International Journal of Health, Exercise, and Sport Sciences (IJOSS) ISSN: 3023-8382

REVIEW ARTICLE / Derleme Makalesi

Open Access/Açık Erişim

Titin mechanism on skeletal muscles: Active force

İskelet kaslarında titin mekanizması: Aktif kuvvet

Atilla Şahan[1], Alay Kesler[2], Kaan Salman[3], Hilal Kılınç[4], Aykut Hocalar[5], Yeliz Kahraman[6]

*Correspondence:
PhD. Yeliz KAHRAMAN
yelizkahramana@hotmail.com.

[1]Burdur Mehmet Akif University and Sport Science, Antalya, Turkey, atilla_sahan3543@hotmail.com. Orcid: 0009-0000-7185-2348

[2]Associate., İstanbul Cerrahpaşa University and Sport Science Faculty, İstanbul, Turkey, alayk@hotmail.com. Orcid: 0000-0002-7232-6072

[3]Research associate., Muğla Sıtkı Koçman University and Sport Science Faculty, Muğla, Turkey, kaansalman@mu.edu.tr. Orcid: 0000-0002-2425-2128

[4]Associate profesör., Dokuz Eylül University, Sport Science Faculty, İzmir, Turkey, kilinc.hilal@deu.edu.tr. Orcid: 0000-0001-6348-9753

[5]Ph.d., Akdeniz University, Health Science Institute, Antalya, Turkey, aykuthocalar@gmail.com. Orcid: 0009-0009-5708-4683

[6]PhD. Akdeniz University and Health Science Institute, Antalya, Turkey, yelizkahramana@hotmail.com; orcid: 0000-0001-8209-4087

Abstract

Titin molecules of skeletal muscle actived muscle gene expression produce active force during passive stiffness indirectly in spring properties. To that the titin activation determines on passive sarcomeres role and active force during molecular lengthening in myofibrils. Titin directly of thick (myosin) and thin (actin) filament localization to enable processes of myofibril elasticities promote molecular energy in sarcomeres. These characteristic physiologic results determine muscle force reactivation both as passive and active muscle. The induction of titin binding to Ca2+ reactivation low and high energy accumulation as (%15), titin directly activated to mechanic force with increasing of Ca2+ as (%85). This suggest noted that sarcomere's PEVK region segmental myofibril composition provides isometric force through elongation arranged on entropy low energy whereas enthalpy high energy. In these direction produce force of connectin (titin) owing to a spring role to slow-twitch fiber than fast-twitch fiber during isometric contraction. After activated force recruit passive elements enable to isometric force. Outcomes of titin, molecular spring properties accompany with active force with passive elements, thus this reported that titin structural condition during force producing changes on active force along with passive stiffness.

Keywords: Titin molecule, spring role, active force, passive tension.

Özet

İskelet kasının aktif genindeki titin molekülleri, pasif sertlik sırasında dolaylı olarak yay özelliklerine bağlı aktif kuvvet üretir. Bu nedenle titin aktivasyonu, pasif sarkomerlerin rolünü ve miyofibrillerdeki moleküler uzama sırasında aktif kuvveti belirler. Titin, miyofibril elastikiyet süreçlerini mümkün kılmak için kalın (miyozin) ve ince (aktin) filamentlerin lokalizasyonunu doğrudan etkileyerek sarkomerlerde moleküler enerjiyi artırır. Bu karakteristik fizyolojik sonuçlar, kas kuvvetinin hem pasif hem de aktif kas olarak yeniden aktivasyonunu belirler. Titin bağlanmasının Ca2+ ile indüklenmesi düşük ve yüksek enerji birikimini (%15) yeniden aktive ederken, titin Ca2+ artışıyla (%85) mekanik kuvvete doğrudan aktif olur. Kısacası, sarkomerin PEVK bölgesindeki segmental miyofibril bileşimi, düşük enerjili entropi ve yüksek enerjili entalpiye göre düzenlenmiş uzama yoluyla izometrik kuvvet sağlar. Bu yönde, izo-koşulda hızlı kas liflerinden ziyade yavaş kas liflerinde yay rolü oluşumunda konnektin (titin) kuvveti üretilir. Aktif hale gelen kuvvet, pasif elemanları harekete geçirerek izometrik kuvveti mümkün kılar. Titin molekülünün yay özelliklerinin sonuçları, aktif kuvvet ve pasif unsurlarla birlikte ortaya çıkar; bu nedenle, aktif kuvvet ve pasif sertlik ile birlikte kuvvet üretimi sırasında titin yapısal olarak değişmektedir.

