Titin in muscular dystrophy and cardiomyopathy: Urinary titin as a novel marker.

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Abstract

Titin, encoded by the gene TTN, is the largest human protein, and plays central roles in sarcomeric structures and functions in skeletal and cardiac muscles. Mutations of TTN are causally related to specific types of muscular dystrophies and cardiomyopathies. A developed methodology of next generation sequencing has recently led to the identification of novel TTN mutations in such diseases. The clinical significance of titin is now emerging as a target for genetic strategies. Titin-related muscular dystrophies include tibial muscular dystrophy, limb-girdle muscular dystrophy, Emery-Dreifuss muscular dystrophy, hereditary myopathy with early respiratory failure, central core myopathy, centronuclear myopathies, and Salih myopathy. Truncation mutations of TTN have been identified as the most frequent genetic cause of dilated cardiomyopathy. In this review article, we highlight the role of titin and impact of TTN mutations in the pathogenesis of muscular dystrophies and cardiomyopathies. Recently, a novel sensitive sandwich enzyme-linked immunosorbent assay (ELISA) for the detection of the urinary titin N-terminal fragments (U-TN) has been established. We discuss the clinical significance of U-TN in the diagnosis of muscular dystrophies and differential diagnosis of cardiomyopathies, as well as risk stratification in dilated cardiomyopathy.

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