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Distinct Fiber Type Signature in Mouse Muscles Expressing a Mutant Lamin A Responsible for Congenital Muscular Dystrophy in a Patient.

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Abstract

Specific mutations in *LMNA*, which encodes nuclear intermediate filament proteins lamins A/C, affect skeletal muscle tissues. Early-onset *LMNA* myopathies reveal different alterations of muscle fibers, including fiber type disproportion or prominent dystrophic and/or inflammatory changes. Recently, we identified the p.R388P *LMNA* mutation as responsible for congenital muscular dystrophy (L-CMD) and lipodystrophy. Here, we asked whether viral-mediated expression of mutant lamin A in murine skeletal muscles would be a pertinent model to reveal specific muscle alterations. We found that the total amount and size of muscle fibers as well as the extent of either inflammation or muscle regeneration were similar to wildtype or mutant lamin A. In contrast, the amount of fast oxidative muscle fibers containing myosin heavy chain IIA was lower upon expression of mutant lamin A, in correlation with lower expression of genes encoding transcription factors MEF2C and MyoD. These data validate this in vivo model for highlighting distinct muscle phenotypes associated with different lamin contexts. Additionally, the data suggest that alteration of muscle fiber type identity may contribute to the mechanisms underlying physiopathology of L-CMD related to R388P mutant lamin A.

KEYWORDS: congenital muscular dystrophy; lamin A; muscle fiber type transition; myosin heavy chain IIA

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