An Integrative Review of Genetic and Non-Genetic Factors Influencing Human Skeletal Muscle Hypertrophy

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Abstract

Muscle growth is a complex biological process that is limited by both environmental and genetic factors. This review paper explores the integration of genetic and non-genetic factors and how they impact muscle growth and variation among individuals. Both of these influences have the potential to significantly guide muscle growth, causing a widespread contrast in muscle mass within individuals.

Key genes, which are the Androgen Receptor gene, Myostatin gene, IGF-1 gene, and the ACTN3 gene, cause the largest impacts on muscle hypertrophy, leading to a widespread variation in muscle mass within humans. Other genes, including KDM5B, OBSCN, GIGYF1, TTN, RB1CC1, and EIF3J, have been found to increase strength. Crucial non-genetic factors have also been identified to significantly impact muscle hypertrophy and largely contribute to the overall variation in muscle mass among humans. These factors are sleep, hormones, physical training, nutrition, and age. This knowledge allows personalized fitness and nutrition practice to maximize muscle growth potential and find applications in varied fields from sports science to interventions in medicine.

Introduction

Muscle mass differences between people is a human characteristic with different environmental and genetic causes. New evidence indicates that specific genes control the kind of muscle fiber produced, the rate of protein synthesis, and the endocrine response to exercise stimulus. Genetic variants that impact fast-twitch muscle fibers, such as ACTN3, as well as IGF-1, which affects muscle growth and repair, will impact how well you respond to strength training (Yang, 2003; Yoshida, 2020). Genetic mutations that change androgen receptors, and those that interfere with myostatin and inhibit muscle hypertrophy, impact muscle strength and muscle mass variation (Walsh 2005; Campbell 2009; Sheppard 2011). Through identification and discussion of such genetic factors, we can further our understanding of causal processes underlying variance in individuals' responses to exercise training, together with inherent variation in muscle strength and performance potential among individuals.

Beyond genetic factors, there is a broad range of environmental influences as well. These environmental influences include nutritional factors, like the consumption of protein and micronutrients, or training and exercise, such as lifting weights. These non-genetic factors are a keystone for muscle growth and muscle mass variation in a population.

Although a great deal of research has been done on the effects on human muscle, further investigation is needed in this complex area. Muscle growth involves a complicated interplay between environment and genetics, so it needs to be researched.,

This paper will provide a deep insight into the various muscle growth factors we currently know of, as well as why there is so much variation in the muscles of humans. Knowing your genetic predispositions can assist you with your fitness, nutrition, and other goals while allowing you to prepare yourself for what is best for you. Because of the understanding it provides of our body, this information can also be helpful in various fields of medicine, such as sports medicine.

In terms of methodology, this review paper will take an integrative approach toward discussing what influences muscle development while causing a variation in muscle mass.

Muscle development

Muscle development, or myogenesis, starts during embryonic development and continues throughout life. This process involves the formation of muscle fibers from precursor cells called myoblasts (Chal, 2017). Muscle stem cells located between the basal lamina and sarcolemma of muscle fibers are called satellite cells. These cells are important for muscle growth, repair, regeneration, and other muscular processes (Chal, 2017). The muscle tissue can adapt to stress and recover from injury thanks to these satellite cells. This indicates the importance of satellite cells in maintaining the structure of muscles. Several transcription factors, including MyoD, Myf5, myogenin, and MRF4, all known as myogenic regulatory factors (MRFs), can control muscle development (Chal, 2017).

The process of myogenesis is composed of several stages. It begins with the determination of muscle progenitor cells which is followed by the myoblast proliferation. Subsequently, they undergo differentiation into myocytes, and ultimately myocytes fuse to form multinucleated myofibers (Chal, 2017).This process ensures the proper formation of functional muscle tissue. Genetic and environmental factors like hormones and mechanical stimuli can affect and influence muscle development (Chal, 2017). Thus, muscles can develop in ways apart from the natural development of muscles. The population as a whole regularly varies in muscle mass because of the different environments they live in and their differing genetics. Skeletal muscle fibers are formed during the first year of life via muscular hyperplasia. Later in life, muscle growth is primarily driven by muscular hypertrophy of the existing fibers, which is caused by various hormonal factors and mechanical stress (Reggiani, 2020). This transition from hyperplasia to hypertrophy demonstrates the changing mechanisms of muscle growth throughout the lifespan. When using a chick embryo model, muscle fiber development is nearly complete at the time of hatch, with embryonic growth characterized by an increase in myoblast cell number through hyperplasia, while posthatch growth occurs through hypertrophy (Velleman, 2007).