Anahtar Kelimeler: Titin molekülü, yay rolü, aktif kuvvet, pasif gerilim.

https://doi.org/10.5281/zenodo.20993999

Received / Gönderim: 02.05.2026

Accepted / Kabul: 12.06.2026

Published / Yayın: 23.06.2026

Volume 3, Issue 2, June, 2026

Cilt 3, Sayı 2, Haziran, 2026

How to Cite This Article

APA 7:

Şahan, A., Kesler, A., Salman, K., Kılınç, H., Hocalar, A., & Kahraman, Y. (2026). Titin mechanism on skeletal muscles: Active force. International Journal of Health, Exercise, and Sport Sciences (IJOSS), 3(2), 509–517. https://www.ijoss.org/Archive/v3-i2/ijoss-Volume3-issue2-07.pdf

Vancouver:
Şahan A, Kesler A, Salman K, Kılınç H, Hocalar A, Kahraman Y. Titin mechanism on skeletal muscles: Active force. Int J Health Exerc Sport Sci (IJOSS). 2026;3(2):509-517. Available from: https://www.ijoss.org/Archive/v3-i2/ijoss-Volume3-issue2-07.pdf

https://www.ijoss.org/Archive/v3-i2/ijoss-Volume3-issue2-07.pdf

IJOSS

Copyright and Open Access Statement: / Telif Hakkı ve Açık Erişim Beyanı : © The Author(s), 2026. This article is published as an open access article by IJOSS. It is distributed under the terms of the Creative Commons Attribution 4.0 International License, which permits unrestricted use, sharing, adaptation, distribution, and reproduction in any medium or format, provided that appropriate credit is given to the original author(s) and the source, a link to the Creative Commons license is provided, and any changes made to the original work are clearly indicated. Unless otherwise stated in a credit line, all images or third-party materials included in this article are covered by the article's Creative Commons license. If any material is not covered by the Creative Commons license and the intended use is not permitted by statutory regulation or exceeds the permitted use, permission must be obtained directly from the copyright holder. To view a copy of this license, visit: http://creativecommons.org/licenses/by/4.0/.

INTRODUCTION

Titin is physiologic topic, the muscle molecular properties of active force generation preceded as gaint sarcomer protein (Maruyama, 1976). Sarcomere working stage is between thick and thin filaments, additional other filaments are intervening space, these gap filaments contain mega-dalton (mD) sized protein as connectin (Horowits & Podolsky, 1987). Titin has been described as a sarcomeric spring that contributes to passive elasticity and may influence force production through its mechanical properties (Bang et al., 2001). It is known structural characteristic history of titin first described "connectin" closely related giant sarcomere proteins which include in slow-twitch fiber larger than fast-twitch fiber (Goto et al., 2003; Maruyama, 1976). It is noted on muscle isometric condition, non-force as shaping of connectins a morphological adaptation associated the slow-to-fast transformation of muscle fibers in account of local changes of contractile proteins, such as myosin heavy chain (MHC) and troponin in slow-twitch muscle progresively than fast-twicth on passive sarcomere (Goto et al., 2003). Titin has also been proposed to function as a molecular spring capable of storing elastic energy within sarcomeres (Nishikawa, 2020). These elastic properties of titin molecules contribute to passive tension in cardiac muscle as modified roles (Bang et al., 2001). In direction, biological achievements of titin sliding filament brought into useful to light microscopy pretioning of biological tissues to electron microscopy (Hoyle, 1983). The innovations ultimate as from (1950-1952) awarded as functional organization of cell in 1974 Nobel Prize in Physiology and Medicine (http://www.nobelprize.org/nobel_prizes/medicine/laureates/1974/). These techniques are presented first organized description of striated muscle in sarcomeres from Hugh Huxley and Jean Hanson (Hanson & Huxley, 1953). In experimental description called filaments within myofibril as thick and thin filaments. Thick filaments composed of myosin and thin filaments, thus, actin detected on sliding filament theory of muscle contraction by early 1960s (Huxley, 1953). By Huxley & Hanson observed on sliding filament elasticity after removal of the thick and thin filaments developing process named hypotetical filament eventually accepted the existence of giant elastic filaments in skeletal muscles, promoting localizated within sarcomeres using term of protein connectin were same protein priority as largest titin (Hanson & Huxley, 1953).

