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Deficiency of emerin contributes differently to the pathogenesis of skeletal and cardiac muscles in LmnaH222P/H222P mutant mice.

Wada E[1], Kato M[1], Yamashita K[1], Kokuba H[2], Liang WC[3,4], Bonne G[5], Hayashi YK[1].

Author information

Abstract

Laminopathies are tissue-selective diseases that affect differently in organ systems. Mutations in nuclear envelopes, emerin (Emd) and lamin A/C (Lmna) genes, cause clinically indistinguishable myopathy called Emery-Dreifuss muscular dystrophy (EDMD) and limb-girdle muscular dystrophy. Several murine models for EDMD have been generated; however, emerin-null (Emd) mice do not show obvious skeletal and cardiac muscle phenotypes, and Lmna H222P/H222P mutant (H222P) mice show only a mild phenotype in skeletal muscle when they already have severe cardiomyopathy. Thus, the underlying molecular mechanism of muscle involvement due to nuclear abnormalities is still unclarified. We generated double mutant (Emd-/-/LmnaH222P/H222P; EH) mice to characterize dystrophic changes and to elucidate interactions between emerin and lamin A/C in skeletal and cardiac muscles. As H222P mice, EH mice grow normally and have breeding productivity. EH mice showed severer muscle involvement compared with that of H222P mice which was an independent of cardiac abnormality at 12 weeks of age. Nuclear abnormalities, reduced muscle fiber size and increased fibrosis were prominent in EH mice. Roles of emerin and lamin A/C in satellite cells function and regeneration of muscle fiber were also evaluated by cardiotoxin-induced muscle injury. Delayed increases in myog and myh3 expression were seen in both H222P and EH mice; however, the expression levels of those genes were similar with control and regenerated muscle fiber size was not different at day 7 after injury. These results indicate that EH mouse is a suitable model for studying skeletal muscle involvement, independent of cardiac function, in laminopathies and an interaction between emerin and lamin A/C in different tissues.

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Conflict of interest statement

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