Genetic factors that impact muscle growth.

One of the most powerful predictors of how far any person can progress in muscular size or strength is genetics. Genetic ability controls everything from early muscle-cell formation to the overall ability of the body to build bigger muscles. Often missing for athletes and coaches alike, these invisible influences are what can let training plans become fine-tuned to the human biological reality and the genetic factors that impose subtle limits.

Androgen Receptor (AR) Gene.

The androgen receptor gene, a gene with a CAG-repeat region of variable length, has a powerful effect on muscle development genes. Receptor activity can increase due to fewer or

shorter repeats. This increase in sensitivity enables androgens to push muscle cells to increase in size and strength (Walsh, 2005; Campbell, 2009). Because the AR protein also partners with diverse myogenic transcription factors and kinase-driven signaling cascades, even minor genetic changes can affect the processes regulating myoblast proliferation and differentiation as well as the muscular phenotype (Braun, 2011; Mohammadabadi, 2021).

Myostatin (MSTN) Gene.

On the contrary, myostatin is a molecular brake. In both animals and humans, rare mutations or lowered expressions of MSTN cause a dismantle of that brake, which results in a tremendous gain in muscle. When myostatin's suppression of the Smad pathway is removed, myoblasts divide and fuse more frequently. Furthermore, resistance exercise produces outsized increases in muscle size, and total skeletal muscle mass rises well above normal (Dennis, 2008; Verbrugge, 2018; Colorado, 2023).

Insulin-like Growth Factor 1 (IGF-1) Gene.

While MSTN restrains growth, IGF-1 propels it. Variants that increase the levels of IGF-1 accelerate protein synthesis through the Akt-mTOR pathway and promote tissue regeneration in the aftermath of high load (Yoshida 2020; Verbrugge 2018; Liu 2020). Cascading growth hormones in the circulation and genes such as GHR2 and IGFR1 functionally associated with the IGF-1 signalling that adapts to a nutrient surplus or resistance work and orchestrates compensatory hypertrophy (Verbrugge, 2018; Liu, 2020).

Alpha-actinin-3 (ACTN3) Gene.

The ACTN3 gene is the cornerstone for explosiveness. The gene encodes the alpha-actinin-3 protein, which is found in fast-twitch fibres. The famous R577X polymorphism shows how simple a single substitution can occur to modify athletic potential. The functional R allele encourages high-powered output, while the homozygous XX state removes the protein altogether and pushes fibres towards endurance properties (Yang, 2003; Mohammadabadi, 2021).

Other genes.

Genes such as KDM5B, OBSCN, GIGYF1, TTN, RB1CC1, and EIF3J have been identified to contribute to hand grip strength, a key measure of overall muscular strength (Huang, 2023). Some other genes like PGC-1α, STARS, JunB, and TRPC1 are involved in muscle metabolism and myogenesis and muscle hypertrophy occurring through transcriptional and signalling mechanisms controlling muscle growth (Braun, 2011; Fu, 2021).

Non-genetic Factors That Impact Muscle Growth

Muscle hypertrophy does not depend on DNA alone; there are also several environmental factors that play a role. Because these variables can steer both performance and

long-term health, anyone hoping to maintain or build an athletic frame must understand these key factors.

Sleep

Across most training programs, the recovery window offered by sleep is still the piece most overlooked, even though deep rest is when growth hormones surge and muscle is built (Morrison, 2022). Remove that nightly repair and the body wakes inside a subtly damaged state, struggling to compensate for incomplete recovery. This can also lead to slower or even stalled hypertrophy. One disturbed or shortened night of sleep is enough to cause an 18 % drop in muscle protein synthesis, illustrating just how sensitive skeletal tissue can be to lost hours of sleep (Lamon, 2020).