Therefore, this narrative review aims to synthesize current evidence on the structural and functional roles of titin in skeletal muscle, with particular emphasis on its contribution to passive tension, active force modulation, sarcomere stability, and contraction mechanics.

Titin

Titin is one of the most abundant proteins in skeletal muscle and spans half of the sarcomere, extending from the Z-disc to the M-line, where it contributes to sarcomere organization and mechanical stability (Freundt & Linke, 2019). One molecular titin located at around A-I band interacts thick filaments along with six-titin but, three titin filaments near to thick filaments (Nishikawa et al., 2012). In the A-band, which consists of repeating fibronectin-associated myosin thick filaments, relatively inelastic distal Ig segments connect the A-band to the I-band titin at the end of the thick filaments

(Bennet, Hodkin & Hawkins, 1997). The elastic I-band region of titin is bound to the isoform consisting of the proximal tandem Ig segment, the N2A sequence, and the PEVK domain, which is rich in P (proline), E (glutamate), V (valine), and K (lysine) (Adewale & Young-Hoon Ahn, 2021). The inelastic residues of titin in the Z-disc bind to actin cytoskeleton, protein α-actinin, from the additional sarcomeres of polarity (Young & Gautel, 2000). Additional titin molecules in the Z-disc and M-line occur along the entire length of the myofibril, including actins are provide length with nebulin (Cooper, 2000) (Fig 1). Two giant protein titin and nebulin contribute sarcomere stability, titin extremely is large protein (3000 kD) (Cooper, 2000). Muscle sarcomere shortening is the process by which the thick filaments move toward the Z disks during movement and the extensible region of titin is stretched in the opposite direction into (I1 to I2) to the sarcomere lengthening, thus producing a force that tends to separate the Z disks and is a factor in determining the lower limit of physiological sarcomere length (Horowits & Podolsky, 1987). Iso-conditioning occurs when titin and α-actinin determines the distance of the thick filament from the Z disk, thereby length of bound PEVK controlling, titin is generate length irregularities between hemisarcomeres and balancing the forces between hemisarcomeres (Nishikawa et al., 2012). Therefore, the behavior of the PEVK region during the transition from passive stretch to active contraction may help explain titin's potential contribution to active force modulation (Nishikawa et al., 2012). In force-length results, A-band movement stretches the elastic filament (titin) in the other half of the sarcomere between the half sarcomeres and transmits the force to the Z-disc (Joumaa et al., 2018). The extent of primary structural sarcomeres during A-band movement depends on the final sarcomere length reached after activation, suggesting that A-band movement is dependent on passive force entiring generated by the elastic filament (Joumaa et al., 2018; Horowits & Podolsky, 1987). At long sarcomere lengths, the titin-based passive force exact the half sarcomere lengths uniform and centers the A-bands in the middle of the sarcomeres (Joumaa et al., 2018).

Taken together, these findings indicate that titin contributes not only to the structural alignment of sarcomeres but also to the regulation of passive mechanical properties during muscle stretch.

