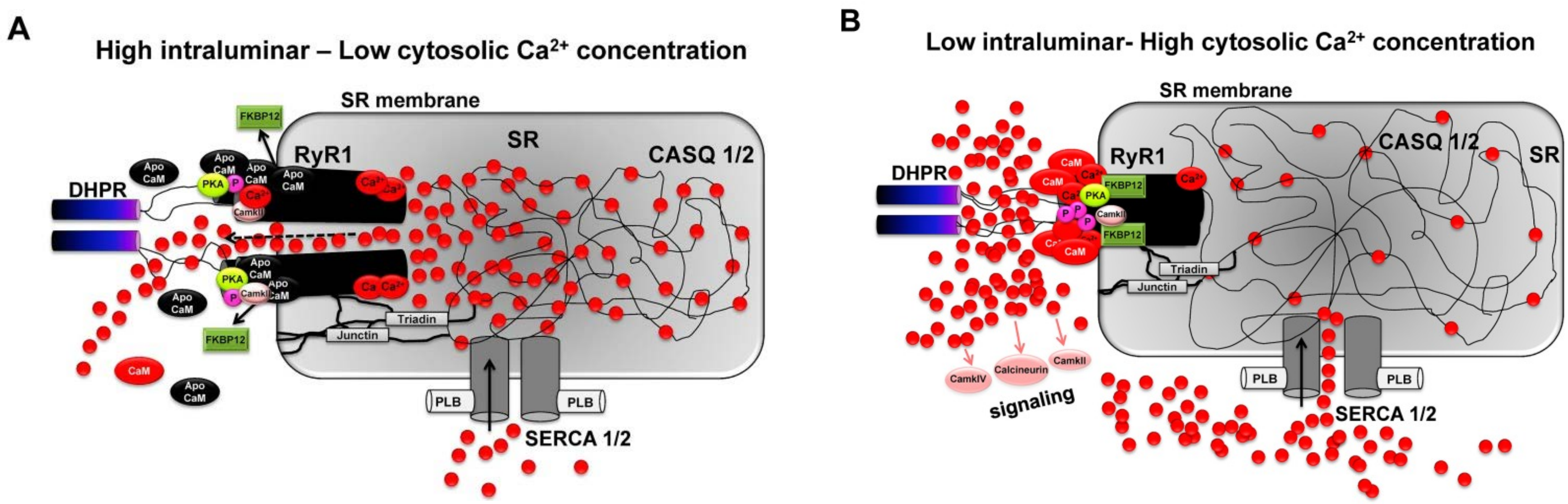
Patrick Wahl[1,2,3†], Udo F. Wehmeier[4†], Felix J. Jansen[5†], Yvonne Kilian[1,3], Wilhelm Bloch[2,3], Nikos Werner[5], Joachim Mester[1,3] and Thomas Hilberg[4]*

Mechanisms of fast loss of muscle power – Loss of speed

- Posttranslational regulation / Protein modulation

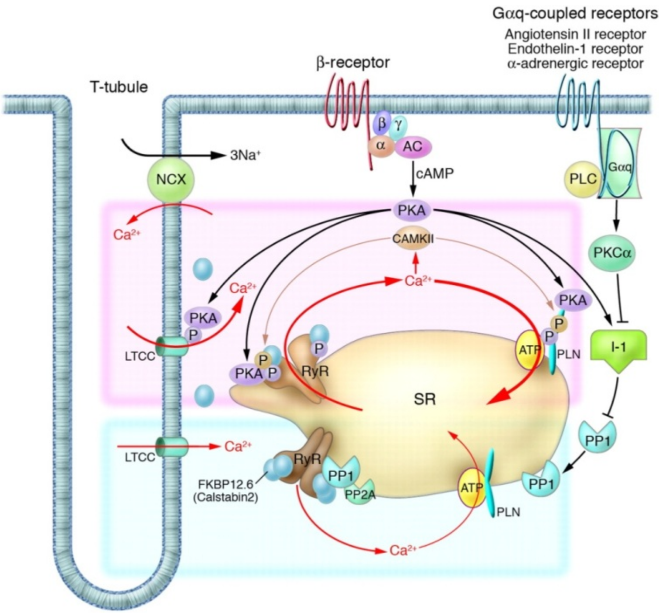
He speed a long - Why?

Fast calclium regulation a principal for fast muscle contraction

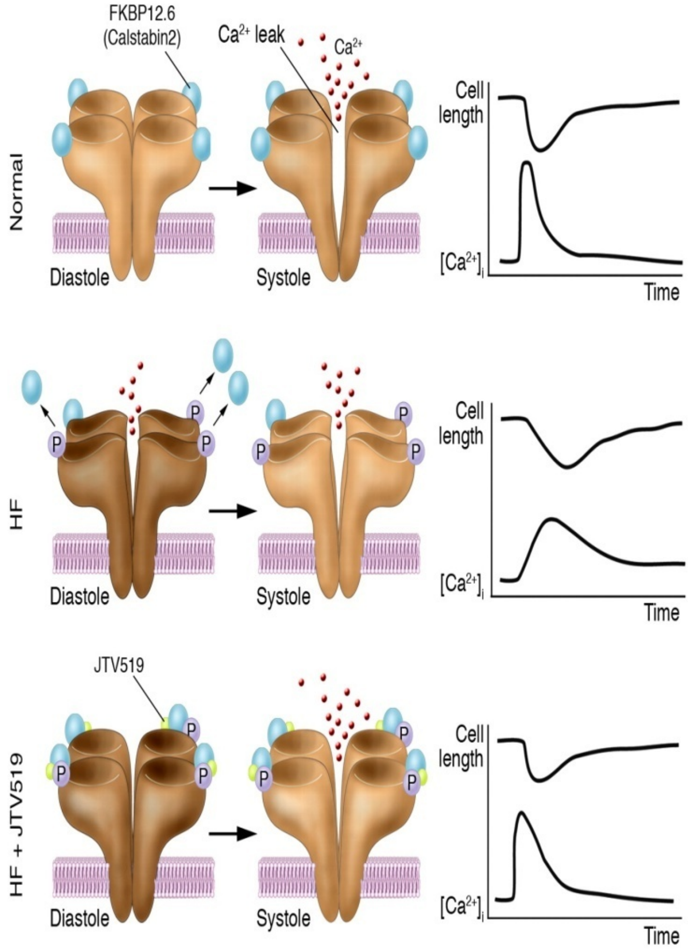


Gehlert, Bloch, Suhr IJMS 2015

Fast calcium oszillation is important for fast muscle contraction – The oszillation is reduced by phosphorylation RyR

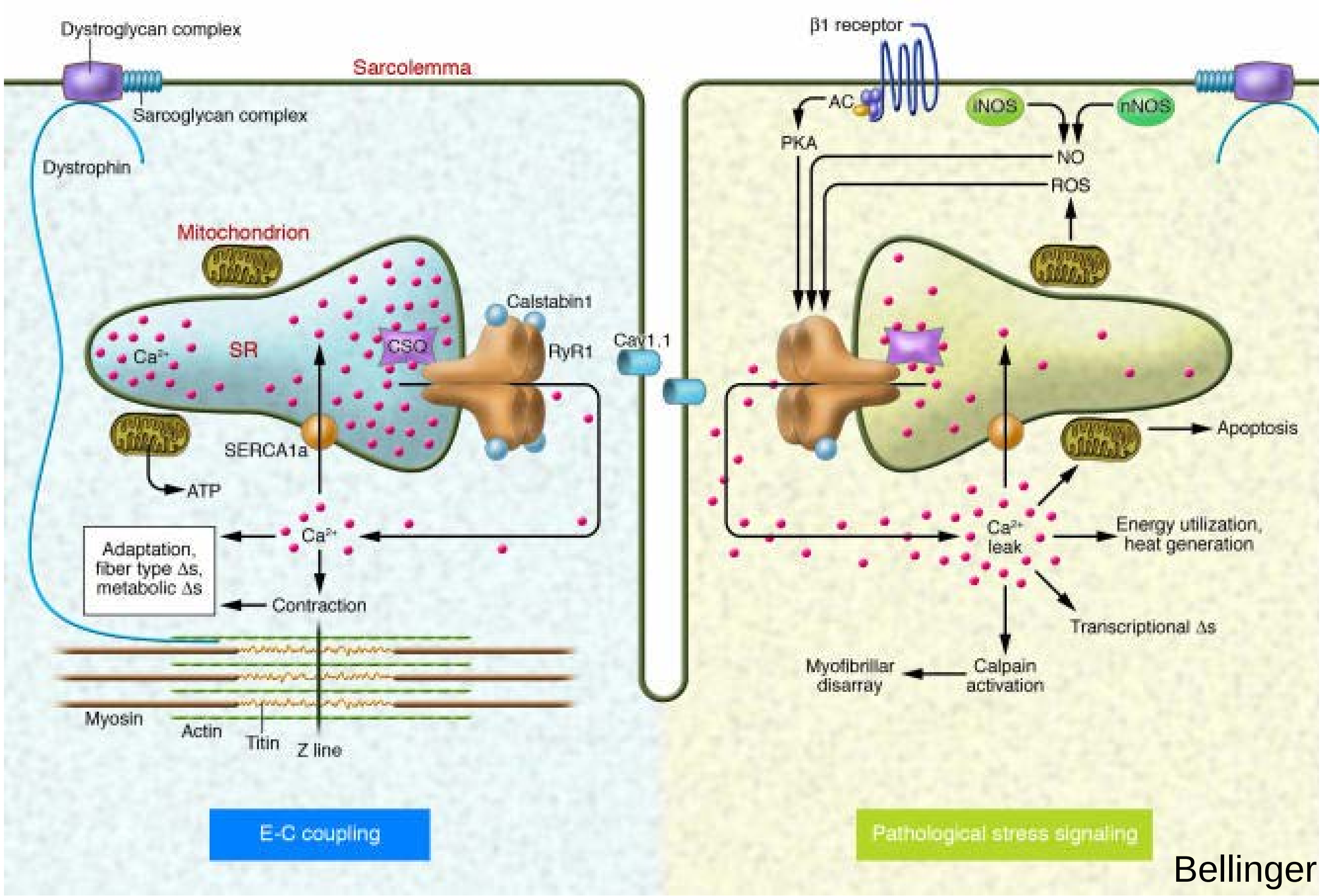


Modified from Yano et al.



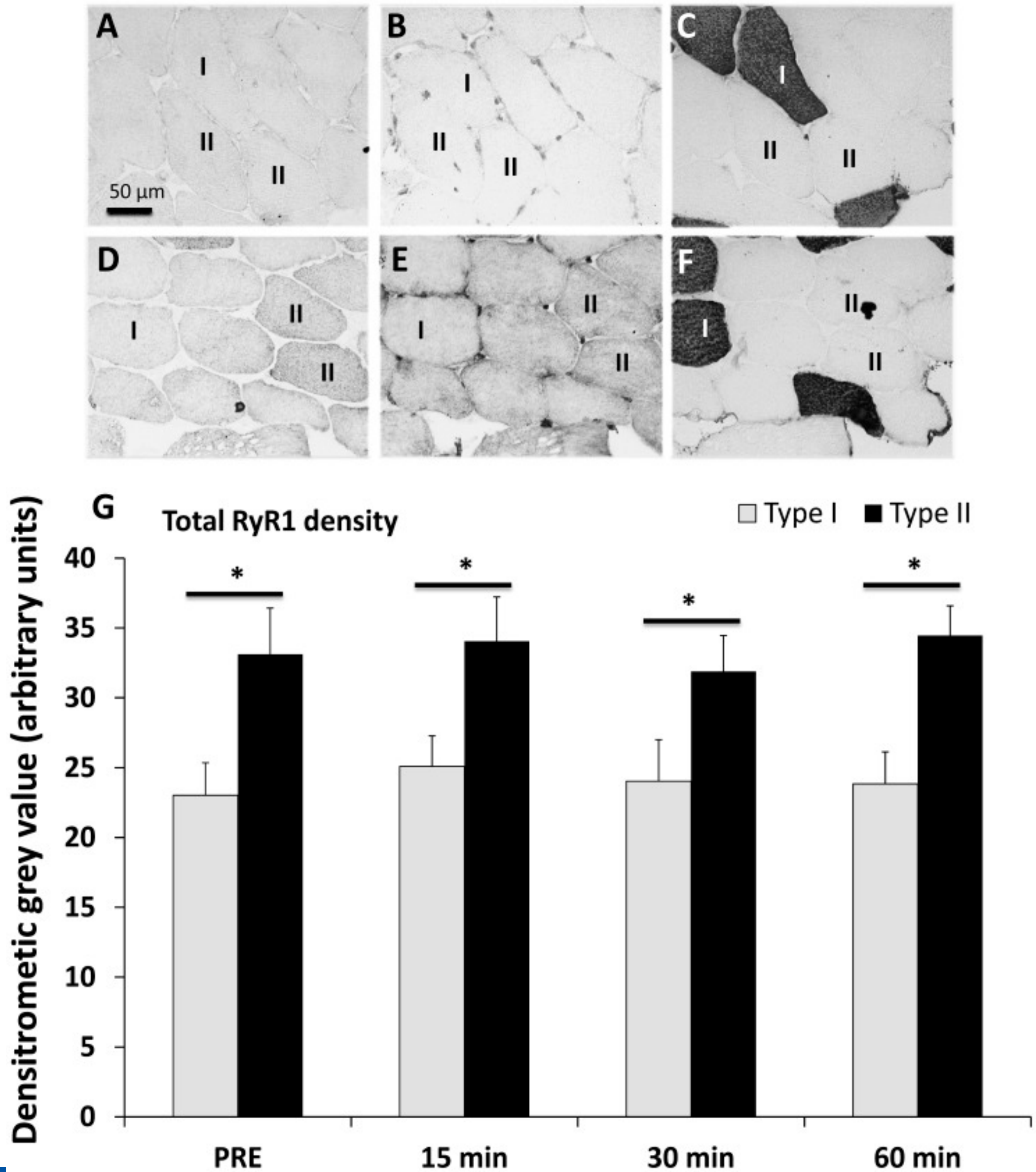
How fast is the process – relevant for sprint?

The RyR is leaky after 30min downhill runing



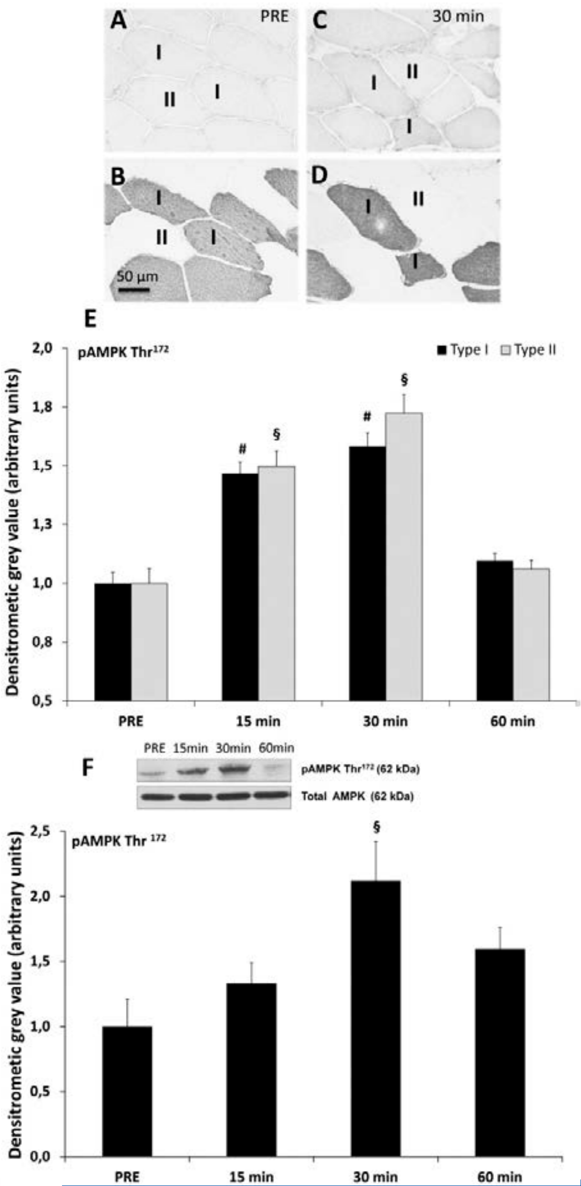
Bellinger et al. 2008

How fast is the process – relevant for sprint?