When poor sleep becomes a habit, the hormones suffer. Sleep deprivation spikes cortisol which pushes testosterone and IGF-1 down. The resulting atmosphere is proteolytic which means it breaks down existing fibers and prevents new ones from developing (Dáttilo, 2011). On the other hand, extending sleep could sharpen performance, dull pain, and enhance the anabolic impact of GH and IGF-I, all substances connected to recovery from exercise-related injury (Chennaoui, 2021). Therefore, restoring adequate, high quality sleep protects from the accumulated damage of hard training while also allowing injured fibers to recover faster (Yang, 2019).

Hormonal Factors

Hormones are a critical factor when regarding muscle hypertrophy. Growth-promoting agents, pituitary growth hormone, thyroid hormones, and insulin, encourage expansion, while glucocorticoids such as cortisol apply the brakes and favor catabolism (Florini, 1987; Kraemer, 2020). Insulin-like growth factors and fibroblast growth factors add further nuance, acting as core anabolic drivers in cultured myoblasts and pushing them toward differentiation and enlargement (Florini, 1987).On the other hand, transforming growth factor-beta and interferon can block differentiation outright, highlighting the multifaceted nature of the role of hormones in muscle cell growth (Florini, 1987). Testosterone, growth hormone, and IGF-1 orchestrate hypertrophy through both genomic and non-genomic routes (Kraemer, 2020). Yet their effectiveness can vary according to IGF-1 binding proteins that fine-tune the peptide's reach and potency. Strategic manipulation of these pathways, whether through natural training methods or, controversially, supraphysiologic courses of anabolic-androgenic steroids, exogenous growth hormone, and IGF-1, can accelerate mass gains. However, such interventions carry well-documented risks (Fink, 2018).

Exercise and Training

Mechanical tension remains the most widely known way to make muscle grow. The tension produced during such movements stimulates local IGF-1 release, which launches protein synthesis and sparks satellite cells into action, two processes essential for muscle

growth (Harridge, 2003). At the microscopic level, hypertrophy arises either by adding new nuclei from stem cells or by expanding the cytoplasm surrounding each nucleus, both of which are triggered most reliably by high-force contractions (Attwaters, 2021). Still, load is not the only driver: metabolic stress also matters. Low-load resistance sets pushed to failure can yield size increases comparable to heavier protocols (Ozaki, 2016), and pairing modest weights with blood-flow restriction produces similar hypertrophic results, thanks largely to elevated metabolic strain (Pearson, 2015).

Growth unfolds through three structural avenues: the increase in muscle cell numbers, fiber diameter, and fiber length, yet adults can exploit only the latter two, since increases in cell number are confined to prenatal and early postnatal life (Pearson, 1990). Both anaerobic and aerobic exercise appear capable of activating the IGF-1 pathway, a phenomenon that becomes especially helpful for preserving function during aging (Li, 2022). Even so, when the goal is maximal size or strength, resistance exercise remains the most effective, outpacing endurance work in its ability to enlarge skeletal muscle (Li, 2022).

Training programs that focus on single-muscle-group training elicit larger hypertrophic responses compared with multi-muscle-group training (Khlaifawi, 2024). While repetition times of 0.5 to 8 seconds have been found beneficial for muscle growth, long repetition times with significant delays (longer than 10 seconds) have been shown to be less effective (Schoenfeld, 2015).

Nutritional Factors

Nutrition plays a significant role in muscle growth and development, affecting a broad range of processes accountable for muscle growth. The anabolic drive is significantly affected by insulin, playing a central role in the perception of indispensable amino acid consumption and the stimulation of muscle protein synthesis, both required for muscle growth (Millward, 1989). Evidence also suggests that the combination of resistance training and proper nutrition is a powerful stimulus for muscle protein synthesis and the overall development of the muscle. The combination of both of these factors has been shown to lead to greater muscle anabolism compared to either resistance training or nutrition alone (Rasmussen, 2003). Nutrition also impacts skeletal muscle growth because of its impact on satellite cells, which contribute greatly to postnatal muscle development. In addition, nutrition has a significant effect on the activity and production of growth hormones such as fibroblast growth factor and IGF-2, both of which play key roles in repairing and increasing muscle (Thornton, 2019).

