

LIFELONG MUSCLE HEALTH THROUGH NUTRITION AND ADAPTIVE CHALLENGES

PHILOSOPHICAL CONTEXT

- Environmental exposure prompts movement on the Biological Spectrum.
- Optimal environmental “dose” depends upon internal capacity.
- Muscle health depends upon regular exposure to tension.

SARCOPENIA

- Sarco = flesh/muscle; Penia = poor
- Characterized by progressive and generalized loss of skeletal muscle mass and strength.
 - 0.8% skeletal muscle loss per year from the fifth decade of life (50+)
- Sarcopenia is strictly correlated with physical disability, poor quality of life, and death.
- Results in:
 1. **Chronic Metabolic Disease**
 - i. Fatty Organ Disease
 2. **Reduced Functional Capability**
- **Fast Twitch** muscle fibers are preferentially targeted (*lost*)
 - *Loss of Strength*
 - *Loss of Speed*
 - *Loss of Control*
- Increased **likelihood of falls**
 - ↓ probability of recovery
 - ↑ dependence on others
 - ↓ quality of life
 - ↑ comorbidities
 - ↓ average life expectancy

UNDERSTANDING SKELETAL MUSCLE

- Preserving muscle means ***promoting regular protein synthesis***

MAMMALIAN TARGET OF RAPAMYCIN (MTOR)

- Protein complex that senses cellular conditions (nutrients, redox state, growth factors, energy charge, and mechanical tension) and **controls protein synthesis**
- Responsive to:
 - **Nutrients** (amino acids)
 - Mechanical **Tension** (eccentric muscle actions)
 - Growth Factors (e.g., IGF-1)
- **Coincidence Detector**: Activates when both tension and nutrients are present.

SATELLITE CELLS

- Stem cell on the periphery of skeletal muscle cells
- Mechanical strain results in their activation:
 - Chemical signaling – growth and repair
 - Proliferation – division (more satellite cells)
 - Fusion and Differentiation (**add nuclei** to existing muscle fibers)

- **Myonuclear Domain**
 - A given myonucleus in the muscle fiber syncytium can only transcriptionally govern a finite jurisdiction.
 - More nuclei = ↑ protein synthesis = HYPERTROPHY
- Satellite cell-mediated myonuclear accretion is **required** for overload-induced hypertrophy.
- **DOMS** is likely needed to induce myonuclear accretion.

TENSION (ADAPTIVE CHALLENGE)

MECHANOTRANSDUCTION

There is a “continuous physical link between the **extracellular matrix, cytoskeleton, sarcomere, and nuclear matrix** as a means to rapidly regulate gene expression following a mechanical stimulus.”

There are several Mechanotransducing Pathways:

- **GPCR** (G-Coupled Protein Receptors)
- **DAG** (Dystrophin-Associated Glycoprotein Complexes)
- **α7β1** (Alpha7β1 Integrin)
- **SAC** (Stretch Activated Channels)
- **MAPK** (Mitogen Activated Protein Kinases)

Mechanical Stimulus → mTORC1 → Protein Synthesis

ECCENTRIC MUSCLE ACTIONS

- DEFINITION: Muscle force is less than the resistance resulting in the **muscle lengthening**.
- Fewer muscle fibers recruited
 - Recruits **more FT** fibers
 - Recruits **less ST** fibers
 - ↑ **mechanical force** by the **working fibers (FT)**.
- Recruitment of rapidly contracting fibers having a short relaxation time is most appropriate for better control of fast movements.
- **Eccentric Actions** Result in:
 - **Increased protein synthesis**
 - Increased mTORC1 signaling
 - Increased satellite cell activation
 - Increased muscle membrane integrity
 - Increased **DOMS**

DOMS (DELAYED ONSET MUSCLE SORENESS)

- Unaccustomed exercise, predominantly **eccentric muscle actions**, results in mechanical muscle damage
- Factors leading to skeletal muscle damage:
 - Longer **duration** (number or repetitions)
 - Higher **intensity** (greater percentage of maximal **eccentric loading**)
 - Higher exercise intensity seems to have more influence than duration of exercise.
- Disrupted Calcium Homeostasis
 - Calcium activated proteases; Lysosomal proteases
 - ROS production
 - Cytokine release

- Neutrophil and Macrophage activation → inflammation
- Cytokines from immune cells play a key role in **satellite cell activation**/recruitment
- Lactic Acid is **NOT** a significant contributor to DOMS

FASTING AND SATELLITE CELLS

- Fasting causes muscle SCs to enter a **deep quiescent state**.
- Deep Quiescent State (DQS)
 - Smaller cell size
 - Less mitochondrial content
 - Less oxygen consumption
 - Less RNA content
- Delayed ROI (return on investment)
 - Lasts for 72 hours after feeding (delayed muscle regeneration)
 - **Enhanced resilience** to nutrient, cytotoxic, and proliferative stress
- Deep Quiescent State Results from:
 - Fasting;
 - Ketogenic Diet or;
 - **Feeding BHB** (Beta Hydroxybutyrate)

NUTRITION

PROTEIN

Window of Opportunity: 48 hours after exercise = ↑ sensitivity to leucine

AMOUNT

The amount is the ideal to maximize protein synthesis for hypertrophy, not an amount to prevent disease.

