Laminin α1 reduces muscular dystrophy in dy2J mice.

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Abstract
Muscular dystrophies, including laminin α2 chain-deficient muscular dystrophy (LAMA2-CMD), are associated with immense personal, social and economic burdens. Thus, effective treatments are urgently needed. LAMA2-CMD is either a severe, early-onset condition with complete laminin α2 chain-deficiency or a milder, late-onset form with partial laminin α2 chain-deficiency. Mouse models dy3K/3K and dy2J/2J, respectively, recapitulate these two forms of LAMA2-CMD very well. We have previously demonstrated that laminin α1 chain significantly reduces muscular dystrophy in laminin α2 chain-deficient dy3K/3K mice. Among all the different pre-clinical approaches that have been evaluated in mice, laminin α1 chain-mediated therapy has been shown to be one of the most effective lines of attack. However, it has remained unclear if laminin α1 chain-mediated treatment is also applicable for partial laminin α2 chain-deficiency. Hence, we have generated dy2J/2J mice (that express a substantial amount of an N-terminal truncated laminin α2 chain) overexpressing laminin α1 chain in the neuromuscular system. The laminin α1 chain transgene ameliorated the dystrophic phenotype, restored muscle strength and reduced peripheral neuropathy. Thus, these findings provide additional support for the development of laminin α1 chain-based therapy for LAMA2-CMD.

KEYWORDS: Basement membrane; Laminin; Muscular dystrophy; Therapy

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