Titin/connectin, encoded by the TTN gene, is the largest protein in humans. It acts as a molecular spring in the sarcomere of striated muscles. Although titin is degraded in the skeletal muscles of patients with muscular dystrophies, studies of titin have been limited by its mammoth size. Mutations in the TTN gene have been detected not only in skeletal muscle diseases but in cardiac muscle diseases. TTN mutations result in a wide variety of phenotypes. Recent proteome analysis has found that titin fragments are excreted into the urine of patients with Duchenne muscular dystrophy (DMD). Enzyme-linked immunosorbent assays (ELISAs) have shown that urinary titin is a useful noninvasive biomarker for the diagnosis and screening of not only DMD, but also of neuromuscular diseases, for predicting the outcome of cardiomyopathy and for evaluating physical activities. The development of ELISA systems to measure urinary titin has opened a door to studying muscle degradation directly and noninvasively. This review provides current understanding of urinary titin and future prospects for measuring this protein.

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KEYWORDS: Connectin; Muscle degradation; Sarcomere; Titin; Urine

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