Adults

- Young: 0.24 g/kg body mass
- Old: 0.40 g/kg of body mass
- **Young: 0.25 g/kg lean body mass**
- **Old: 0.60 g/kg of lean body mass**

220lbs = 100kg 100kg (.75 lean) = 75kg lean body mass 0.25(75) = 20 grams of protein (per meal) 0.6(75) = 42 grams of protein (per meal)

QUALITY

Certain Amino Acids are critical for stimulating mTORC1:

- **Leucine**
- Methionine
- Arginine
- Glutamate/Glutamine

Maximal mTORC1 Activation (meal)

- | |
|--|
| <ul style="list-style-type: none">• >2.2g leucine younger adults• >2.5g leucine for older individuals |
|--|

Upper Limit for leucine is over 500 mg/kg/d (38 g/d for a 75 kg person)

AVAILABILITY

PDCAAS – protein digestibility-corrected amino acid score

DIAAS – digestible indispensable amino acid score

EAA-9 – essential amino acid 9 score

ANTINUTRIENTS

- Natural or synthetic compounds that interfere with the absorption of nutrients.
 - Drugs, Chemicals, Dietary Fiber, Proteins, Overconsumption of nutrients

EXCESSIVE PROTEIN

Consumption of 2g/kg (bodyweight)/day is safe for healthy adults.

Tolerable upper limit of 3.5 g/kg(bodyweight)/day for well-adapted persons.

UNBALANCED DISTRIBUTION

Most adults >60% of daily protein consumed during a single evening meal and ≤ 15 g at breakfast.

Overnight fast = Breakfast starts with negative net protein balance.

ADDITIONAL ONLINE CONTINUING EDUCATION

- **INTERMITTENT FASTING**
- **GUT MICROBIOTA**
- **GLUTEN AND CELIAC DISEASE**

<https://palmerce.learningexpressce.com/index.cfm?eventTypeID=0&categoryIDs=&q=weinert>

REFERENCES

- Daniel R. Moore, Tyler A. Churchward-Venne, Oliver Witard, Leigh Breen, Nicholas A. Burd, Kevin D. Tipton, Stuart M. Phillips, Protein Ingestion to Stimulate Myofibrillar Protein Synthesis Requires Greater Relative Protein Intakes in Healthy Older Versus Younger Men, *The Journals of Gerontology: Series A*, Volume 70, Issue 1, January 2015, Pages 57–62, <https://doi.org/10.1093/gerona/glu103>
- Murach, K. A., Fry, C. S., Dupont-Versteegden, E. E., McCarthy, J. J., & Peterson, C. A. (2021). Fusion and beyond: satellite cell contributions to loading-induced skeletal muscle adaptation. *The FASEB Journal*, 35(10).
- Benjamin, D. I., Both, P., Benjamin, J. S., Nutter, C. W., Tan, J. H., Kang, J., ... & Rando, T. A. (2022). Fasting induces a highly resilient deep quiescent state in muscle stem cells via ketone body signaling. *Cell Metabolism*, 34(6), 902-918.
- Park, SY., Kim, JS. A short guide to histone deacetylases including recent progress on class II enzymes. *Exp Mol Med* 52, 204–212 (2020). <https://doi.org/10.1038/s12276-020-0382-4>
- Lim C, Nunes EA, Currier BS, McLeod JC, Thomas ACQ, Phillips SM. An Evidence-Based Narrative Review of Mechanisms of Resistance Exercise-Induced Human Skeletal Muscle Hypertrophy. *Med Sci Sports Exerc.* 2022 Sep 1;54(9):1546-1559. doi: 10.1249/MSS.0000000000002929. Epub 2022 Apr 6. PMID: 35389932; PMCID: PMC9390238.
- Sergeeva, K., & Tambovtseva, R. (2019, November). Differences in activation patterns between eccentric and concentric muscle contractions. In 4th International Conference on Innovations in Sports, Tourism and Instructional Science (ICISTIS 2019) (pp. 240-244). Atlantis Press.
- Coletti C, Acosta GF, Kessler S, Coletti D. Exercise-mediated reinnervation of skeletal muscle in elderly people: An update. *Eur J Transl Myol.* 2022 Feb 28;32(1):10416. doi: 10.4081/ejtm.2022.10416. PMID: 35234025; PMCID: PMC8992679.
- Larsson, L., Degens, H., Li, M., Salviati, L., Lee, Y. I., Thompson, W., ... & Sandri, M. (2019). Sarcopenia: aging-related loss of muscle mass and function. *Physiological reviews*, 99(1), 427-511.
- Olsen, L. A., Nicoll, J. X., & Fry, A. C. (2019). The skeletal muscle fiber: a mechanically sensitive cell. *European journal of applied physiology*, 119, 333-349.
- Barclay, R. D., Burd, N. A., Tyler, C., Tillin, N. A., & Mackenzie, R. W. (2019). The role of the IGF-1 signaling cascade in muscle protein synthesis and anabolic resistance in aging skeletal muscle. *Frontiers in nutrition*, 6, 146.
- Forester, S. M., Jennings-Dobbs, E. M., Sathar, S. A., & Layman, D. K. (2023). Perspective: Developing a Nutrient-Based Framework for Protein Quality. *The Journal of Nutrition*.
- Paul, G. L., Gautsch, T. A., & Layman, D. K. (2022). Amino acid and protein metabolism during exercise and recovery. In *Nutrition in Exercise and Sport, Third Edition* (pp. 125-158). CRC Press.
- Larsen, M. S., Witard, O. C., Holm, L., Scaife, P., Hansen, R., Smith, K., ... & Hansen, M. (2023). Dose-response of myofibrillar protein synthesis to ingested whey protein during energy restriction in overweight postmenopausal women: a randomized, controlled trial. *The Journal of Nutrition*.

Day, L., Cakebread, J. A., & Loveday, S. M. (2022). Food proteins from animals and plants: Differences in the nutritional and functional properties. *Trends in Food Science & Technology*, 119, 428-442.

Amino Acid Profiles from
food sources (tables)