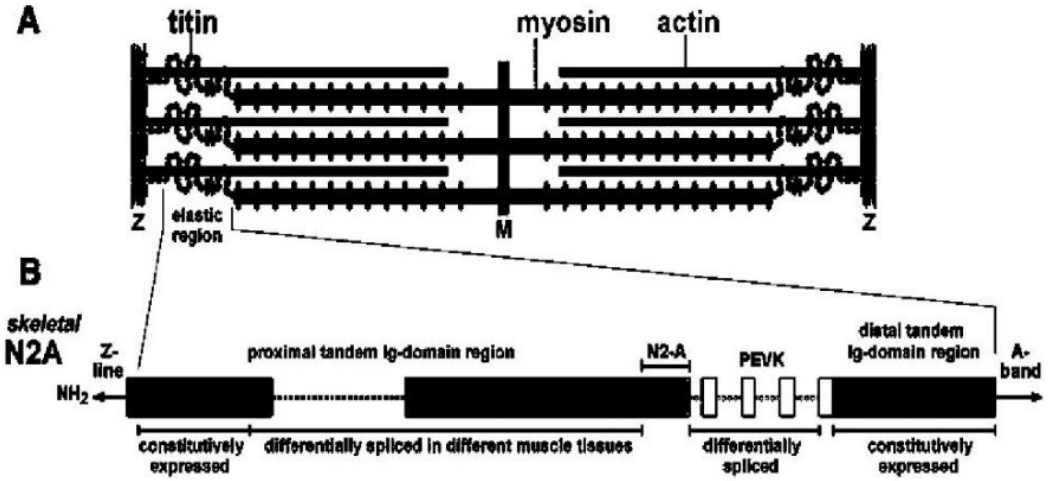

Figure 1. Schematic localization of titin within the sarcomere, extending from the Z-disc to the M-line.

Passive tension role of titin: regional activity

Connectin (titin) role efforts skeletal muscle intracellular elastic protein account for elastic function communication within sarcomeres (Maruyama, 1976). Protein molecular titin activation Z disc along from M line overlap myofibrillar lengthening complex tasks continuously included this topic (Nishikawa et al., 2012). The elastic properties of titin are evident when single myofibrils are stretched, as changes in the I-band region contribute to the development of passive tension (Maruyama, 1976). Stretching beyond the overlap of thick and thin filaments highlights the role of titin in maintaining sarcomere integrity and passive force transmission (Leonard & Herzog, 2010). In that resulted passive force behaviour of myofibrils is consistent straightens the folded proximal tandem Ig domains as the strecth of sarcomeres with little increase in passive tension due to activated sarcomere lenght of 2.4 μm to 5 μm (Leonard & Herzog, 2010). As these indicated that, myo section of sarcomeres are length longer, proximal tandem Ig domain straighten toward the stiffer PEVK domain (35 to 560 μm) about 0.18 nm at 15 μm elongates and passive tension increases titin functional role (Forbes et al., 2005). Titin function of passive spring in muscles is that stiffer PEVK region not elongates at physiologic lengths, during active contraction of muscles, titin shorter I-band region located mechanical demands (Powers et al., 2014). In that is entropic PEVK activation to spring low energy production, but as enthalpic reactivation produce higher energy during elongation of myofibrils (Nishikawa et al., 2012; Forbes et al., 2005). Actual lengths of proximal tandem Ig domain region determine the slack length of sarcomere and stiffer occurs the length of PEVK sequences corraleted passive tension, thus anterior muscles than posterior muscles may be important detection of isoform expression (Nishikawa et al., 2012) (Fig 2).

Therefore, titin-based passive tension appears to depend primarily on sarcomere length, titin isoform composition, and the mechanical behavior of the Ig and PEVK regions.