Recent studies have found that certain forms of supplementation, such as amino acids, creatine, and β-hydroxy-β-methylbutyrate, have shown substantial gains in muscle mass in older adults (Martin-Cantero, 2020). Yet, supplements such as protein alone were discovered to have no contribution to any noticeable increase in muscle mass. This shows the emphasis on utilizing diverse sources of nutrients to optimize muscle development (Martin-Cantero, 2020). A study on the diets of a specific type of fish species, Megalobrama amblycephalae, also known as Wuchang Bream, shows that high-energy diets rich in lipids and carbohydrates support the

hyperplasia of muscles. High-energy dietary factors may thus play extremely crucial roles in muscle growth (Huang, 2021). Moreover, the examination shows that a diet rich in lipids increases the fiber diameter of muscles and the cross-sectional area of muscles when contrasted with diets rich in carbohydrates (Huang, 2021).

The combination of a diet rich in protein and vitamin D with exercise has proven to stimulate skeletal muscle growth effectively in elderly people (Voulgaridou, 2023). It was further found that essential amino acids like leucine, arginine, cysteine, and glutamine play an essential role in optimizing the production of muscles and combating the loss of muscle across different population groups (Voulgaridou, 2023). Nutrition studies on Kenyan children have indicated that meat-containing food supplements have significantly contributed to lean body mass, where the children who received the meat supplement had 30-80% greater muscle mass in the mid-upper arm than other diets (Grillenberger, 2003).

Other experiments have noted that high-fat diets in mice tend to cause a reduced response of muscle growth with no apparent muscle atrophy (De Sousa, 2020). The evidence shows that certain reactions towards certain nutritional components differ and change with time. Omega-3 fatty acids have also proven significant in maintaining the health of muscles and building greater muscle mass due to their contribution towards cellular signaling pathways, with the inhibition of inflammation-induced oxidative stress (Alfonso, 2019).

Age-Related

Age is a significant factor in muscle hypertrophy. Muscle strength reduces with age, but this can be corrected or delayed with dedication and careful planning (Moore, 2009). It is notably an issue in cases of sarcopenia, a condition that is related to old age and involves diminishing muscle strength and muscle mass. Muscles affected by sarcopenia have also been documented with a shortage of contractile protein and poor force-producing ability (Haddad, 2006). Furthermore, the process of aging suppresses the process of hypertrophy and disrupts muscle regeneration. The muscles of the elderly also contain a higher ratio of RNA-to-protein, indicating decreased efficiency in translating genetic codes for new protein synthesis (Haddad, 2006). Aging affects muscle mass since the body loses 3–8% with each decade of age beyond 30 years, with this process further accelerating past 60 years of age (Volpi, 2005).

Despite the worsened hypertrophic response and the other age-related challenges, it is important to note that aging does not impair training-induced increases in specific tension (Welle, 1996). This means that older individuals are still able to yield significant benefits from training. However, literature supports the fact that high-training intensity is not the most appropriate for this population. For example, a study determined that intensification in training resulted in a reduced increase in myosin heavy chain (MHC) II fiber amount, suggesting that older adults might not be as responsive to high-load training (Straight, 2020).

Conclusion

In summary, human muscle hypertrophy is regulated by non-genetic and genetic factors that influence muscle growth, strength, and physical function. Muscle hypertrophy can be influenced by both non-genetic and genetic factors such as androgen receptor (AR) gene, myostatin (MSTN) gene, insulin-like growth factor 1 (IGF-1) gene, ACTN3 gene, sleep, hormone levels, exercise and diet. Quality sleep promotes muscle repair and protein synthesis. Disturbed or low-quality sleep prevents growth by disrupting hormone levels. It also prevents skeletal muscle from synthesizing protein. The two important ways to initiate muscle hypertrophy are training, exercise and hormonal status for protein synthesis and the satellite cell activation. The elderly adults require specific nutritional components of a diet i.e. protein, essential amino acids, vitamin D, etc. for the growth of skeletal muscle. As we get older, our body experiences a lot of changes that cannot be reversed. Aging causes age-associated atrophy and other disorders like sarcopenia. Thus, it is important to learn and reverse the impact of ageing on muscle hypertrophy. There must be a thorough understanding of, and appropriate regulation of these factors for the maximization of muscle growth and to grasp the science of sport, medicine and fitness. This information could also find practical applications in physiotherapy for the physically disabled, but also for several other conditions such as age-related muscle atrophy, and genetic defects affecting muscles.

