Novel filament systems in normal, regenerating and diseased muscle

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(Introduced by Gordon Lynch.)

Tropomyosin isoforms confer functional diversity on actin filament systems. The best characterized isoforms of tropomyosin are those found in association with the sarcomeric actin thin filaments in striated muscles that mediate the interaction between actin and myosin to bring about contraction. However, a nonmuscle or cytoskeletal tropomyosin, Tm5NM1, also is present in skeletal muscle fibres where it defines a novel compartment, the Z-line adjacent cytoskeleton (Z-LAC) (Kee *et al.*, 2004). In addition, we have found that another cytoskeletal isoform, Tm4, compartmentalizes in muscle fibres to form two distinct microdomains, one transverse or Z-LAC in orientation found in normal muscles and one longitudinal found in muscles undergoing remodelling and repair in response to injury, stretch and disease. In the Z-line adjacent cytoskeleton, Tm5NM1 and Tm4 define distinct actin-based filament systems within close proximity, where Tm5NM1 associates with the T-tubule system. The transition in localization of Tm4 from longitudinal filaments to Z-LAC orientation is observed during the course of muscle regeneration. Tm4-defined longitudinal filaments are present in muscles from mouse models and human patients with myopathies characterized by regeneration and repair. The discovery of these 'nonmuscle' filament systems in skeletal muscle demonstrates that, in parallel with all other cell systems examined, skeletal muscle contains compartmentalised actin cytoskeletal systems characterized by the segregation of different cytoskeletal tropomyosins.

Kee AJ, Schevzov G, Nair-Shalliker V, Robinson CS, Vrhovski B, Ghoddusi M, Qiu MR, Lin JJ, Weinberger R, Gunning PW, Hardeman EC. (2004) *Journal of Cell Biology*, **166**:685-96. Mice were anaesthetized with 20 mg/Kg body weight of Ketamine/Xylazine delivered by interperitoneal injection. Muscle injury/regeneration was induced by intramuscular injection of 0.2-0.4 micrograms of Notexin. -->