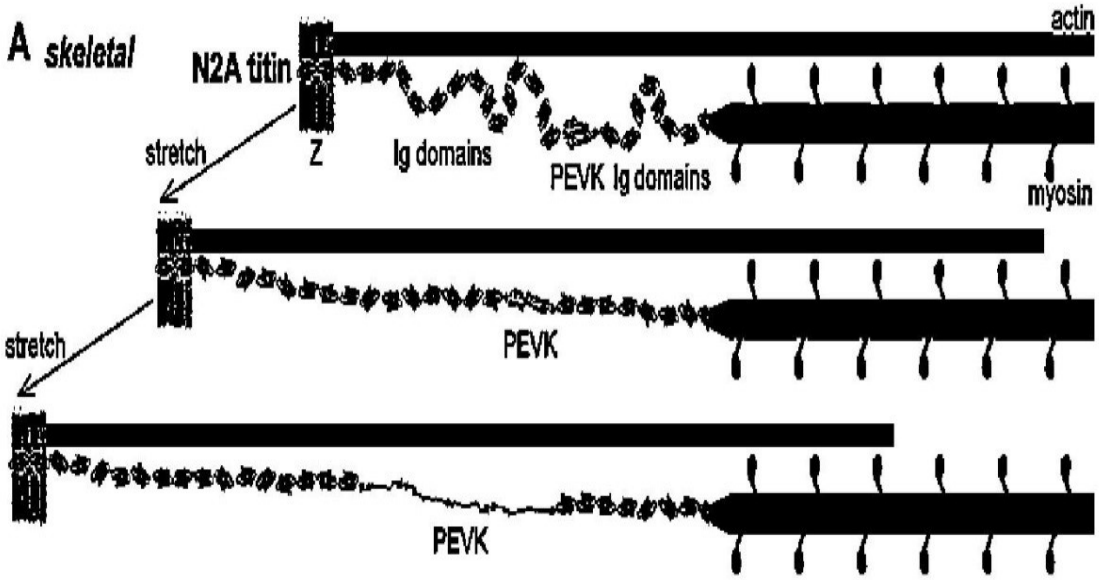

Fig 2. The role of titin as a molecular spring contributing to passive tension during sarcomere stretch

Potential Contribution of Titin to Active Force Generation

The possibility that titin contributes to active force generation has been increasingly discussed in relation to actin–titin interactions and calcium-dependent changes in titin stiffness (Fig 3). Titin isoforms in skeletal and cardiac muscle play different roles (ie., titin genes) in passive and active force generation (Horowits, 1992). Active muscles displace in purified I-band from localization of titin to obtain Ca^{2+} in vitro, it condition explains N2A region signal factor recruit force generation (Stronczek et al., 2021). Active fibers (thick filaments) increase Ca^{2+} influx, increasing tension and stiffness in the non-crossing bridge structure, probably titin (Stronczek et al., 2021). Thus, PEVK fragments and single fibers show not only mechanically Ca^{2+} influx but also Ca^{2+} increases, causing a change in the force-extension curve upon calcium activation and active stretch through titin molecules (Monroy et al., 2012). During active stretches were due to the activation as this removal of troponin C in active force, however, active and passive viscoelastic structures, myofibrils increased by Ca^{2+} influx able to sarcomere length about 6 μm (Monroy et al., 2012). In the stabilities, passive tension condition determines active lengthening during calcium activation, after activated force recruit passive elements enable to isometric force (Nishikawa et al., 2012). Enhanced force and energy storage during active stretch of skeletal muscle experienced by cross bridge including eccentric contraction, a role of titin in force generation acts at N2A-actin binding providing calcium dependence associated with thid interaction to high force, evidences suggested that proximal PEVK domains like stabilize N2A-actin binding in active muscle (Gage & Nishikawa, 2026). The effect of Ca^{2+} on titin

stiffness (three titin) is direct, it can bind to actin when Ca^{2+} is present during free length and increase its stiffness, it condition promotes active force production (Herzog, 2014). For example, α-actinin increasing along with radial PEVK increase indirectly during active stretching based on titin and α-actinin, which is stabile supporting to filaments generate isometric force (Nishikawa et al., 2012). During all of mechanic forces high or low Ca^{2+} activation it is knowing Ca^{2+} binding to titin may contribute as (15%), but all titin activated Ca^{2+} interaction may contribute as (85%), directly to small force and stiffness are expect from Ca^{2+} binding to PEVK (Freundt and Linke, 2019). During potential force generation, skeletal muscle working take in actomyosin cross bridges identif as the partial molecule structures account for active muscle tension, and the plateau as the isometric force-length relationship of skeletal muscles was determined by predictions of the myofibril sliding filaments with the rate of actomyosin ATP hydrolysis at different temperatures, in this condition that muscle energetics in account of predicting force during isometric contraction (Nishikawa, 2020). Hill-type force–length models suggest that the spring-like properties of titin may contribute to muscle force regulation across different contraction velocities (Kloock et al., 2026). I-band titin spans and determines the length sarcomres in muscle type specific to generate myosin filament feedback mechanism modulated in myosin contractile forms (Loreau et al., 2025).