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References

1. Attwaters, M., & Hughes, S. (2022). Cellular and molecular pathways controlling muscle size in response to exercise. *The FEBS Journal, 289*(5), 15820. https://doi.org/10.1111/febs.15820

2. Baig, M. H., Ahmad, K., Moon, J. S., Park, S. Y., Ho Lim, J., Chun, H. J., Qadri, A. F., Hwang, Y. C., Jan, A. T., Ahmad, S. S., Ali, S., Shaikh, S., Lee, E. J., & Choi, I. (2022). Myostatin and its regulation: A comprehensive review of myostatin inhibiting strategies. *Frontiers in Physiology, 13*, 876078. https://doi.org/10.3389/fphys.2022.876078

3. Braun, T., & Gautel, M. (2011). Transcriptional mechanisms regulating skeletal muscle differentiation, growth, and homeostasis. *Nature Reviews Molecular Cell Biology, 12*(6), 349–361. https://doi.org/10.1038/nrm3118

4. Burgerhout, E., Mommens, M., Johnsen, H., Aunsmo, A., Santi, N., & Andersen, Ø. (2017). Genetic background and embryonic temperature affect DNA methylation and expression of myogenin and muscle development in Atlantic salmon (Salmo salar). *PLoS ONE, 12*(6), e0179918. https://doi.org/10.1371/journal.pone.0179918

5. Campbell, B. C., Gray, P. B., Eisenberg, D. T. A., Ellison, P., & Sorenson, M. D. (2009). Androgen receptor CAG repeats and body composition among Ariaal men. *International Journal of Andrology, 32*(2), 140–148. https://doi.org/10.1111/j.1365-2605.2007.00825.x

6. Chennaoui, M., Vanneau, T., Trignol, A., Arnal, P., Gomez-Mérino, D., Baudot, C., Perez, J., Pochettino, S., Eirale, C., & Chalabi, H. (2021). How does sleep help recovery from exercise-induced muscle injuries? *Journal of Science and Medicine in Sport*. Advance online publication. https://doi.org/10.1016/j.jsams.2021.05.007

7. Colorado, M., Jaramillo, R., & Arango, L. (2023). Influence of genetics and epigenetics on the process of muscle hypertrophy: A systematic review. *Movement & Sport Sciences - Science & Motricité*. Advance online publication. https://doi.org/10.1051/sm/2023007

8. Cruz-Jentoft, A. J., Dawson Hughes, B., Scott, D., Sanders, K. M., & Rizzoli, R. (2020). Nutritional strategies for maintaining muscle mass and strength from middle age to later life: A narrative review. *Maturitas, 132*, 57–64. https://doi.org/10.1016/j.maturitas.2019.11.007

9. Dáttilo, M., Antunes, H., Medeiros, A., Neto, M., Souza, H., Tufik, S., & Mello, M. (2011). Sleep and muscle recovery: Endocrinological and molecular basis for a new and promising hypothesis. *Medical Hypotheses, 77*(2), 220–222. https://doi.org/10.1016/j.mehy.2011.04.017

10. Dáttilo, M., Antunes, H., Nunes-Galbes, N., Mônico-Neto, M., Souza, H., Quaresma, M., Lee, K., Ugrinowitsch, C., Tufik, S., & De Mello, M. (2019). Effects of sleep deprivation on the acute skeletal muscle recovery after exercise. *Medicine & Science in Sports &*

Exercise. Advance online publication. https://doi.org/10.1249/MSS.0000000000002137

11. De Sousa, L., Marshall, A., Norman, J., Fuqua, J., Lira, V., Rutledge, J., & Bodine, S. (2020). The effects of diet composition and chronic obesity on muscle growth and function. *Journal of Applied Physiology*. Advance online publication. https://doi.org/10.1152/japplphysiol.00156.2020

