Format: Abstract

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Postnatal Development of Mice with Combined Genetic Depletions of Lamin A/C, Emerin and Lamina-associated Polypeptide 1.

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Abstract

Mutations in LMNA encoding lamin A/C and EMD encoding emerin cause cardiomyopathy and muscular dystrophy. Lmna null mice develop these disorders and have a lifespan of 7-8 weeks. Emd null mice show no overt pathology and have normal skeletal muscle but with regeneration defects. We generated mice with germline deletions of both Lmna and Emd to determine the effects of combined loss of the encoded proteins. Mice without lamin A/C and emerin are born at the expected Mendelian ratio, are grossly normal at birth but have shorter lifespans than those lacking only lamin A/C. However, there are no major differences between these mice with regards to left ventricular function, heart ultrastructure or electrocardiographic parameters except for slower heart rates in the mice lacking both lamin A/C and emerin. Skeletal muscle is similarly affected in both of these mice. Lmna+/- mice also lacking emerin live to at least one year and have no significant differences in growth, heart or skeletal muscle compared to Lmna+/- mice. Deletion of the mouse gene encoding lamina-associated protein 1 leads to prenatal death; however, mice with heterozygous deletion of this gene lacking both lamin A/C and emerin are born at the expected Mendelian ratio but had a shorter lifespan than those only lacking lamin A/C and emerin. These result show that mice with combined deficiencies of three interacting nuclear envelope proteins have normal embryonic development and that early postnatal defects are primarily driven by loss of lamin A/C or lamina-associated polypeptide 1 rather than emerin.

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