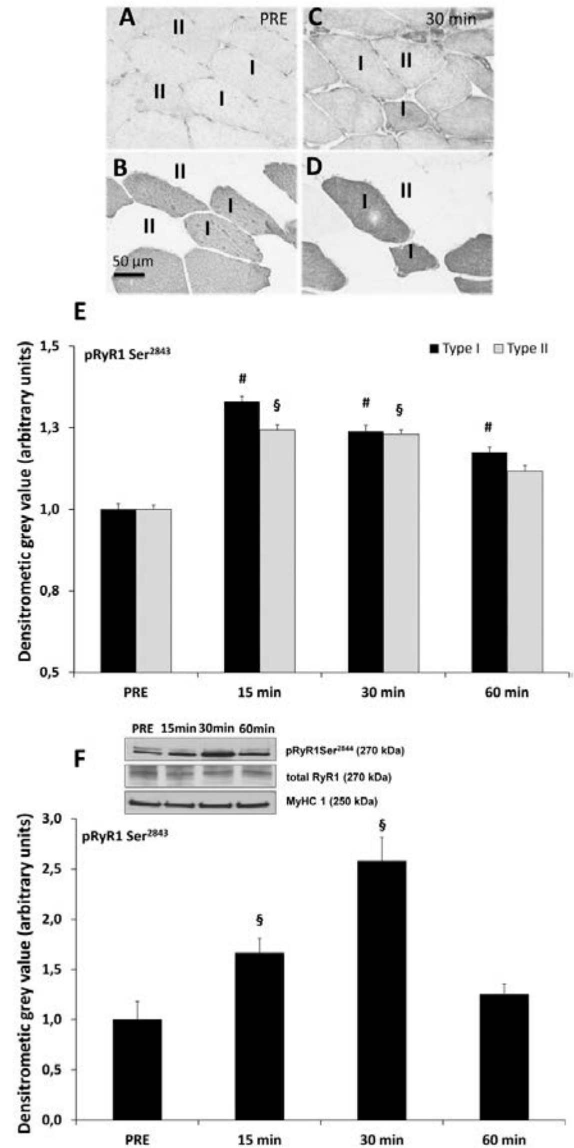


65 sec under tension

Gehlert et al. PLOSone 2012



65 sec under tension

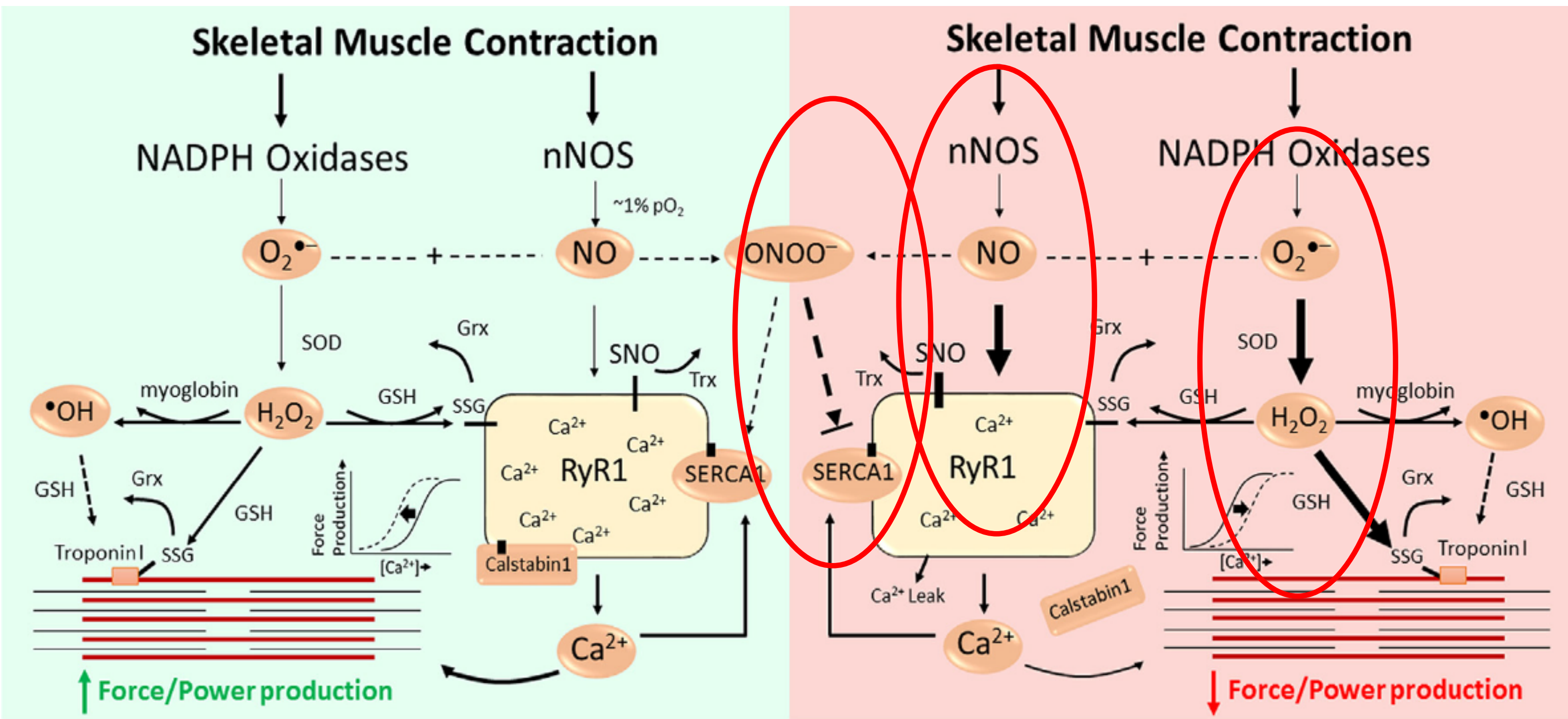


Gehlert et al. PLOSone 2012

RyR phosphorylation is a fast process and stays for relevant time.

Reduction of calcium regulation should be avoided before competion.

Nitric oxide (NO) - additional post transcriptional modulation of calcium release and myofilaments

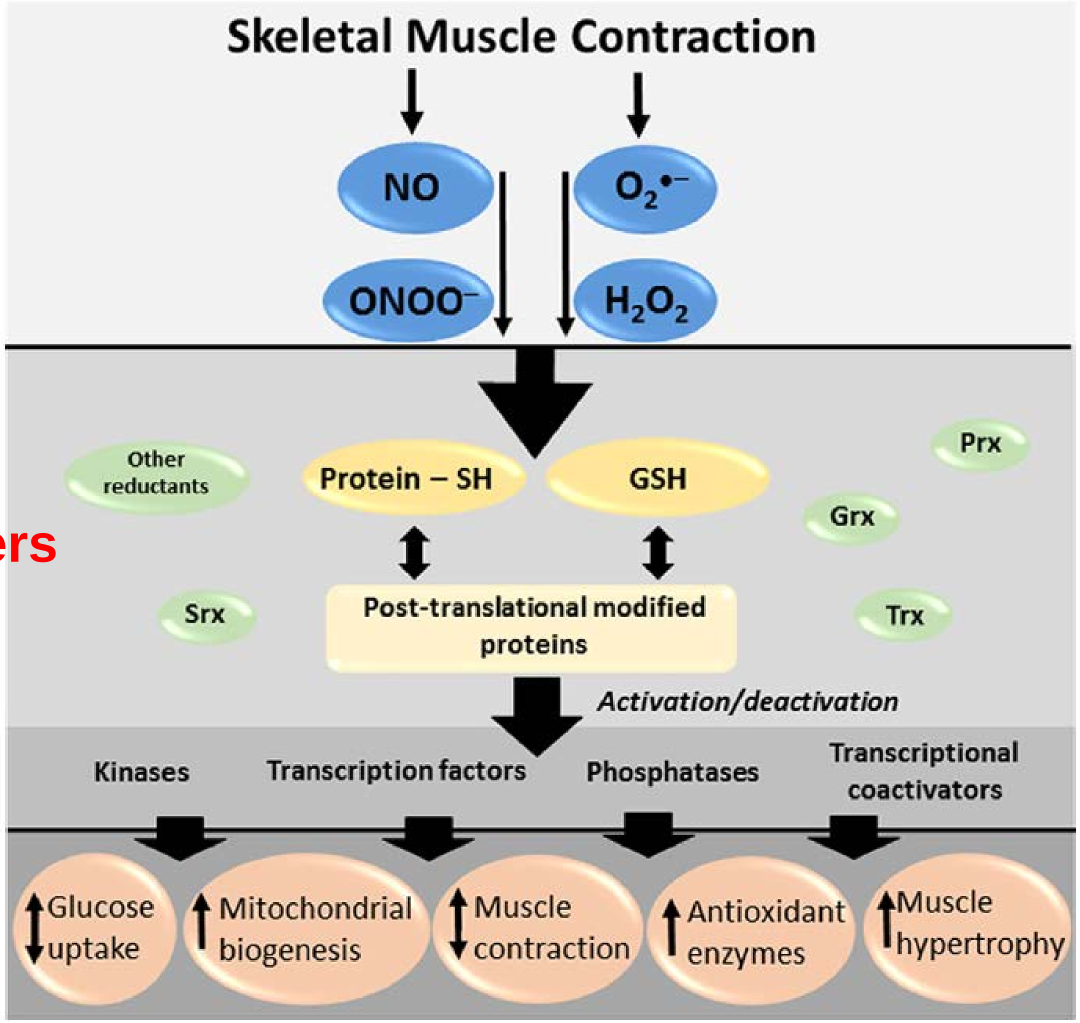


Mason et al. / Free Radical Biology and Medicine 98 (2016)

Free Radicals (ROS and NO) – post translational modification

Cave!

Antioxidants / Radical scavengers



Mason et al. / Free Radical Biology and Medicine 98 (2016)

Titin modulation

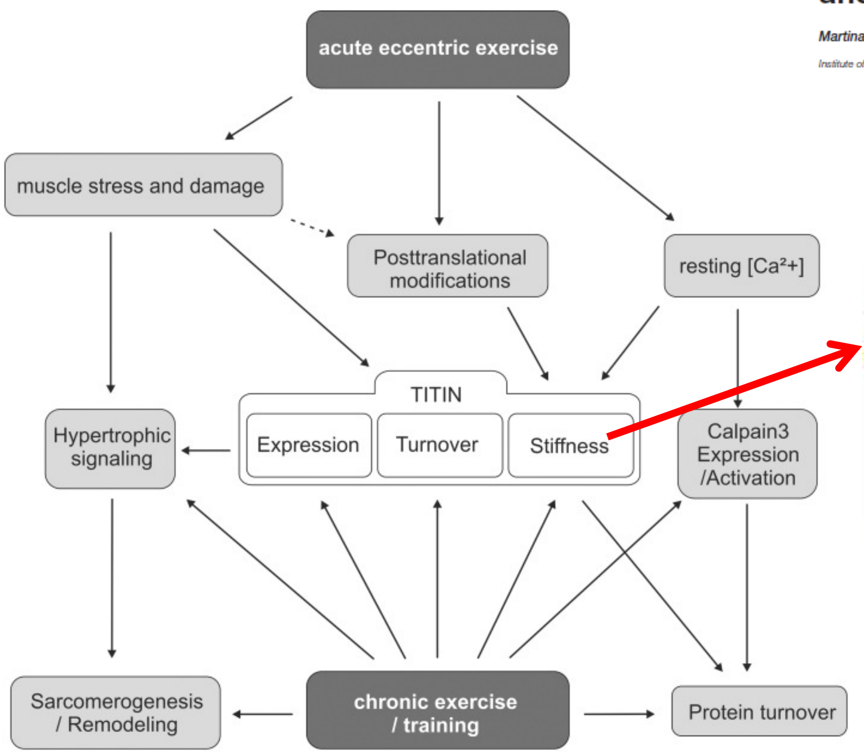
frontiers in Physiology

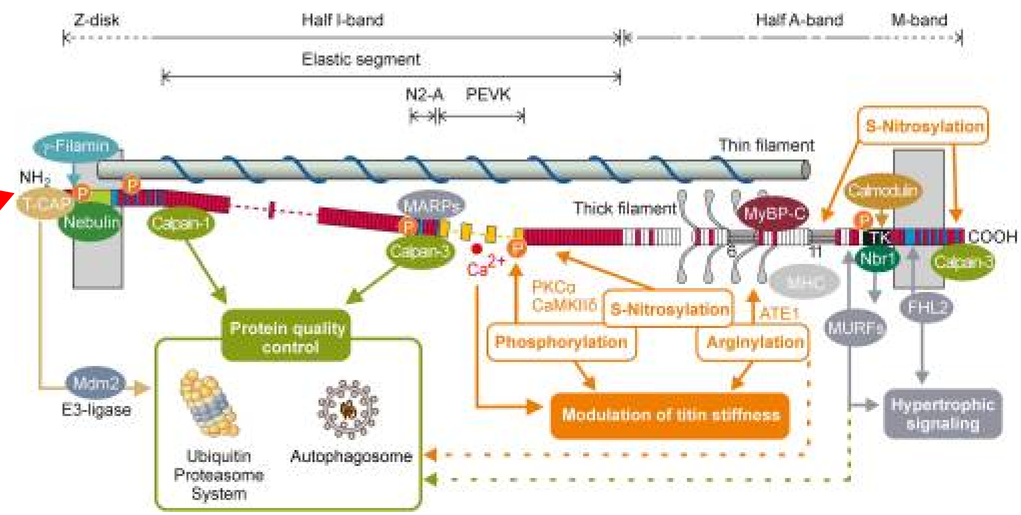
MINI REVIEW
published: 01 March 2016
doi: 10.3389/fphys.2016.00076

Titin, a Central Mediator for Hypertrophic Signaling, Exercise-Induced Mechanosignaling and Skeletal Muscle Remodeling

*Martina Krüger * and Sebastian Kötter*

Institute of Cardiovascular Physiology, Heinrich Heine University Düsseldorf, Düsseldorf, Germany





Titin modulation

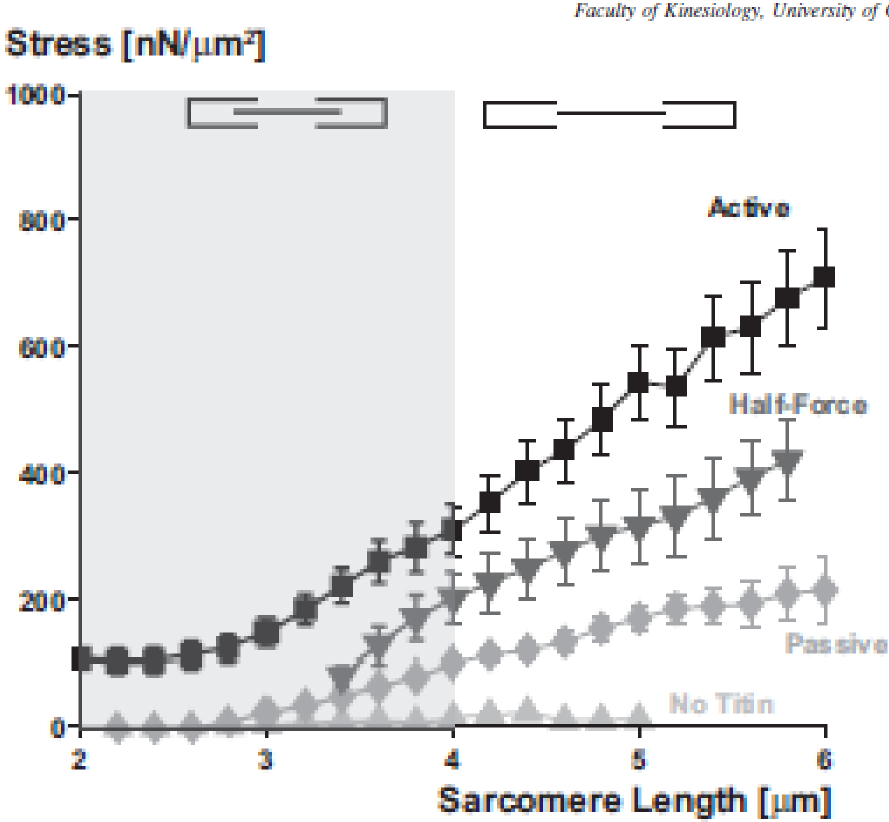
J Appl Physiol 116: 1407–1417, 2014.
First published February 21, 2013; doi:10.1152/japplphysiol.00069.2013.