12. Dennis, R., Przybyla, B., Gurley, C., Kortebein, P., Simpson, P., Sullivan, D., & Peterson, C. (2008). Aging alters gene expression of growth and remodeling factors in human skeletal muscle both at rest and in response to acute resistance exercise. *Physiological Genomics, 32*(3), 393–400. https://doi.org/10.1152/physiolgenomics.00191.2007

13. Fink, J., Schoenfeld, B., & Nakazato, K. (2018). The role of hormones in muscle hypertrophy. *The Physician and Sportsmedicine, 46*(2), 129–134. https://doi.org/10.1080/00913847.2018.1406778

14. Florini, J. (1987). Hormonal control of muscle growth. *Muscle & Nerve, 10*(7), 577–598. https://doi.org/10.1002/mus.880100702

15. Frost, R., & Lang, C. (2007). Protein kinase B/Akt: A nexus of growth factor and cytokine signaling in determining muscle mass. *Journal of Applied Physiology, 103*(1), 378–387. https://doi.org/10.1152/japplphysiol.00089.2007

16. Fu, Y., Shang, P., Zhang, B., Tian, X., Nie, R., Zhang, R., & Zhang, H. (2021). Function of the porcine TRPC1 gene in myogenesis and muscle growth. *Cells, 10*(1), 147. https://doi.org/10.3390/cells10010147

17. Fushimi, S., Nohno, T., & Katsuyama, H. (2023). Chronic Stress Induces Type 2b Skeletal Muscle Atrophy via the Inhibition of mTORC1 Signaling in Mice. Medical Sciences, 11(1), 19. https://doi.org/10.3390/medsci11010019.

18. Grillenberger, M., Neumann, C., Murphy, S., Bwibo, N., Veer, V., Hautvast, J., & West, C. (2003). Food supplements have a positive impact on weight gain and the addition of animal source foods increases lean body mass of Kenyan schoolchildren. *The Journal of Nutrition, 133*(11 Suppl 2), 3957S–3964S. https://doi.org/10.1093/jn/133.11.3957S

19. Haddad, F., & Adams, G. (2006). Aging-sensitive cellular and molecular mechanisms associated with skeletal muscle hypertrophy. *Journal of Applied Physiology, 100*(4), 1188–1203. https://doi.org/10.1152/japplphysiol.01227.2005

20. Harridge, S. (2003). Ageing and local growth factors in muscle. *Scandinavian Journal of Medicine & Science in Sports, 13*(1), 1–5. https://doi.org/10.1034/j.1600-0838.2003.20235.x

21. Huang, Y., Jiang, G., Abasubong, K., Wang, C., Zhang, L., Dai, Y., Zheng, X., Cao, X., He, C., Wang, X., Xiao, K., Li, X., Wu, Y., & Liu, W. (2021). High lipid and high carbohydrate diets affect muscle growth of blunt snout bream (Megalobrama amblycephala) through different signaling pathways. *Aquaculture, 539*, 737495. https://doi.org/10.1016/j.aquaculture.2021.737495

22. Huang, Y., Bodnar, D., Chen, C. Y., Sanchez-Andrade, G., Sanderson, M., Biogen Biobank Team, Shi, J., Meilleur, K. G., Hurles, M. E., Gerety, S. S., Tsai, E. A., & Runz, H. (2023). Rare genetic variants impact muscle strength. *Nature Communications, 14*(1), 3449. https://doi.org/10.1038/s41467-023-39247-1

23. Chal, J., & Pourquié, O. (2017). Making muscle: Skeletal myogenesis in vivo and in vitro. *Development, 144*(12), 2104–2122. https://doi.org/10.1242/dev.151035

24. Khlaifawi, M., Kadhim, H., Alsaedi, H., Alfadhli, B., & Alali, A. (2024). Comparative analysis of single vs. two-muscle training programs on upper body muscle growth. *Retos*. https://doi.org/10.47197/retos.v62.110738

25. Kraemer, W., Ratamess, N., Hymer, W., Nindl, B., & Fragala, M. (2020). Growth hormone(s), testosterone, insulin-like growth factors, and cortisol: Roles and integration for cellular development and growth with exercise. *Frontiers in Endocrinology, 11*, 33. https://doi.org/10.3389/fendo.2020.00033

