Elevated Expression of Moesin in Muscular Dystrophies.


Abstract

Fibrosis is the main complication of muscular dystrophies. We identified moesin, a member of the ezrin-radixin-moesin family, in dystrophic muscles of mice representing Duchenne and congenital muscular dystrophies (DMD and CMD, respectively) and dysferlinopathy, but not in the wild type. High levels of moesin were also observed in muscle biopsy specimens from DMD, Ullrich CMD, and merosin-deficient CMD patients, all of which present high levels of fibrosis. The myofibroblasts, responsible for extracellular matrix protein synthesis, and the macrophages infiltrating the dystrophic muscles were the source of moesin. Moesin-positive cells were embedded within the fibrotic areas between the myofibers adjacent to the collagen type I fibers. Radixin was also synthesized by the myofibroblasts, whereas ezrin colocalized with the myofiber membranes. In animal models and patients' muscles, part of the moesin was in its active phosphorylated form. Inhibition of fibrosis by halofuginone, an antifibrotic agent, resulted in a major decrease in moesin levels in the muscles of DMD and CMD mice. In summary, the results of this study may pave the way for exploiting moesin as a novel target for intervention in MDs, and as part of a battery of biomarkers to evaluate treatment success in preclinical studies and clinical trials.

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