Nishikawa (2020) was the future direction that when a muscle is active stretched, the energy required to produce a given force is significantly reduced compared to isometric contraction, energy economy is higher during active lengthening, however, preceding stretch or shortening altered the muscle force observed at a length, resulting of stretch of the active muscle was greater than the isometric force at the same final length.

These findings suggest that titin may contribute to residual force enhancement and energy efficiency during active lengthening contractions, although the exact molecular mechanisms remain under investigation.

Importantly, the available evidence does not imply that titin independently generates active force; rather, titin may modulate force production through its interaction with actomyosin-based contraction, sarcomere length, calcium activation, and passive elastic elements.

Limitations and Future Directions

This review has several limitations. First, it is a narrative review rather than a systematic review; therefore, the literature was not selected through a predefined search strategy, and some relevant studies may have been missed. Second, many mechanistic findings on titin are derived from isolated muscle fibres, myofibrils, or animal models, which may limit their direct translation to whole-muscle function in humans. Third, the precise contribution of titin to active force generation remains debated because titin-based stiffness interacts with calcium activation, actomyosin cross-bridge cycling, sarcomere length, and muscle-specific titin isoforms. Future studies should combine

molecular, single-fibre, and in vivo approaches to clarify how titin contributes to force regulation during eccentric, concentric, and isometric contractions.

CONCLUSION

Titin is a giant sarcomeric protein that contributes to skeletal muscle mechanics through its structural, elastic, and regulatory properties. Current evidence suggests that titin plays an important role in passive tension development, sarcomere stability, and force transmission during muscle lengthening. Beyond its classical function as a passive molecular spring, titin may also contribute to active force modulation through calcium-dependent changes in stiffness, titin–actin interactions, and alterations in the mechanical behavior of the Ig and PEVK regions. However, the precise extent to which titin contributes to active force generation remains under investigation and should not be interpreted as a fully established causal mechanism. Overall, titin should be considered a dynamic regulatory protein that links passive stiffness, active force enhancement, sarcomere stability, and energy efficiency during skeletal muscle contraction. A better understanding of titin mechanics may provide new insights into skeletal muscle performance, fatigue resistance, eccentric contraction, and muscle adaptation.

Kısaltmalar / Abbreviations

A-band	: Anisotropic band
ATP	: Adenosine triphosphate
Ca^{2+}	: Calcium ion
I-band	: Isotropic band
Ig	: Immunoglobulin-like domain
kDa	: Kilodalton
Mda	: Megadalton
MHC	: Myosin heavy chain
M-line	: Middle line of the sarcomere
N2A	: N2A region of titin
NH_2-terminal	: Amino-terminal region
PEVK	: Proline, glutamate, valine, and lysine-rich domain
Z-disc	: Z-line / Z-disc of the sarcomere

Beyanlar / Declarations

Etik Onay ve Katılım Onayı / Ethics approval and consent to participate

Bu çalışmanın hazırlanma ve yazım sürecinde "Yükseköğretim Kurumları Bilimsel Araştırma ve Yayın Etiği Yönergesi" kapsamında bilimsel, etik ve alıntı kurallarına uyulmuş olup, toplanan veriler üzerinde herhangi bir tahrifat yapılmamış ve bu çalışma başka herhangi bir akademik yayın ortamına değerlendirilmek üzere gönderilmemiştir. Araştırma süreci Helsinki Bildirgesi ilkelerine uygun olarak yürütülmüştür. Makale ile ilgili doğabilecek her türlü etik ve hukuki sorumluluk yazarlara aittir.

During the preparation and writing of this study, scientific, ethical, and citation rules were followed in accordance with the "Higher Education Institutions Scientific Research and Publication Ethics Guidelines". No alterations were made to the collected data, and this study has not been submitted to any other academic publication venue for evaluation. The study was conducted in accordance with the principles of the Declaration of Helsinki. The authors are solely responsible for any ethical or legal issues that may arise regarding this article.

Veri Ve Materyal Erişilebilirliği / Availability of data and material

Bu çalışmanın bulgularını destekleyen veriler, makul talepler üzerine sorumlu yazardan temin edilebilir. Veri seti yalnızca akademik amaçlar için erişilebilir olacak ve verilerin herhangi bir kullanımı, orijinal çalışmayı referans gösterecek ve katılımcıların gizliliğini koruyacaktır.