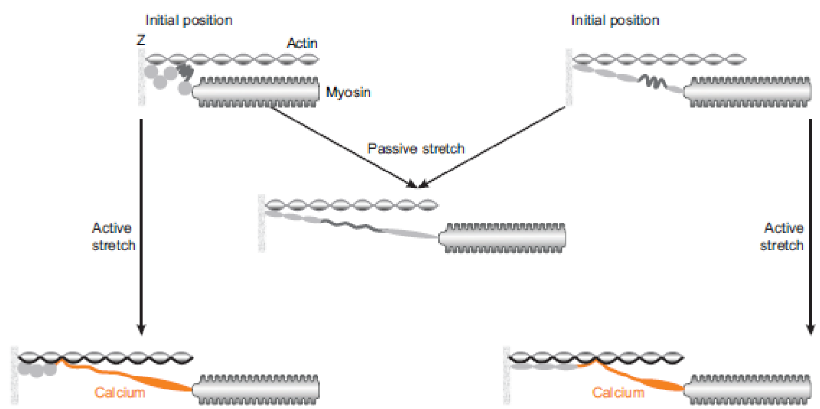
Review

HIGHLIGHTED TOPIC | *Eccentric Exercise*

Mechanisms of enhanced force production in lengthening (eccentric) muscle contractions

Walter Herzog
Faculty of Kinesiology, University of Calgary, Alberta, Canada





Titin modulation

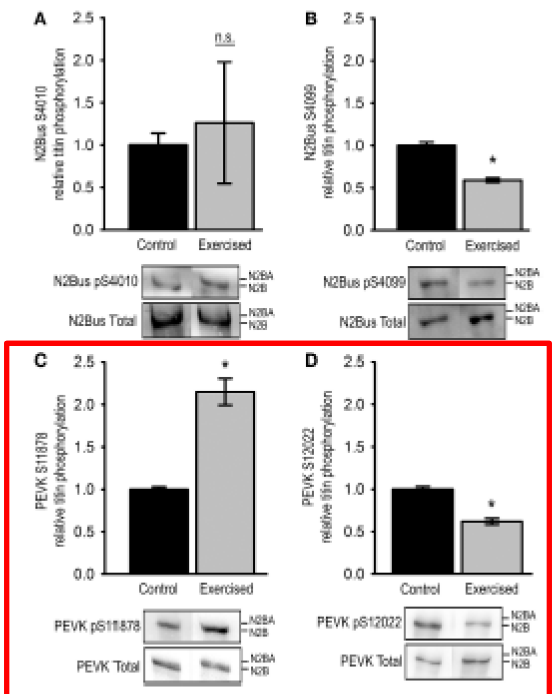
frontiers in PHYSIOLOGY
ORIGINAL RESEARCH ARTICLE
published: 20 November 2014
doi: 10.3389/fphys.2014.00449

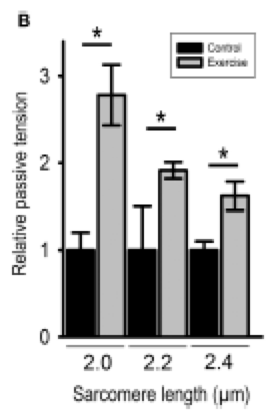
Acute exercise modifies titin phosphorylation and increases cardiac myofilament stiffness

Anna E. Müller[1†], *Matthias Kreiner*[1†], *Sebastian Kötter*[1†], *Philipp Lassak*[1], *Wilhelm Bloch*[2], *Frank Suhr*[2*] *and Martina Krüger*[1*]

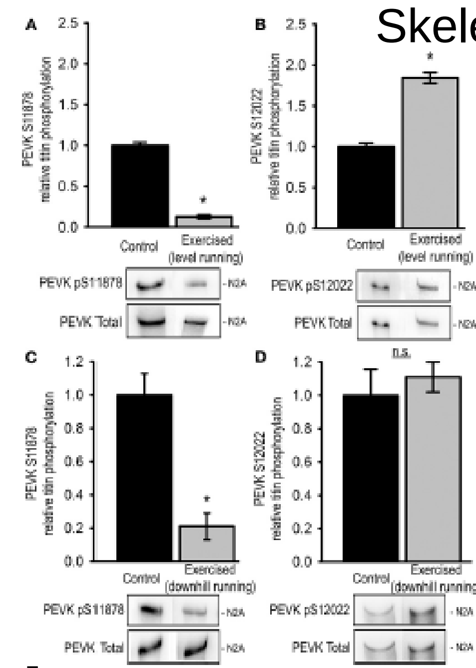
[1] *Department of Cardiovascular Physiology, Heinrich Heine University Düsseldorf, Düsseldorf, Germany*
[2] *Department of Molecular and Cellular Sport Medicine, Institute of Cardiovascular Research and Sport Medicine, German Sport University Cologne, Cologne, Germany*

Heart





Skeletal muscle



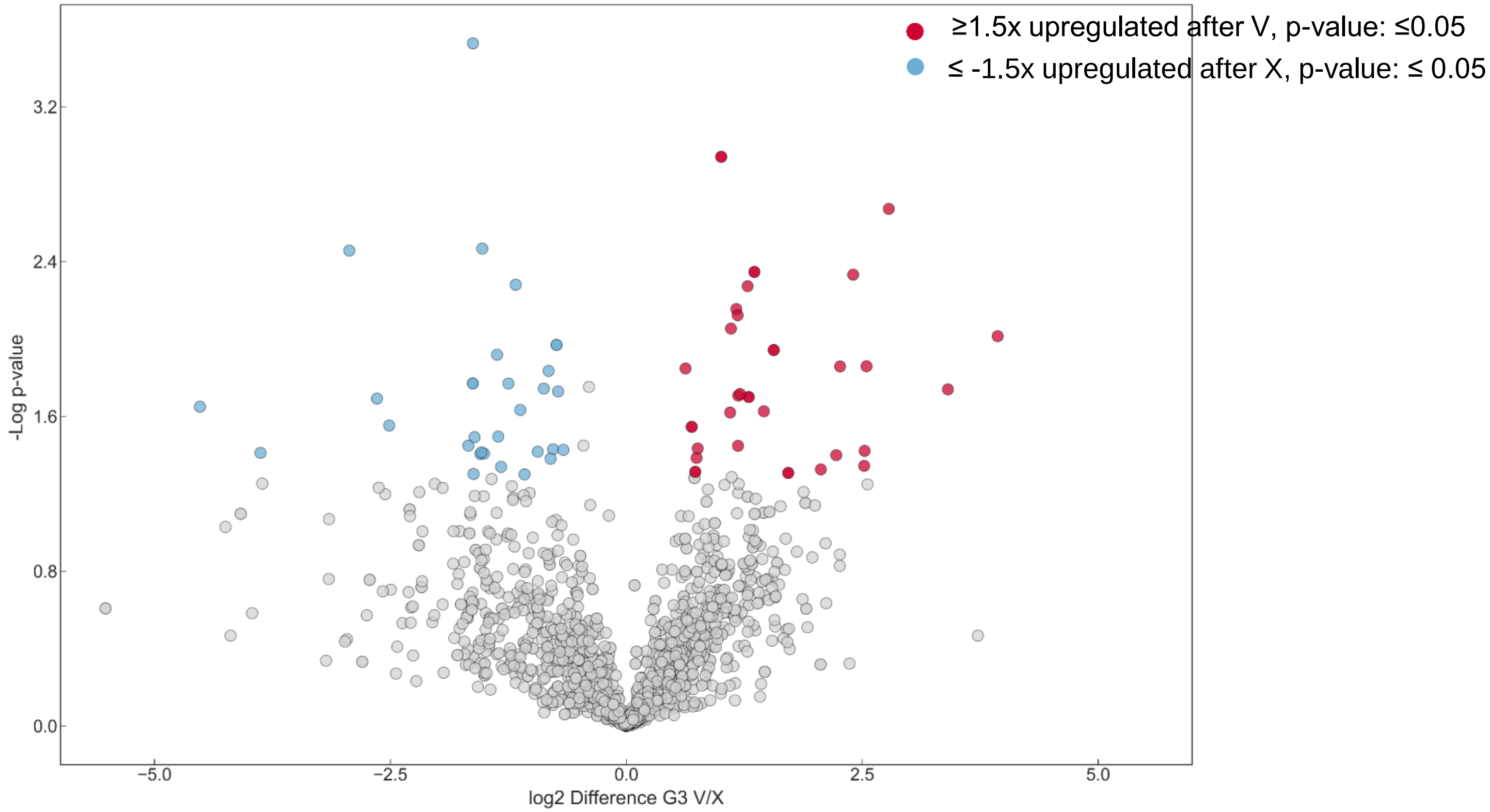
↑ **Stiffness** ↓

Rat 15 min treadmill runing

Phospho-proteomics

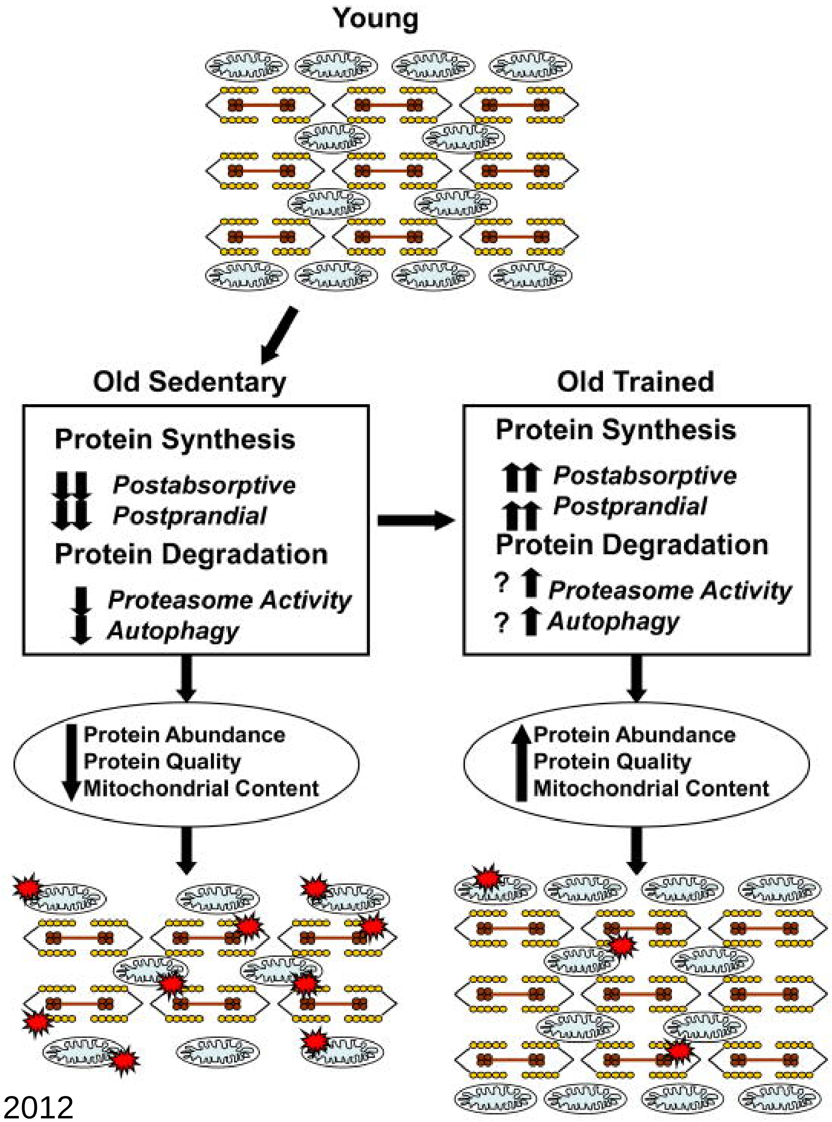
Gropup 3 (KA: 10 Wdh/Set)
- pre
- 5 Sets (V)
- 10 Sets (X)
M. Vastus lateralis

Volcano Plot G3 V/X



Muscle needs permanent turnover

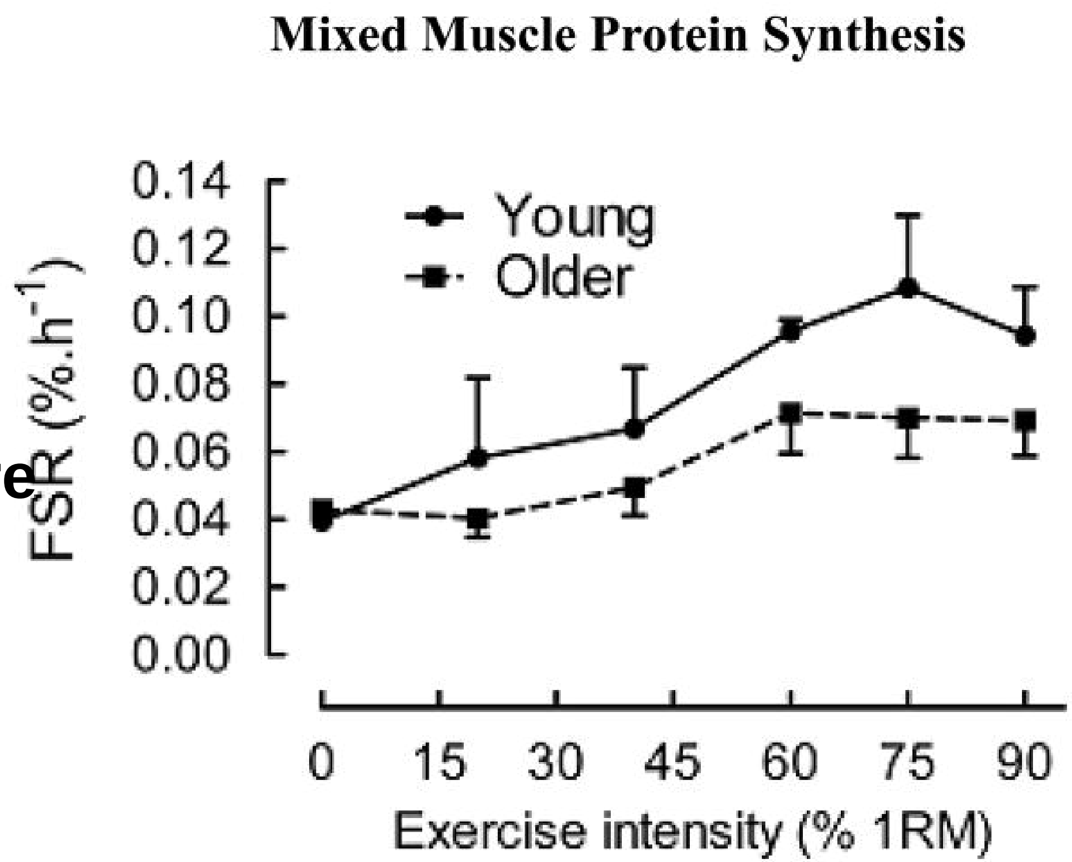
1-2% of muscle proteins are changed per day



