

## Publication

### Accumulation of muscle ankyrin repeat protein transcript reveals local activation of primary myotube endcompartments during muscle morphogenesis

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The characteristic shapes and positions of each individual body muscle are established during the process of muscle morphogenesis in response to patterning information from the surrounding mesenchyme. Throughout muscle morphogenesis, primary myotubes are arranged in small parallel bundles, each myotube spanning the forming muscles from end to end. This unique arrangement potentially assigns a crucial role to primary myotube end regions for muscle morphogenesis. We have cloned muscle ankyrin repeat protein (MARF) as a gene induced in adult rat skeletal muscle by denervation. MARF is the rodent homologue of human C-193 (Chu, W., D.K. Burns, R.A. Swerick, and D.H. Presky. 1995. J. Biol. Chem. 270:10236-10245) and is identical to rat cardiac ankyrin repeat protein. (Zou, Y., S. Evans, J. Chen, H.-C. Kuo, R.P. Harvey, and K.R. Chien. 1997. Development. 124:793-804). In denervated muscle fibers, MARF transcript accumulated in a unique perisynaptic pattern. MARF was also expressed in large blood vessels and in cardiac muscle, where it was further induced by cardiac hypertrophy. During embryonic development, MARF was expressed in forming skeletal muscle. In situ hybridization analysis in mouse embryos revealed that MARF transcript exclusively accumulates at the end regions of primary myotubes during muscle morphogenesis. This closely coincided with the expression of thrombospondin-4 in adjacent prospective tendon mesenchyme, suggesting that these two compartments may constitute a functional unit involved in muscle morphogenesis. Transfection experiments established that MARF protein accumulates in the nucleus and that the levels of both MARF mRNA and protein are controlled by rapid degradation mechanisms characteristic of regulatory early response genes. The results establish the existence of novel regulatory muscle fiber subcompartments associated with muscle morphogenesis and denervation and suggest that MARF may be a crucial nuclear cofactor in local signaling pathways from prospective tendon mesenchyme to forming muscle and from activated muscle interstitial cells to denervated muscle fibers.

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