to the physiologic and pathophysiologic significances in modifying the contractility of skeletal and cardiac muscles during development and in adaptation to stress and disease conditions, the hyperplasticity of the N-terminal region of TnT demonstrates an informative example for the evolution of protein three-dimensional structure and provides insights into the molecular evolution and functional potential of proteins.

1. INTRODUCTION

The contractile machinery of striated muscles (represented by skeletal and cardiac muscles of vertebrates) is the myofibrils that consist of tandem repeats of sarcomeres. A sarcomere is composed of overlapping myosin thick filaments and actin thin filaments. Contraction is powered by actin-activated myosin ATPase-catalyzed ATP hydrolysis during actomyosin cross-bridge cycling. This process is regulated by the thin filament-associated regulatory proteins troponin under the control of cytosolic Ca^{2+} (Gordon et al., 2000).

Residing at ~37-nm intervals along the thin filament in the form of F-actin-tropomyosin double helices (Galinska-Rakoczy et al., 2008; Lehman et al., 2009; Ohtsuki et al., 1967), the troponin complex consists of three protein subunits: the Ca^{2+}-binding subunit troponin C (TnC^1), actomyosin ATPase-inhibiting subunit troponin I (TnI), and tropomyosin-binding subunit troponin T (TnT) (Greaser and Gergely, 1971). To convert the cellular signal of cytosolic Ca^{2+} transient originated from sarcolemmal electrical activity to myofilament movements during each excitation–contraction–relaxation cycle, troponin functions through cooperative interactions among the three subunits and with tropomyosin (Gordon et al., 2000; Tobacman, 1996). Whereas TnC is a relative of the calmodulin gene family (Collins, 1991) and functions as the Ca^{2+} receptor of the thin filament regulatory system in striated muscle, TnI and TnT are striated-muscle-specific proteins encoded by closely linked genes and have coevolved into three pairs of fiber-type-specific isoforms (Chong and Jin, 2009; Jin et al., 2008).

In addition to anchoring the troponin complex to the thin filament, TnT directly interacts with multiple proteins in the thin filament regulatory system to play an organizer role in the troponin complex (Perry, 1998). Through isoform gene regulation, alternative RNA splicing, and posttranslational modifications, structural and functional variations of TnT provide a mechanism to modulate striated muscle contraction and relaxation.

To understand the structure–function relationship of TnT, this review outlines the evolution of muscle type-specific TnT isoform genes, the