Irving et al. 2012

Muscle needs permanent turnover

1-2% of muscle proteins are changed per day

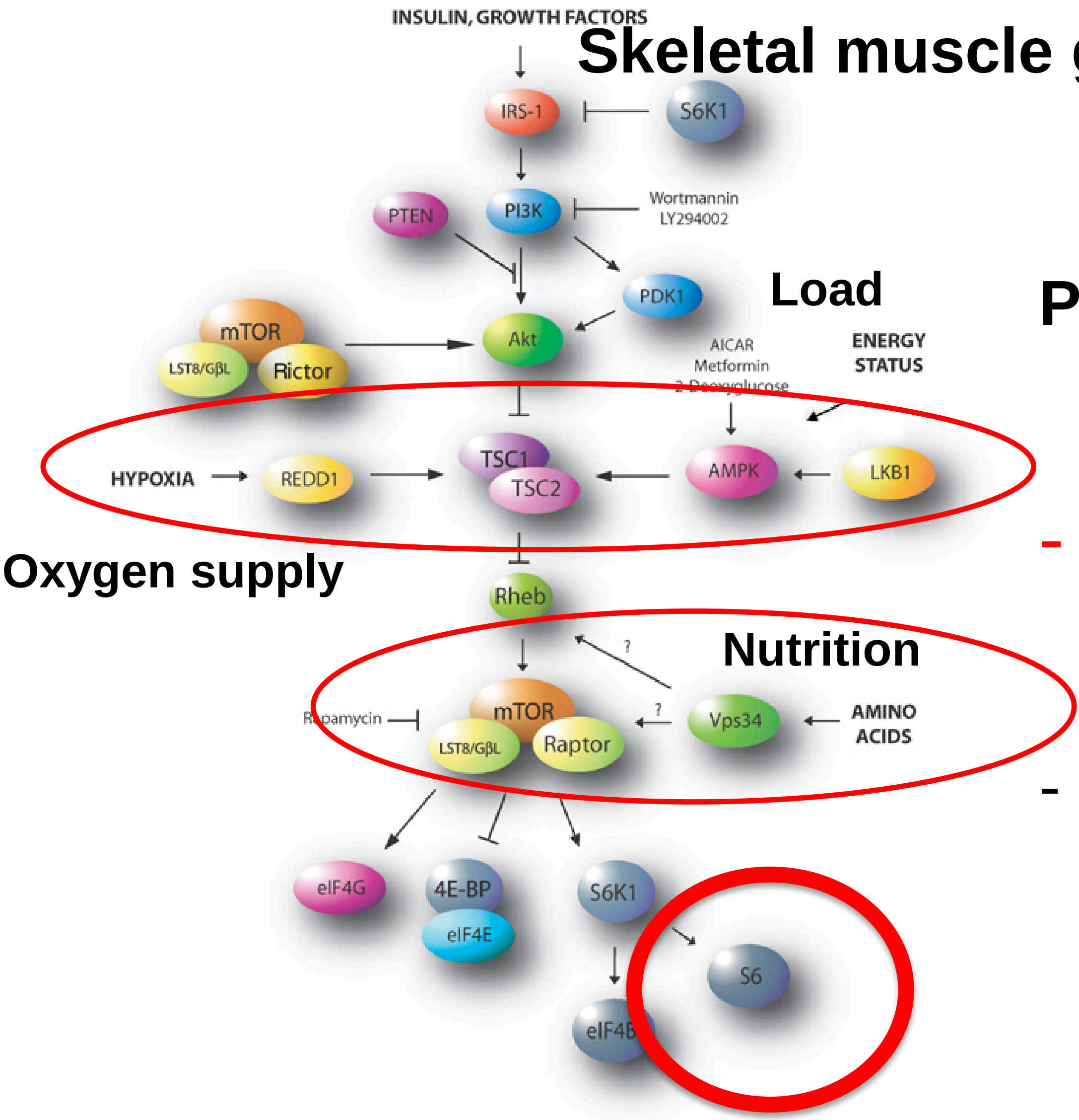


Irving et al. 2012

Skeletal muscle growth and maintenance

↓

Protein synthesis



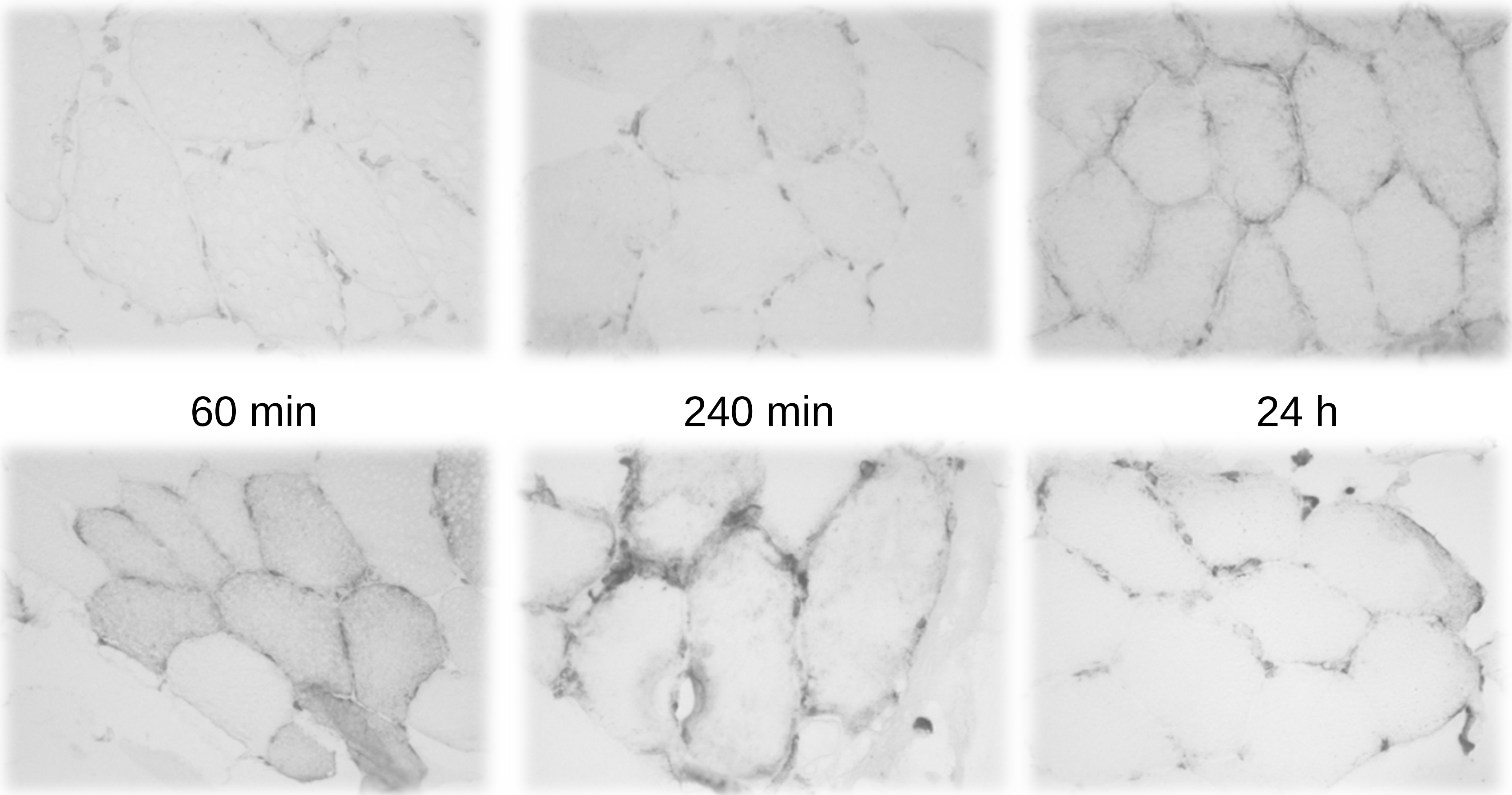
- **during regeneration**
- **S6 a key molecule in protein synthesis**

Dynamic of S6 phosphorylation

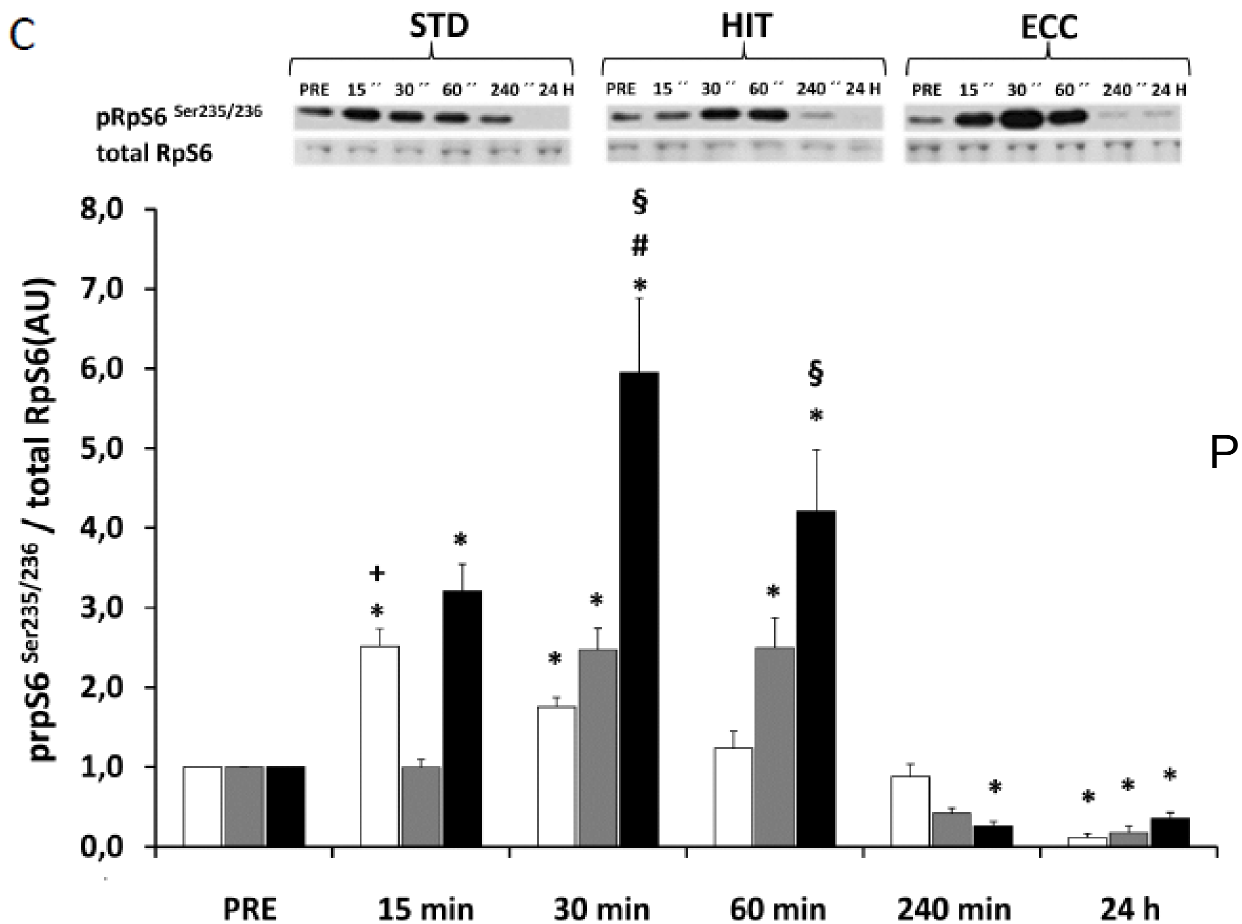
Pre

15 min

30 min



Comparison hypertrophy, eccentric, concentric resistance training

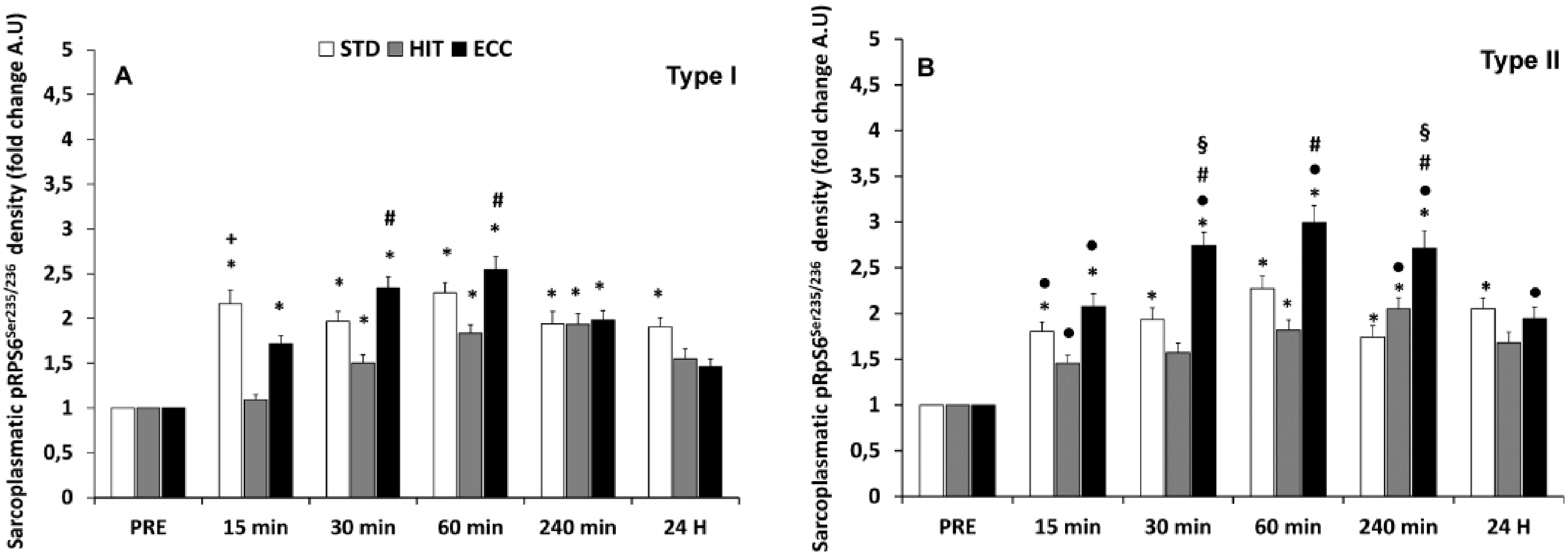


Phospho-S6

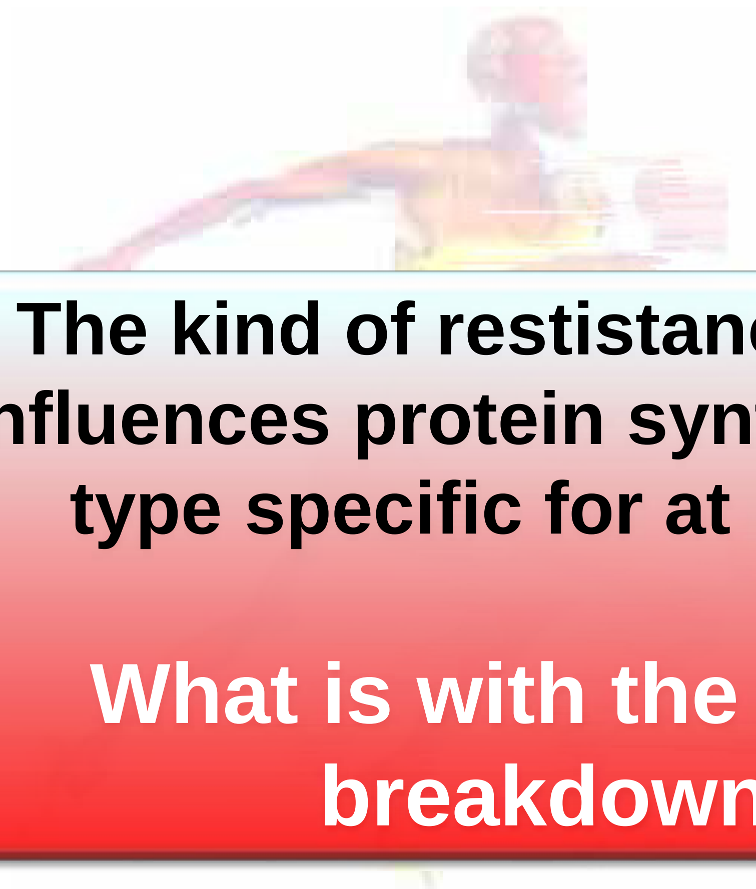
Gehlert et al Pflugers Arch 2014

Comparison hypertrophy, eccentric, concentric resistance training

Phospho-S6



Gehlert et al Pflugers Arch 2014

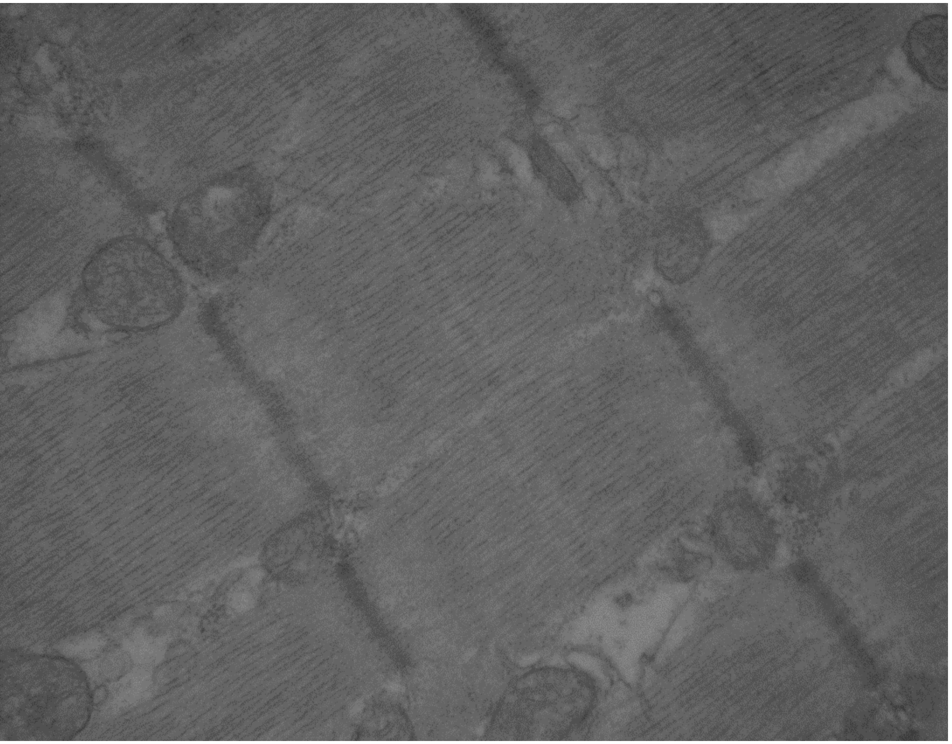


The kind of restistance training influences protein synthesis fibre-type specific for at least 24h

What is with the protein breakdown?

