Structural Studies on Titin and Titin Kinase's Downstream Signaling Pathway

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Titin is the third filament system in vertebrate striated muscles where it spans half of the sarcomere from the Z-disc to the M-line. The giant multi-domain protein titin consists of about three hundred domains, most of them immunoglobulin (Ig)-like domains and fibronectin III (FnIII) domains showing typical patterns assigned to specific regions in the sarcomere, interposed by unique sequences. One of these is a serine/threonine kinase domain, titin kinase [1], located at the interface between A-band and M-line. It has been shown by Centner et al. [2] that MURF-1, a member of the RING finger proteins, binds to the two Ig-domains A168 and A169 in proximity to the kinase. Thus, its binding might be involved in the regulation of titin kinase. The structure of this tandem Ig domain has been solved. Ig domains, also in titin, are involved in many protein-protein interactions and this interconnects titin with other muscle proteins and pathways. Here, we will present new structures near titin kinase and from a downstream signaling pathway of titin kinase (Gautel et al., unpublished data).

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