The data that support the findings of this study are available from the corresponding author upon reasonable request. The dataset will be accessible only for academic purposes, and any use of the data will recognize the original study and maintain the confdentiality of the participants.

Çıkar Çatışması / Competing interests

Yazarlar, bu makalede sunulan çalışmayı etkileyebilecek herhangi bir çıkar çatışması veya kişisel ilişkiye sahip olmadıklarını beyan etmektedirler.

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Yazar Katkıları / Authors' Contribution Statement

Yazarlar çalışmaya eşit oranda katkı sağlamış, makalenin son halini okuyup onaylamış ve yayımlanmasından doğacak sorumluluğu paylaşmıştır.

The authors contributed equally to the study, reviewed and approved the final version of the manuscript, and agreed to be accountable for all aspects of the work.

Fon Desteği / Funding

Bu çalışma, kamu, özel veya kar amacı gütmeyen sektörlerdeki fon sağlayıcı kurumlardan herhangi bir özel destek almamıştır.

This research received no external funding.

Teşekkür / Acknowledgements

None.

References / Kaynaklar

Adewale, A. O., & Ahn, Y. H. (2021). Titin N2A Domain and Its Interactions at the Sarcomere. *International journal of molecular sciences*, *22*(14), 7563. https://doi.org/10.3390/ijms22147563.

Bang, M. L., Centner, T., Fornoff, F., Geach, A. J., Gotthardt, M., McNabb, M., Witt, C. C., Labeit, D., Gregorio, C. C., Granzier, H., & Labeit, S. (2001). The complete gene sequence of titin, expression of an unusual approximately 700-kDa titin isoform, and its interaction with obscurin identify a novel Z-line to I-band linking system. *Circulation research*, *89*(11), 1065–1072. https://doi.org/10.1161/hh2301.100981.

Bennett, P. M., Hodkin, T. E., & Hawkins, C. (1997). Evidence that the tandem Ig domains near the end of the muscle thick filament form an inelastic part of the I-band titin. *Journal of structural biology*, *120*(1), 93–104. https://doi.org/10.1006/jsbi.1997.3898.

Cooper, G.M. (2000) The Cell: A Molecular Approach. 2nd Edition, Sunderland (MA): Sinauer Associates, The Development and Causes of Cancer.

Forbes, J. G., Jin, A. J., Ma, K., Gutierrez-Cruz, G., Tsai, W. L., & Wang, K. (2005). Titin PEVK segment: charge-driven elasticity of the open and flexible polyampholyte. *Journal of muscle research and cell motility*, *26*(6-8), 291–301. https://doi.org/10.1007/s10974-005-9035-4.

Freundt, J. K., & Linke, W. A. (2019). Titin as a force-generating muscle protein under regulatory control. *Journal of applied physiology (Bethesda, Md. : 1985)*, *126*(5), 1474–1482. https://doi.org/10.1152/japplphysiol.00865.2018.

Gage, M., & Nishikawa, K. (2026). Roles of N2A Titin in Signaling and Muscle Mechanics. Medical Research Archives, 14(3). doi:10.18103/mra.v14i3.7328.

Goto, K., Okuyama, R., Honda, M., Uchida, H., Akema, T., Ohira, Y., & Yoshioka, T. (2003). Profiles of connectin (titin) in atrophied soleus muscle induced by unloading of rats. *Journal of applied physiology (Bethesda, Md. : 1985)*, *94*(3), 897–902. https://doi.org/10.1152/japplphysiol.00408.2002.

Hanson, J., & Huxley, H. E. (1953). Structural basis of the cross-striations in muscle. *Nature*, *172*(4377), 530–532. https://doi.org/10.1038/172530b0.

Horowits, R., & Podolsky, R. J. (1987). The positional stability of thick filaments in activated skeletal muscle depends on sarcomere length: evidence for the role of titin filaments. *The Journal of cell biology*, *105*(5), 2217–2223. https://doi.org/10.1083/jcb.105.5.2217.