Acute changes in the muscle after eccentric load

Pre eccentric load

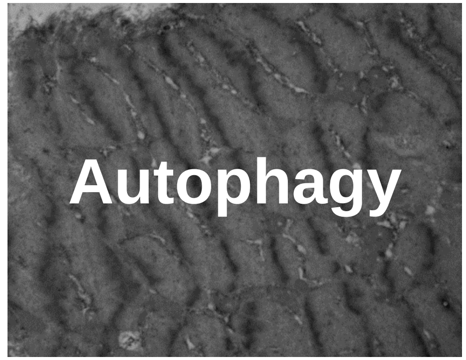


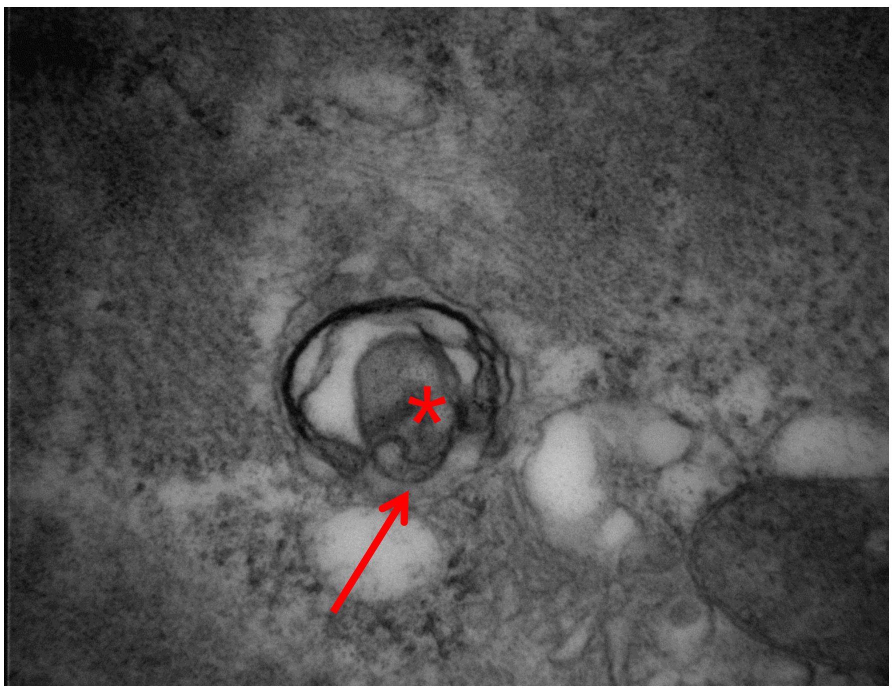
After eccentric load

Z-line

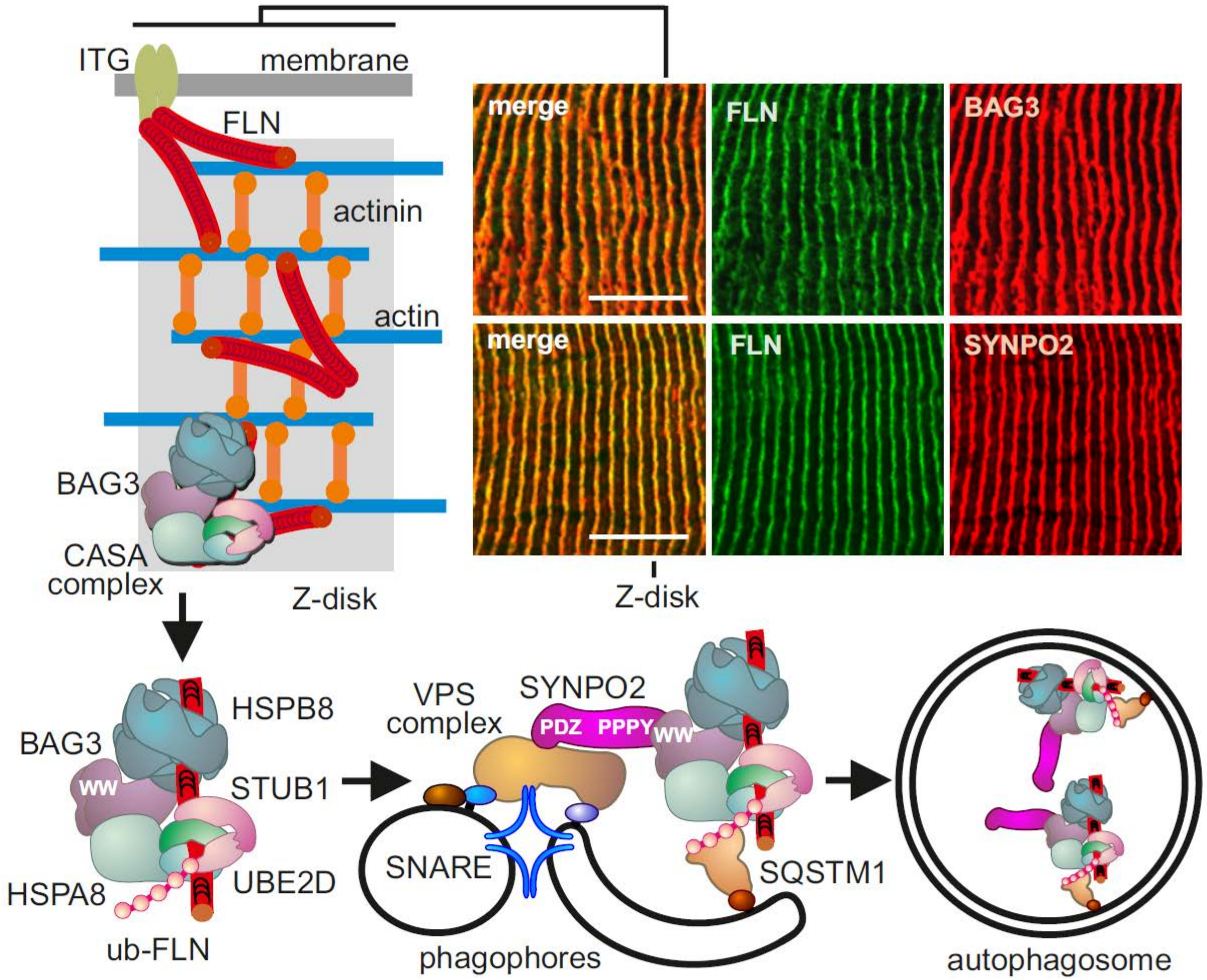
70s „time under tension“

Acute changes in the muscle after eccentric load



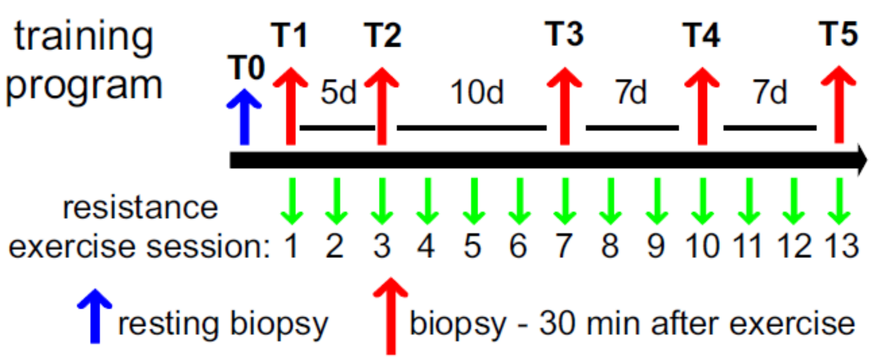


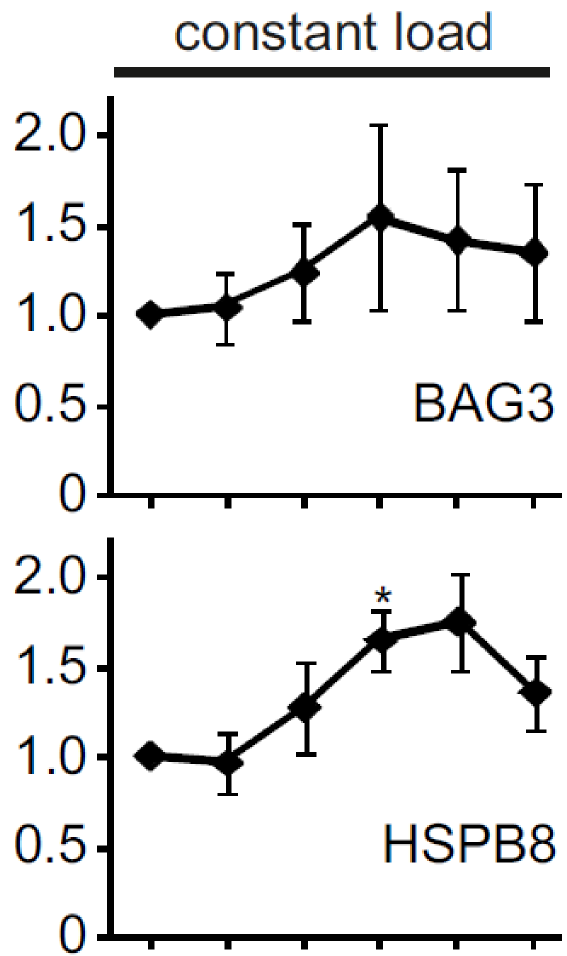
Induction of autophagy by eccentric load



Ulbricht, Gehlert et al. submitted

Induction of autophagy by eccentric load



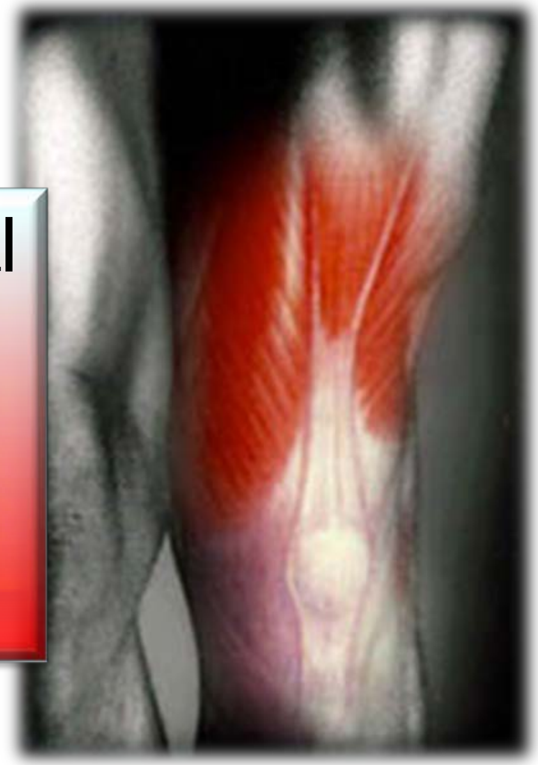


Ulbricht, Gehlert et al. submitted

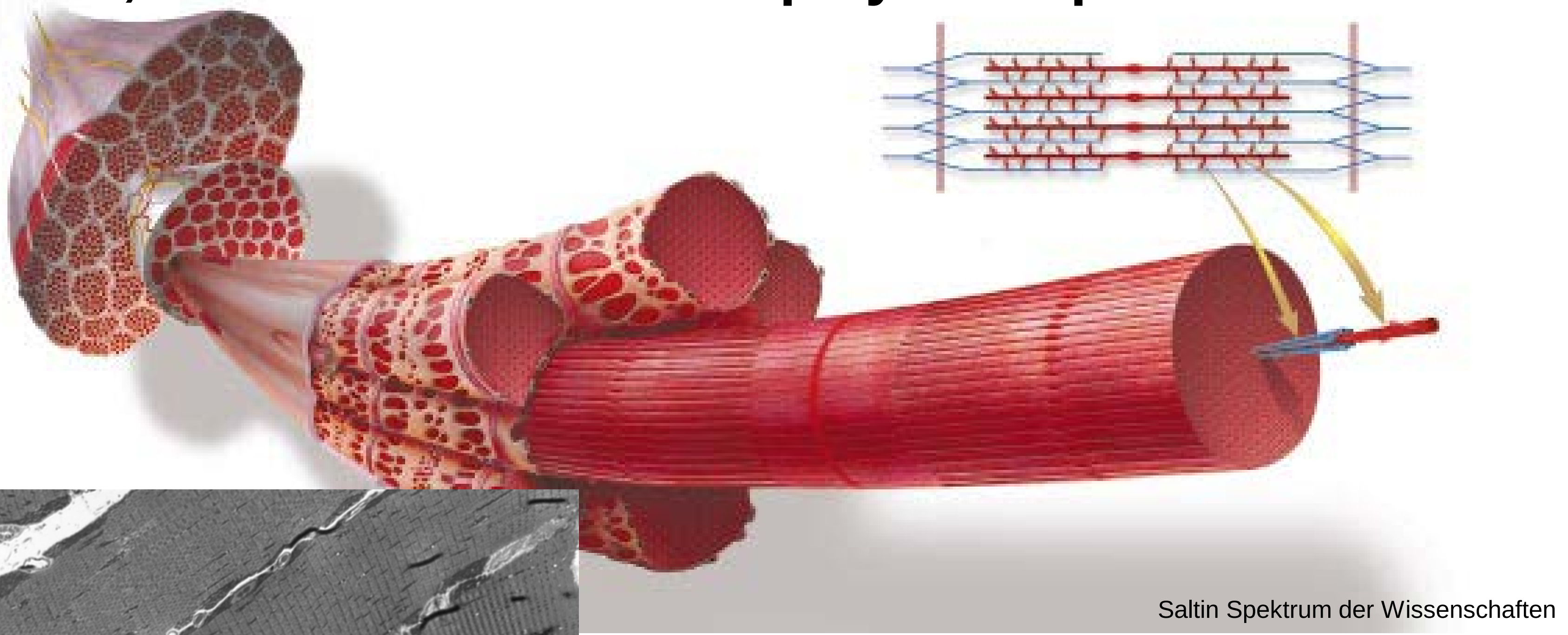
Muscle plasticity is higher as principal estimated