26. Krzysztofik, M., Wilk, M., Wojdała, G., & Gołaś, A. (2019). Maximizing muscle hypertrophy: A systematic review of advanced resistance training techniques and methods. *International Journal of Environmental Research and Public Health, 16*(24), 4897. https://doi.org/10.3390/ijerph16244897

27. Lamon, S., Morabito, A., Arentson-Lantz, E., Knowles, O., Vincent, G., Condo, D., Alexander, S., Garnham, A., Paddon-Jones, D., & Aisbett, B. (2021). The effect of acute sleep deprivation on skeletal muscle protein synthesis and the hormonal environment. *Physiological Reports, 9*(2), e14660. https://doi.org/10.14814/phy2.14660

28. Li, B., Feng, L., Wu, X., Cai, M., Yu, J., & Tian, Z. (2022). Effects of different modes of exercise on skeletal muscle mass and function and IGF-1 signaling during early aging in mice. *The Journal of Experimental Biology*. https://doi.org/10.1242/jeb.244650

29. Liu, X., Zeng, S., Liu, S., Wang, G., Lai, H., Zhao, X., Bi, S., Guo, D., Chen, X., Yi, H., Su, Y., Zhang, Y., & Li, G. (2020). Identifying the related genes of muscle growth and exploring the functions by compensatory growth in mandarin fish (Siniperca chuatsi). *Frontiers in Physiology, 11*, 553563. https://doi.org/10.3389/fphys.2020.553563

30. Martin-Cantero, A., Reijnierse, E., Gill, B., & Maier, A. (2021). Factors influencing the efficacy of nutritional interventions on muscle mass in older adults: A systematic review and meta-analysis. *Nutrition Reviews, 79*(3), 315–330. https://doi.org/10.1093/nutrit/nuaa064

31. Millward, D. (1989). The nutritional regulation of muscle growth and protein turnover. *Aquaculture, 79*(1-4), 1–28. https://doi.org/10.1016/0044-8486(89)90441-9

32. Mohammadabadi, M., Bordbar, F., Jensen, J., Du, M., & Guo, W. (2021). Key genes regulating skeletal muscle development and growth in farm animals. *Animals, 11*(3), 835. https://doi.org/10.3390/ani11030835

33. Moore, D. R., & Burd, N. A. (2009). Exercise intensity matters for both young and old muscles. *The Journal of Physiology, 587*(3), 511–512. https://doi.org/10.1113/jphysiol.2008.166744

34. Morrison, M., Halson, S. L., Weakley, J., & Hawley, J. A. (2022). Sleep, circadian biology and skeletal muscle interactions: Implications for metabolic health. Sleep Medicine Reviews, 66, 101700. https://doi.org/10.1016/j.smrv.2022.101700

35. Ozaki, H., Loenneke, J., Buckner, S., & Abe, T. (2016). Muscle growth across a variety of exercise modalities and intensities: Contributions of mechanical and metabolic stimuli. *Medical Hypotheses, 88*, 22–26. https://doi.org/10.1016/j.mehy.2015.12.026

36. Pearson, A. (1990). Muscle growth and exercise. *Critical Reviews in Food Science and Nutrition, 29*(3), 167–196. https://doi.org/10.1080/10408399009527522

37. Pearson, S., & Hussain, S. (2015). A review on the mechanisms of blood-flow restriction resistance training-induced muscle hypertrophy. *Sports Medicine, 45*(2), 187–200. https://doi.org/10.1007/s40279-014-0264-9

38. Rasmussen, B., & Phillips, S. (2003). Contractile and nutritional regulation of human muscle growth. *Exercise and Sport Sciences Reviews, 31*(3), 127–131. https://doi.org/10.1097/00003677-200307000-00005

39. Reggiani, C., & Schiaffino, S. (2020). Muscle hypertrophy and muscle strength: Dependent or independent variables? A provocative review. *European Journal of Translational Myology, 30*(3), 9311. https://doi.org/10.4081/ejtm.2020.9311

40. Schoenfeld, B., Ogborn, D., & Krieger, J. (2015). Effect of Repetition Duration During Resistance Training on Muscle Hypertrophy: A Systematic Review and Meta-Analysis. Sports Medicine, 45, 577-585. https://doi.org/10.1007/s40279-015-0304-0.

