Structural diversity in the atomic resolution 3D fingerprint of the titin M-band segment.

Chatziefthimiou SD, Hornburg P, Sauer F, Mueller S, Ugurlar D, Xu ER, Wilmanns M.

Abstract

In striated muscles, molecular filaments are largely composed of long protein chains with extensive arrays of identically folded domains, referred to as "beads-on-a-string". It remains a largely unresolved question how these domains have developed a unique molecular profile such that each carries out a distinct function without false-positive readout. This study focuses on the M-band segment of the sarcomeric protein titin, which comprises ten identically folded immunoglobulin domains. Comparative analysis of high-resolution structures of six of these domains – M1, M3, M4, M5, M7, and M10 – reveals considerable structural diversity within three distinct loops and a non-conserved pattern of exposed cysteines. Our data allow to structurally interpreting distinct pathological readouts that result from titinopathy-associated variants. Our findings support general principles that could be used to identify individual structural/functional profiles of hundreds of identically folded protein domains within the sarcomere and other densely crowded cellular environments.

PMID: 31856237 DOI: 10.1371/journal.pone.0226693
Structural diversity in the atomic resolution 3D fingerprint of the titin M-band segment. - PubMed - NCBI

LinkOut - more resources