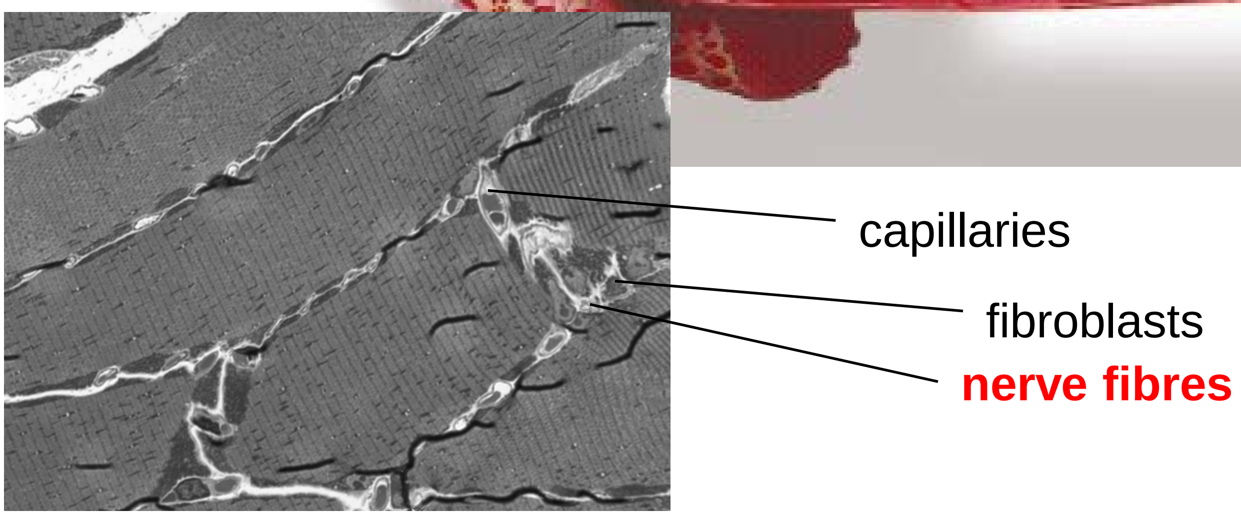
–

Posttranscritpional mechanisms are strongly involved



Tissue adaptation isn‘t only dependent from muscle fibres: **Vessels, ECM and nerve fibres play an important role**





OPEN ACCESS Freely available online · PLOS ONE

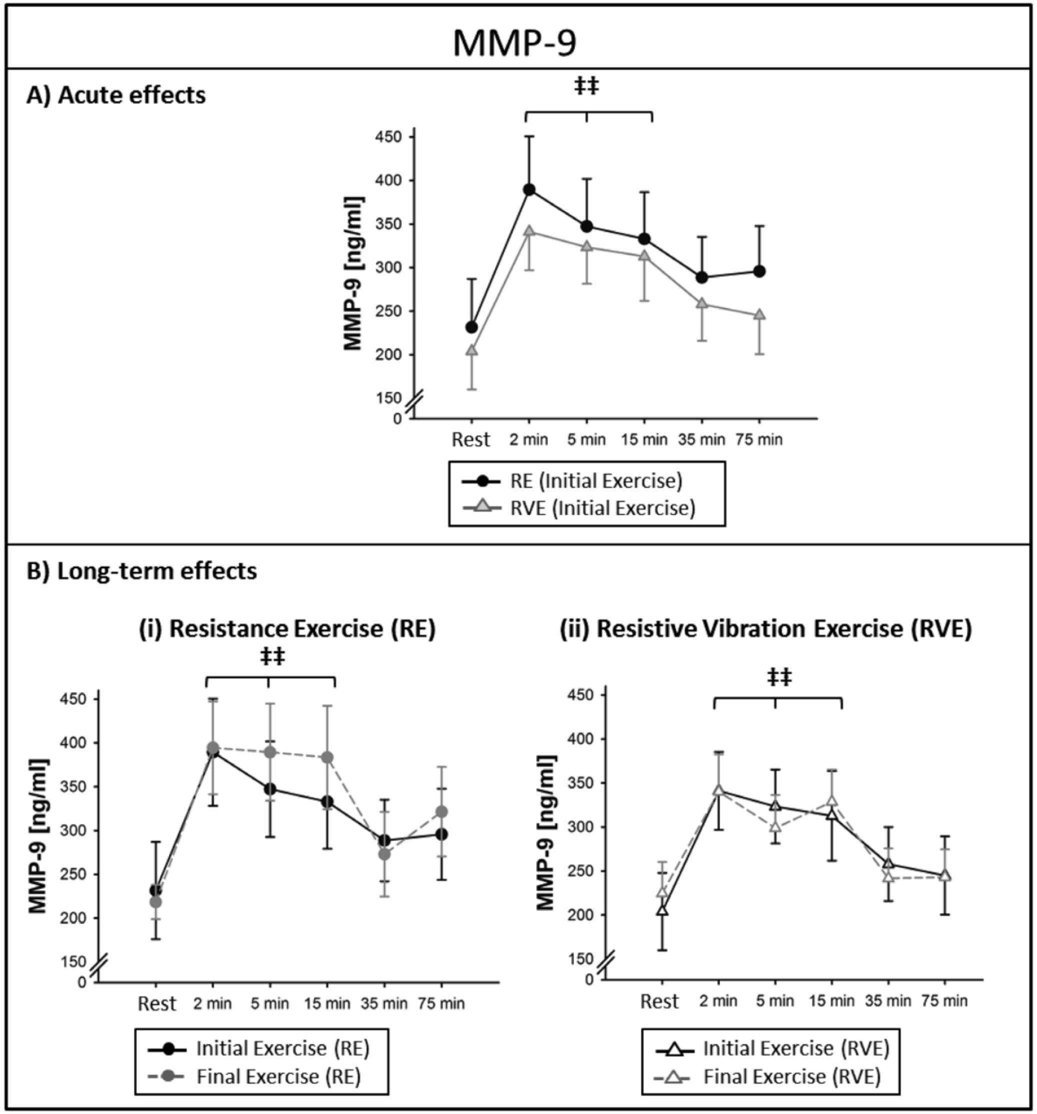
Whole-Body Vibrations Do Not Elevate the Angiogenic Stimulus when Applied during Resistance Exercise

Åsa Beijer[1,2]*, André Rosenberger[1,3], Birgit Bölck[2], Frank Suhr[2], Jörn Rittweger[1,4], Wilhelm Bloch[2]

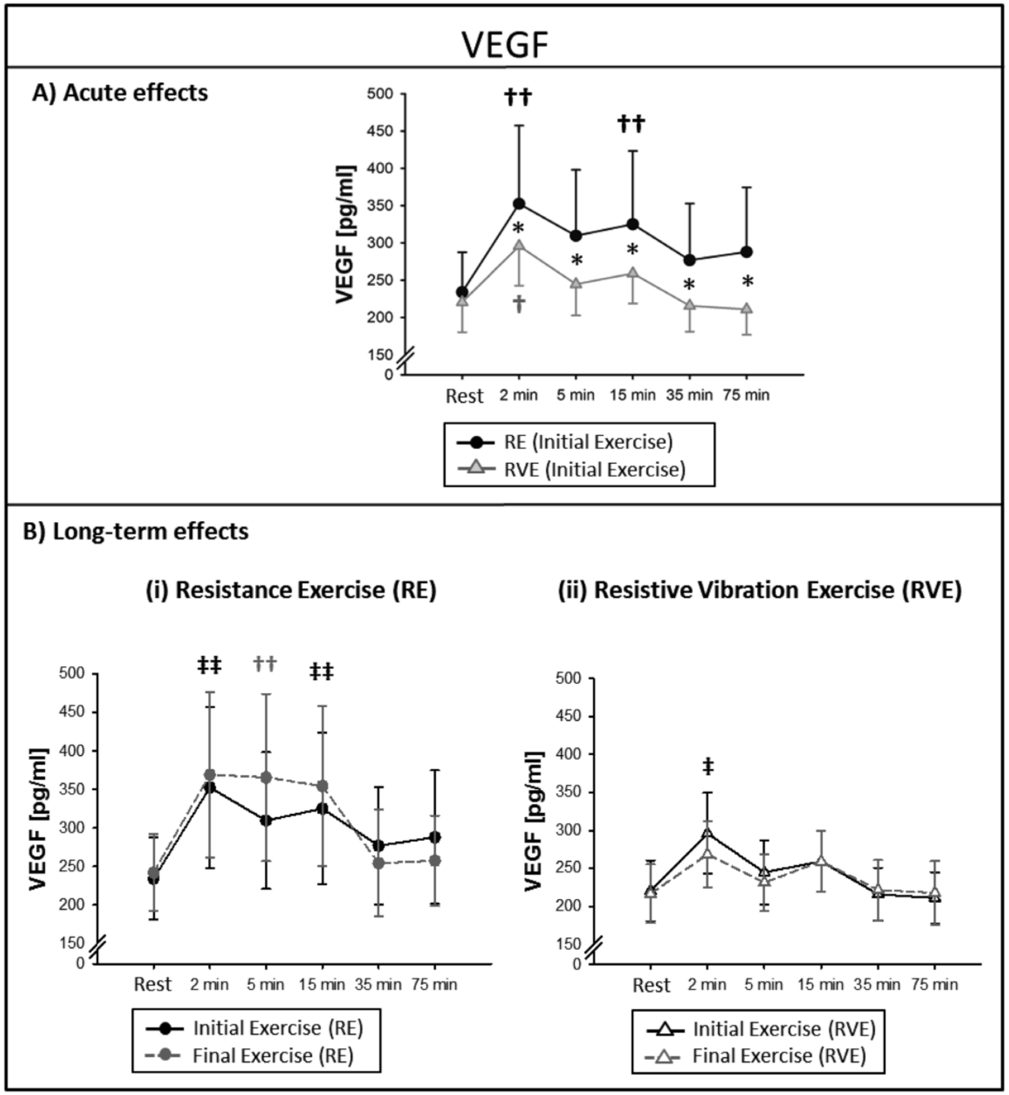
1 German Aerospace Center, Institute of Aerospace Medicine and Space Physiology, Cologne, Germany, **2** German Sport University Cologne, Department of Molecular and Cellular Sport Medicine, Cologne, Germany, **3** German Sport University Cologne, Institute of Training Science and Sports Informatics, Cologne, Germany, **4** Institute for Biomedical Research into Human Movement and Health, Manchester Metropolitan University, Manchester, United Kingdom

6 week resistance training with and without vibration (16 training units)
80% RM

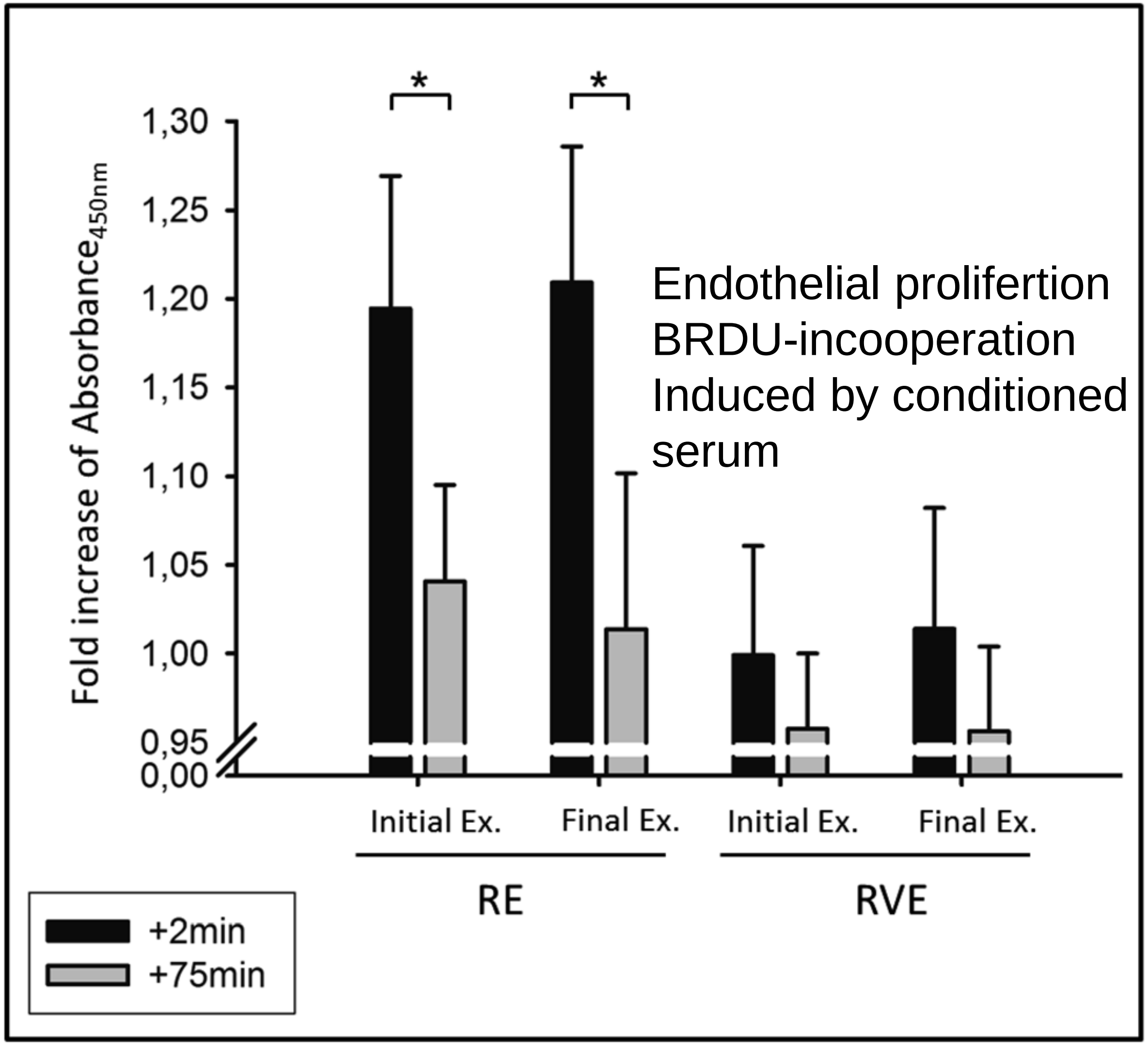
Resistance training leads to release of proteases –cleavage of ECM



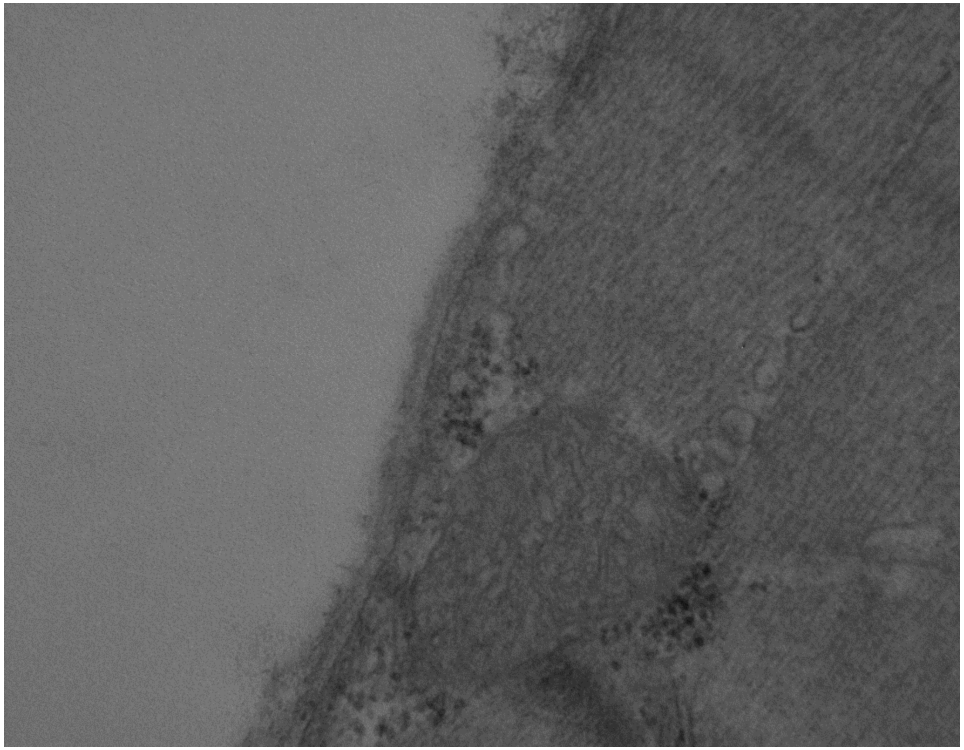
Resistance training leads to release of angiogenic factors