41. Schoenfeld, B. J., & Grgic, J. (2020). Effects of range of motion on muscle development during resistance training interventions: A systematic review. *SAGE Open Medicine, 8*, 2050312120901559. https://doi.org/10.1177/2050312120901559

42. Sheppard, R. L., Spangenburg, E. E., Chin, E. R., & Roth, S. M. (2011). Androgen receptor polyglutamine repeat length affects receptor activity and C2C12 cell development. *Physiological Genomics, 43*(21), 1135–1143.

https://doi.org/10.1152/physiolgenomics.00049.2011

43. Straight, C., Fedewa, M., Toth, M., & Miller, M. (2020). Improvements in skeletal muscle fiber size with resistance training are age-dependent in older adults: A systematic review and meta-analysis. *Journal of Applied Physiology*. https://doi.org/10.1152/japplphysiol.00170.2020

44. Thornton, K. (2019). Triennial growth symposium: The nutrition of muscle growth: Impacts of nutrition on the proliferation and differentiation of satellite cells in livestock species. *Journal of Animal Science, 97*(5), 2258–2269. https://doi.org/10.1093/jas/skz081

45. Verbrugge, S., Schönfelder, M., Becker, L., Nezhad, F., De Angelis, H., & Wackerhage, H. (2018). Genes whose gain or loss-of-function increases skeletal muscle mass in mice: A systematic literature review. *Frontiers in Physiology, 9*, 553. https://doi.org/10.3389/fphys.2018.00553

46. Velleman, S. (2007). Muscle development in the embryo and hatchling. *Poultry Science, 86*(5), 1050–1054. https://doi.org/10.1093/ps/86.5.1050

47. Volpi, E., Nazemi, R., & Fujita, S. (2004). Muscle tissue changes with aging. *Current Opinion in Clinical Nutrition and Metabolic Care, 7*(4), 405–410. https://doi.org/10.1097/01.mco.0000134362.76653.b2

48. Voulgaridou, G., Papadopoulou, S., Spanoudaki, M., Kondyli, F., Alexandropoulou, I., Michailidou, S., Zarogoulidis, P., Matthaios, D., Giannakidis, D., Romanidou, M., & Papadopoulou, S. (2023). Increasing muscle mass in elders through diet and exercise: A literature review of recent RCTs. *Foods, 12*(6), 1218. https://doi.org/10.3390/foods12061218

49. Walsh, S., Zmuda, J. M., Cauley, J. A., Shea, P. R., Metter, E. J., Hurley, B. F., et al. (2005). Androgen receptor CAG repeat polymorphism is associated with fat-free mass in men. *Journal of Applied Physiology, 98*(1), 132–137. https://doi.org/10.1152/japplphysiol.00537.2004

50. Welle, S., Totterman, S., & Thornton, C. (1996). Effect of age on muscle hypertrophy induced by resistance training. *The Journals of Gerontology: Series A, Biological Sciences and Medical Sciences, 51*(6), M270–M275. https://doi.org/10.1093/gerona/51A.6.M270

51. Yang D, Shen Y, Wu C, Huang Y, Lee P, Er N, Huang W, & Tung Y. (2019). Sleep deprivation reduces the recovery of muscle injury induced by high-intensity exercise in a mouse model.. Life sciences, 116835. https://doi.org/10.1016/j.lfs.2019.116835.

52. Yang, N., MacArthur, D. G., Gulbin, J. P., Hahn, A. G., Beggs, A. H., Easteal, S., & North, K. (2003). ACTN3 genotype is associated with human elite athletic performance.

American Journal of Human Genetics, 73(3), 627–631. https://doi.org/10.1086/377590

53. Yoshida, T., & Delafontaine, P. (2020). Mechanisms of IGF-1-mediated regulation of skeletal muscle hypertrophy and atrophy. *Cells, 9*(9), 1970. https://doi.org/10.3390/cells9091970