Horowits R. (1992). Passive force generation and titin isoforms in mammalian skeletal muscle. *Biophysical journal*, *61*(2), 392–398. https://doi.org/10.1016/S0006-3495(92)81845-3.

Hoyle G. (1983). Forms of modulatable tension in skeletal muscles. *Comparative biochemistry and physiology. A, Comparative physiology*, *76*(2), 203–210. https://doi.org/10.1016/0300-9629(83)90316-x.

Huxley H. E. (1953). Electron microscope studies of the organisation of the filaments in striated muscle. *Biochimica et biophysica acta*, *12*(3), 387–394. https://doi.org/10.1016/0006-3002(53)90156-5.

Joumaa, V., Bertrand, F., Liu, S., Poscente, S., & Herzog, W. (2018). Does partial titin degradation affect sarcomere length nonuniformities and force in active and passive myofibrils?. *American journal of physiology. Cell physiology*, *315*(3), C310–C318. https://doi.org/10.1152/ajpcell.00183.2017.

Kloock, L., Lauren de Graaf, M., Boström, K.J., Wagner, H. (2026). Spring–damper titin model improves the estimation of muscle forces during force enhancement measurements, Journal of Biomechanics, 2, 113306. https://doi.org/10.1016/j.jbiomech.2026.113306.

Leonard, T. R., & Herzog, W. (2010). Regulation of muscle force in the absence of actin-myosin-based cross-bridge interaction. *American journal of physiology. Cell physiology*, *299*(1), C14–C20. https://doi.org/10.1152/ajpcell.00049.2010.

Loreau, V., Koolhaas, W. H., Chan, E. H., De Boissier, P., Brouilly, N., Avosani, S., Sane, A., Pitaval, C., Reiter, S., Luis, N. M., Mangeol, P., von Philipsborn, A. C., Rupprecht, J. F., Görlich, D., Habermann, B. H., & Schnorrer, F. (2025). Titin-dependent biomechanical feedback tailors sarcomeres to specialized muscle functions in insects. Science advances, 11(19), eads8716. https://doi.org/10.1126/sciadv.ads8716.

Maruyama K. (1976). Connectin, an elastic protein from myofibrils. *Journal of biochemistry*, *80*(2), 405–407. https://doi.org/10.1093/oxfordjournals.jbchem.a131291.

Monroy, J. A., Powers, K. L., Gilmore, L. A., Uyeno, T. A., Lindstedt, S. L., & Nishikawa, K. C. (2012). What is the role of titin in active muscle?. *Exercise and sport sciences reviews*, *40*(2), 73–78. https://doi.org/10.1097/JES.0b013e3182458.

Nishikawa, K. C., Monroy, J. A., Uyeno, T. E., Yeo, S. H., Pai, D. K., & Lindstedt, S. L. (2012). Is titin a 'winding filament'? A new twist on muscle contraction. *Proceedings. Biological sciences*, *279*(1730), 981–990. https://doi.org/10.1098/rspb.2011.1304.

Nishikawa K. (2020). Titin: A Tunable Spring in Active Muscle. *Physiology (Bethesda, Md.)*, *35*(3), 209–217. https://doi.org/10.1152/physiol.00036.2019.

Powers, K., Schappacher-Tilp, G., Jinha, A., Leonard, T., Nishikawa, K., & Herzog, W. (2014). Titin force is enhanced in actively stretched skeletal muscle. *The Journal of experimental biology*, *217*(Pt 20), 3629–3636. https://doi.org/10.1242/jeb.105361.

Stronczek, C., Lange, S., Bullard, B., Wolniak, S., Börgeson, E., Mayans, O., & Fleming, J. R. (2021). The N2A region of titin has a unique structural configuration. *The Journal of general physiology*, *153*(7), e202012766. https://doi.org/10.1085/jgp.202012766.

Young, P., & Gautel, M. (2000). The interaction of titin and alpha-actinin is controlled by a phospholipid-regulated intramolecular pseudoligand mechanism. *The EMBO journal*, *19*(23), 6331–6340. https://doi.org/10.1093/emboj/19.23.6331.

Disclaimer / Publisher's Note

The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and do not necessarily reflect the views of **IJOSS** and/or the editor(s). **IJOSS** and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content. **IJOSS** remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.