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Titin N2A Domain and Its Interactions at the Sarcomere

Adeleye O Adewale [1], Young-Hoon Ahn [1]

Affiliations

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Abstract

Titin is a giant protein in the sarcomere that plays an essential role in muscle contraction with actin and myosin filaments. However, its utility goes beyond mechanical functions, extending to versatile and complex roles in sarcomere organization and maintenance, passive force, mechanosensing, and signaling. Titin's multiple functions are in part attributed to its large size and modular structures that interact with a myriad of protein partners. Among titin's domains, the N2A element is one of titin's unique segments that contributes to titin's functions in compliance, contraction, structural stability, and signaling via protein-protein interactions with actin filament, chaperones, stress-sensing proteins, and proteases. Considering the significance of N2A, this review highlights structural conformations of N2A, its predisposition for protein-protein interactions, and its multiple interacting protein partners that allow the modulation of titin's biological effects. Lastly, the nature of N2A for interactions with chaperones and proteases is included, presenting it as an important node that impacts titin's structural and functional integrity.

Keywords: N2A domain; protein–protein interaction; titin.