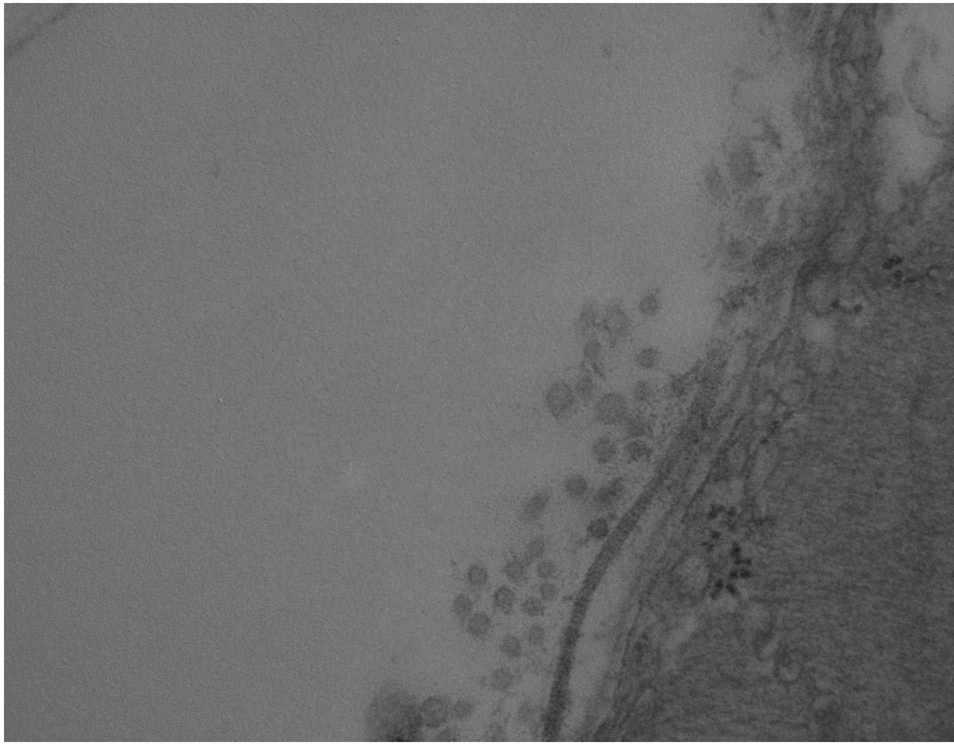


Resistance training enhances angiogenesis



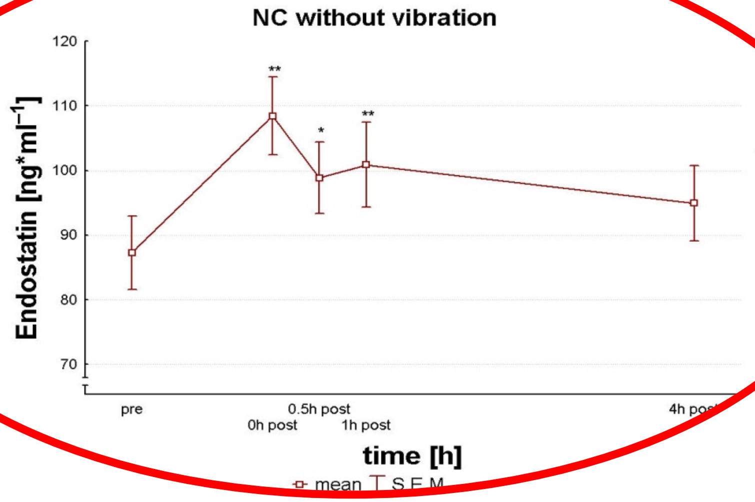
Alteration of endomysium after 6 weeks downhill runing

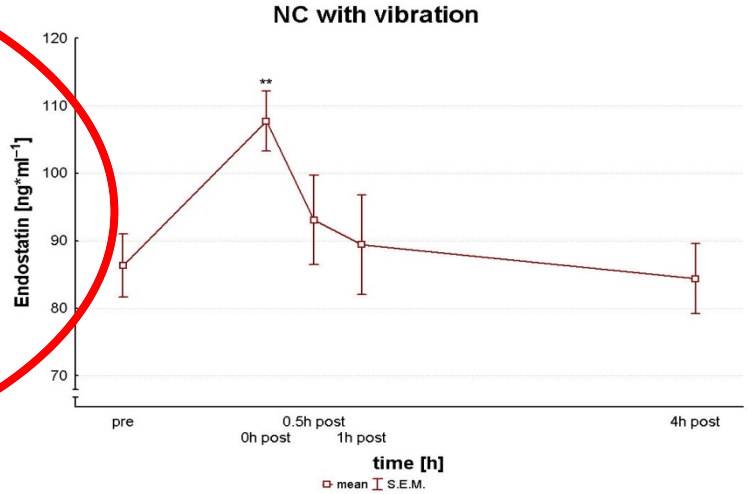


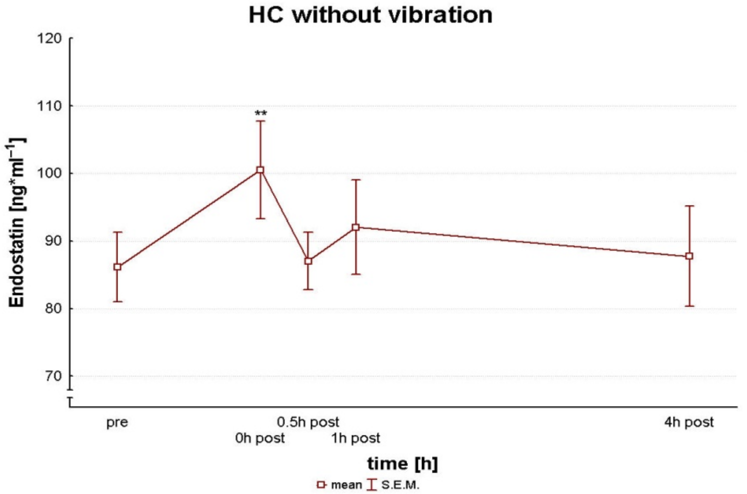


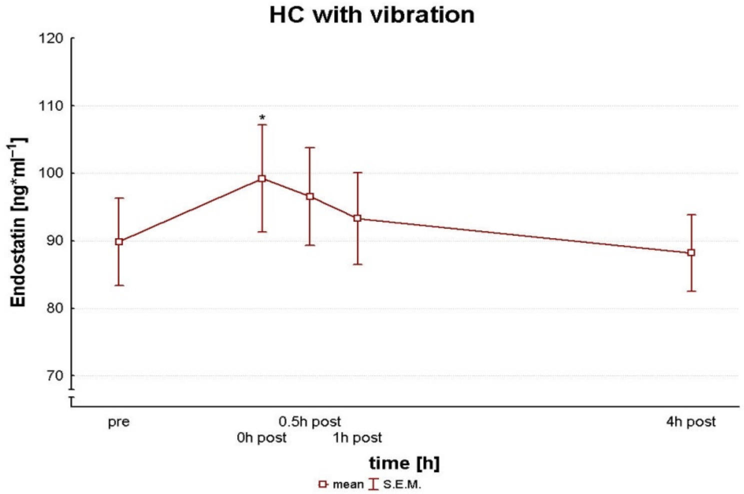
Relevance for function and structure?

ECM processing







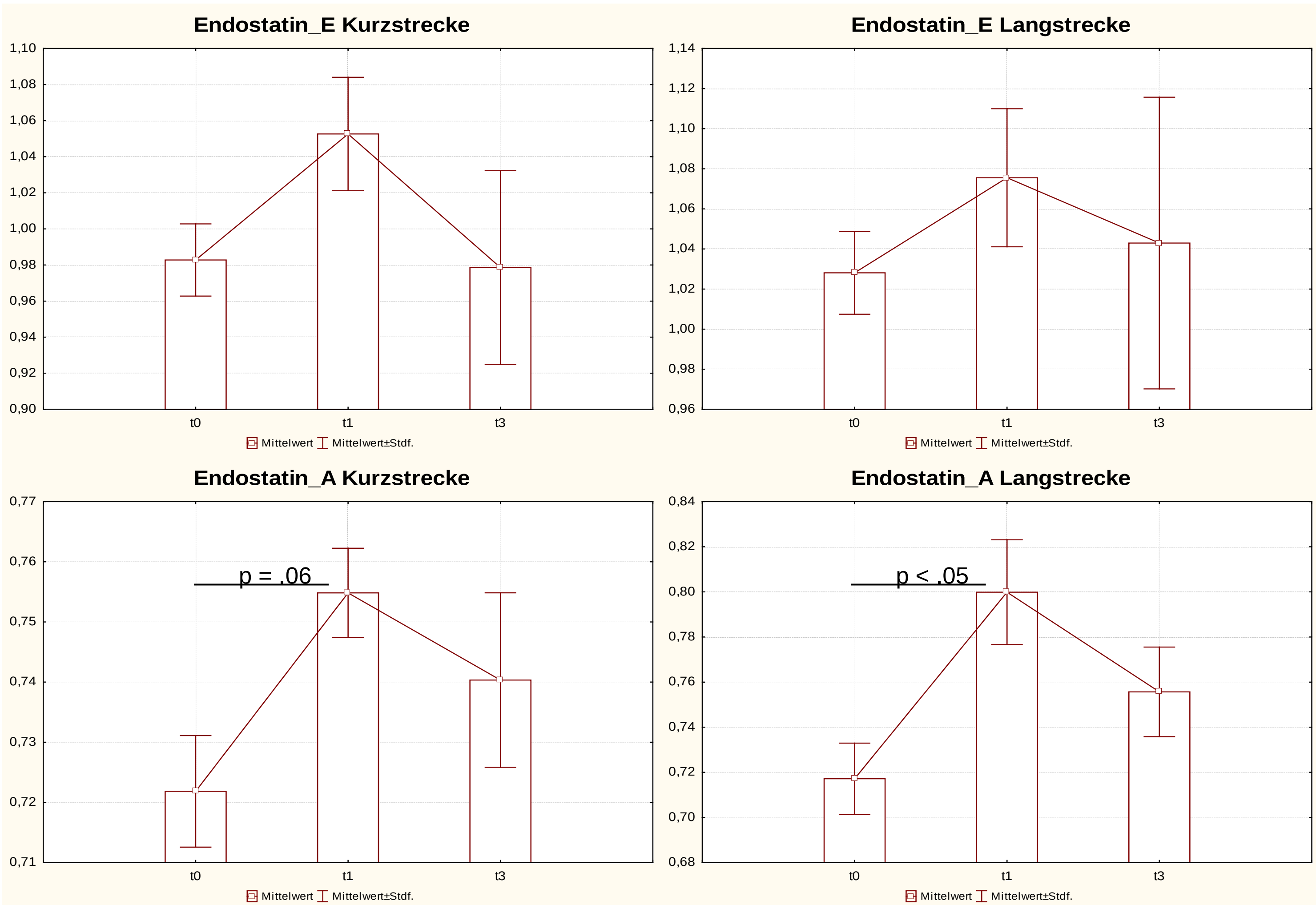


Suhr et al. J Appl Physiol 103:474-483 2007

Etlite athlets
Winter training
30min step test runing

before

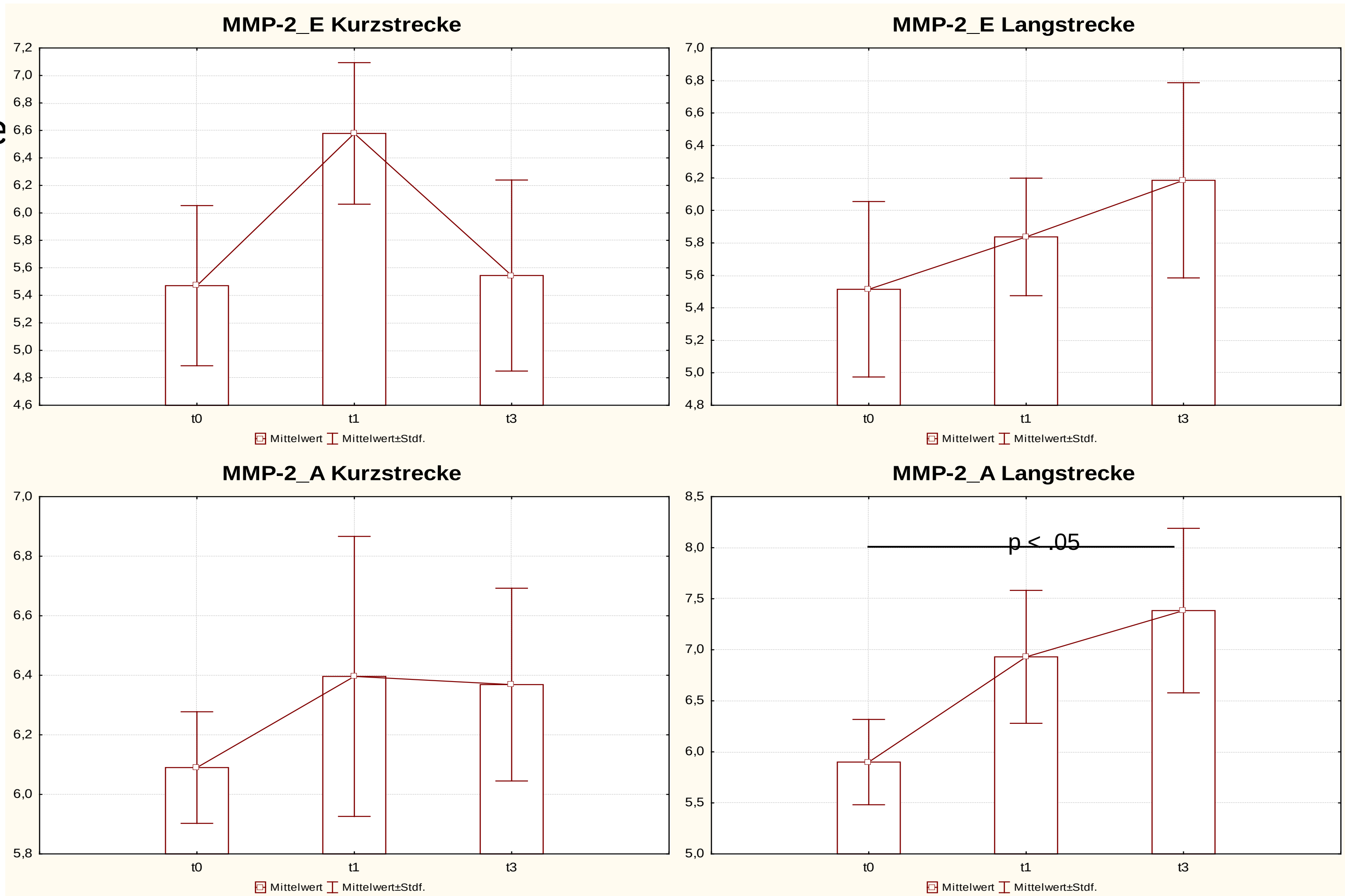
after

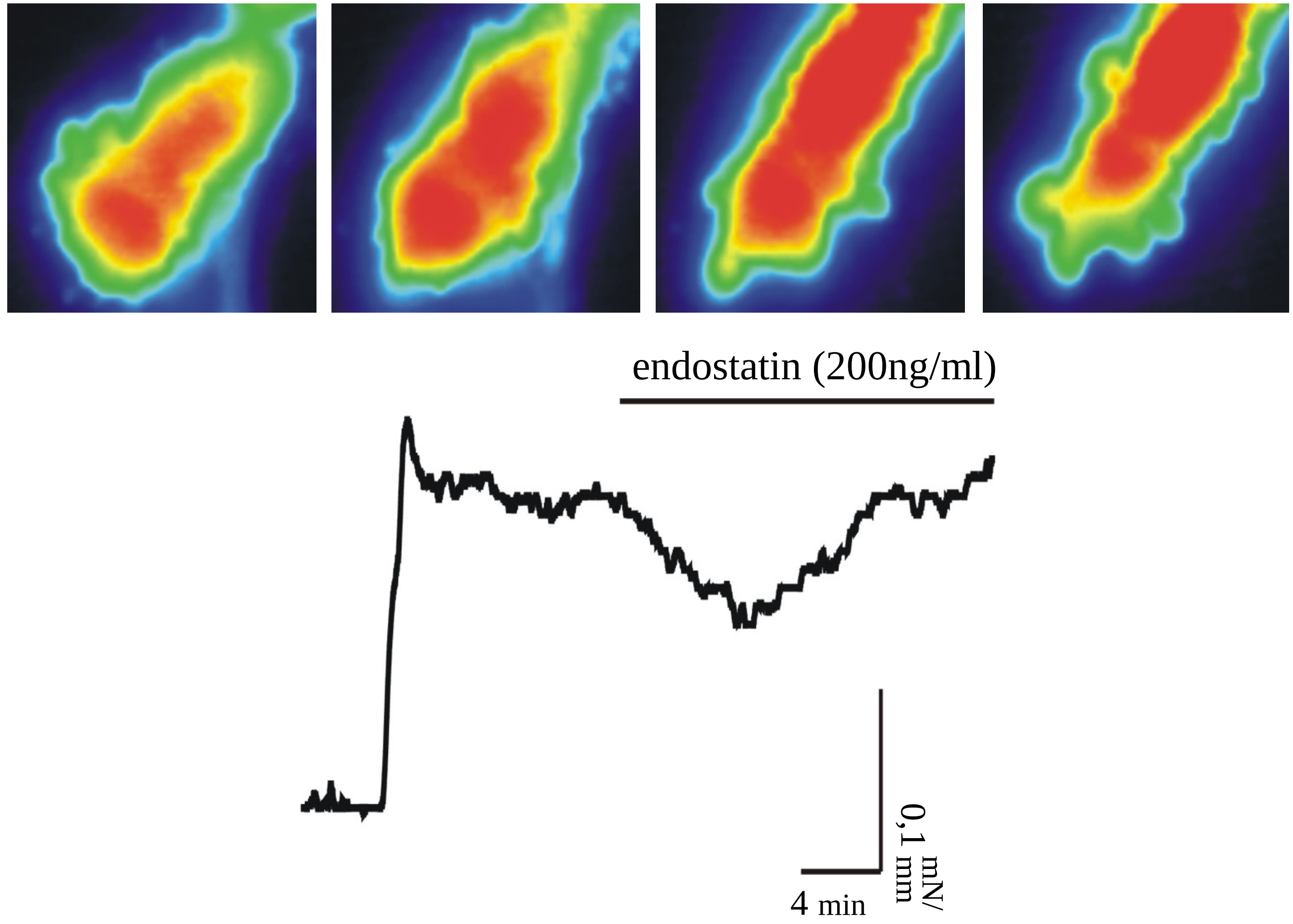


Etlite athlets
Winter training
30min step test runing

before

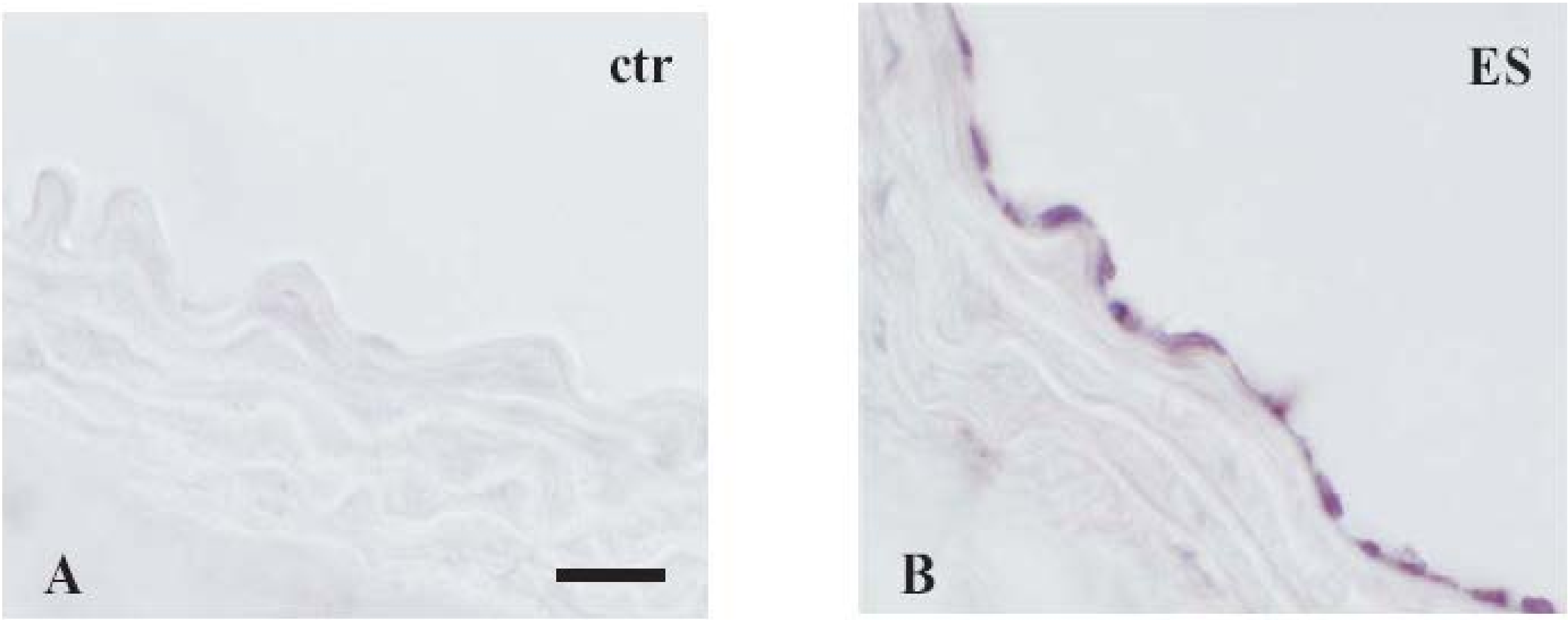
after



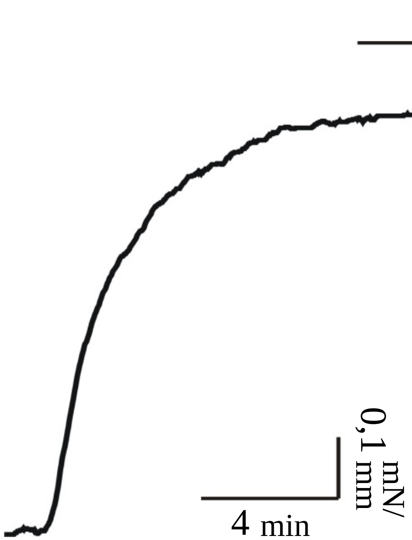


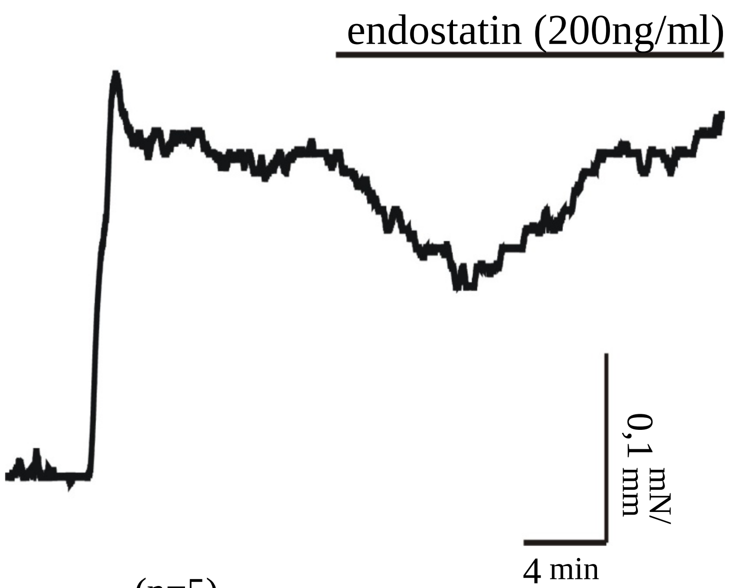
Wenzel et al. Circulation Research. 2006;98:1203

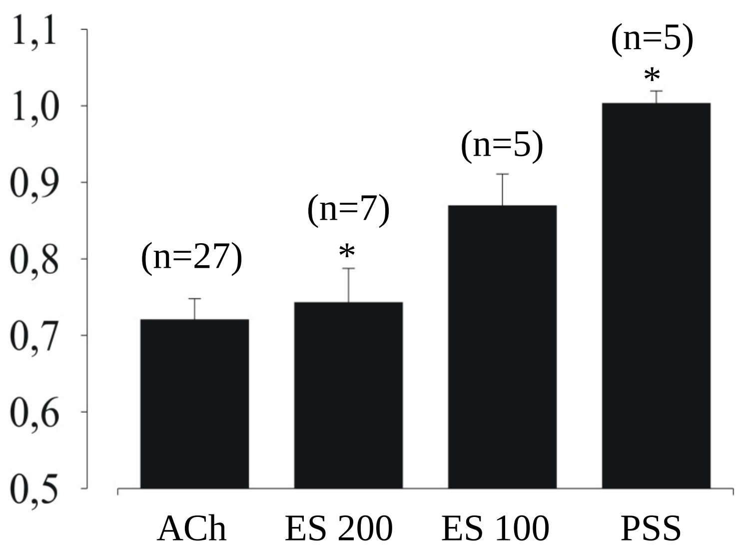
ECM cleavage product influence endothelial function by eNOS activation



Wenzel et al. Circulation Research. 2006;98:1203

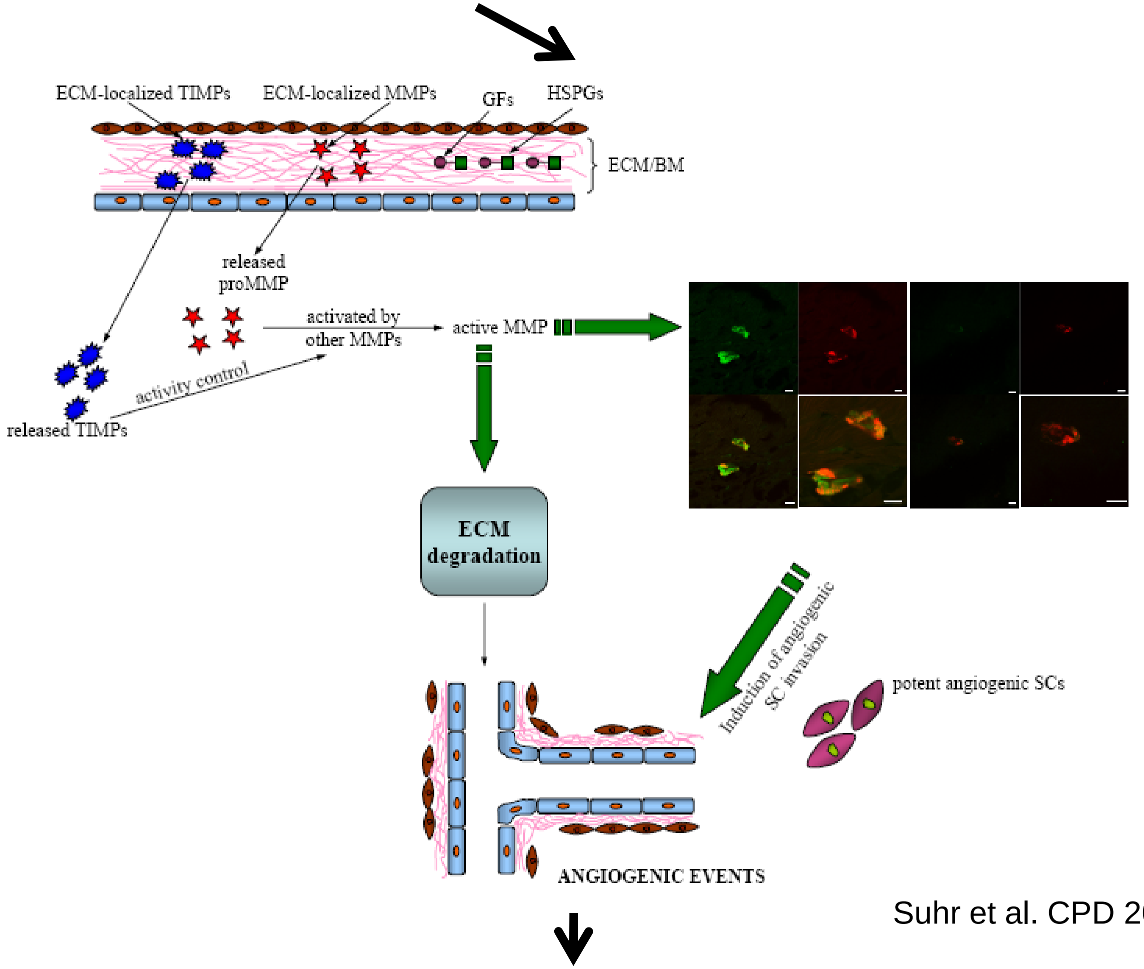






Wenzel et al. Circulation Research. 2006;98:1203

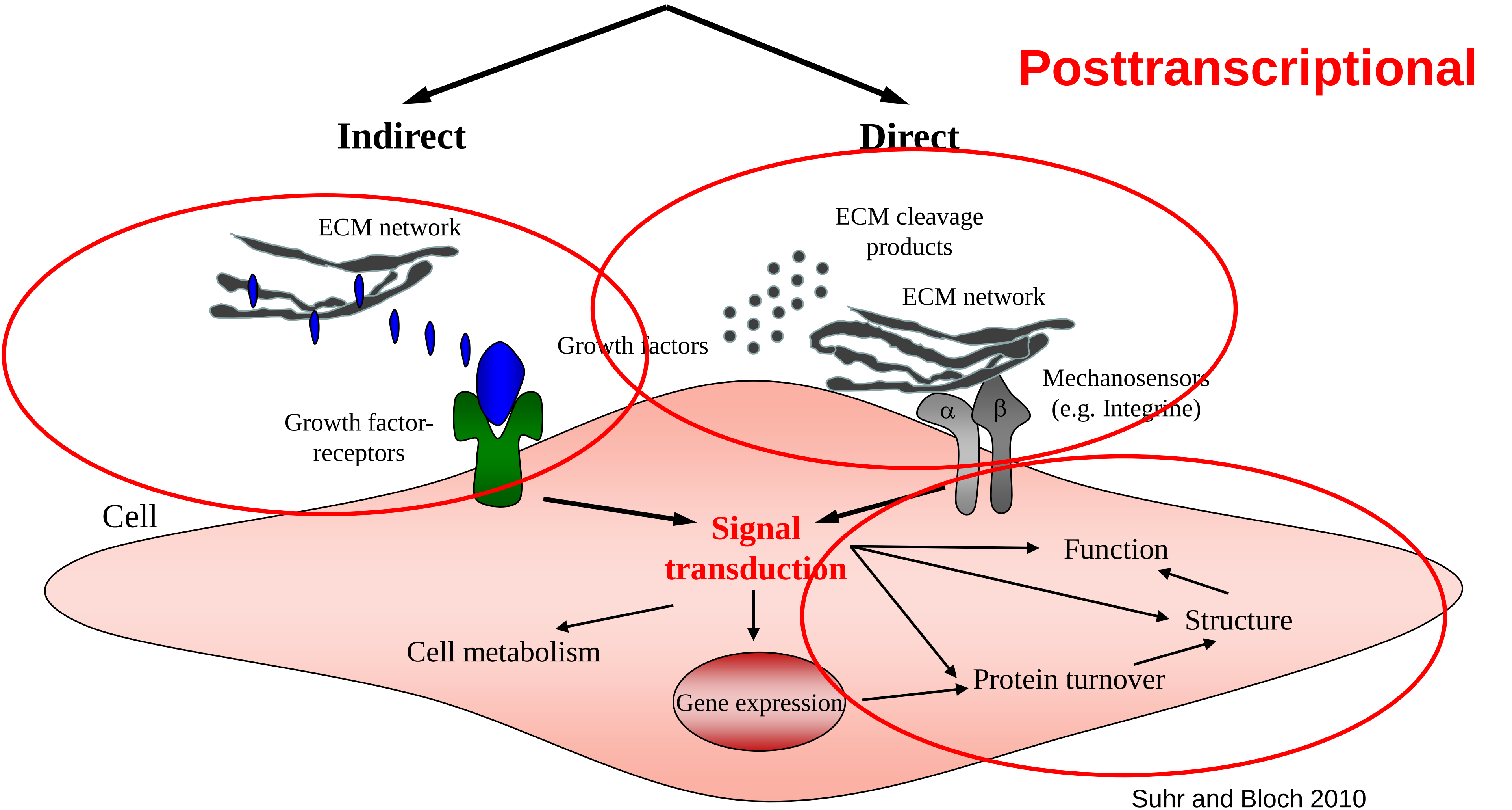
ECM Cleavage



Suhr et al. CPD 2009

New Vessels (Modulation of angiogenesis)

Mediator of mechanical stimuli



Suhr and Bloch 2010

Muscle adaptation isn‘t only dependent from muscle fibres – ECM, blood and lymphatic vessels, nerve fibres and immune cells at posttranscriptional level

Thank you for your attention!