Lamin A/C deficiency is 'unnerving'

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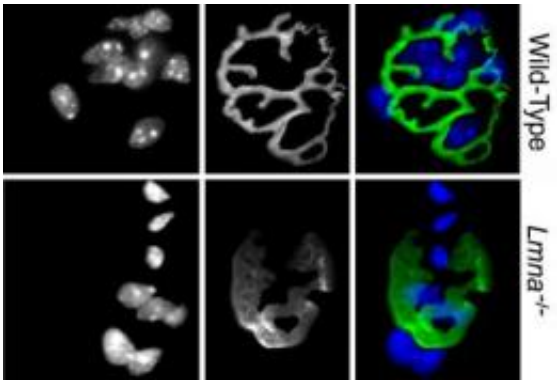

Lmna -/- animals have disorganized neuromuscular synapses (green) without postsynaptic nuclei (blue). Credit: Méjat, A., et al. 2008. J. Cell Biol.

Mutations in the nuclear intermediate filament lamin A/C (LMNA) gene are associated with Emery-Dreifuss muscular dystrophy, but cause the disease by unknown mechanisms. Méjat et al. show that one mechanism involves the disruption of neuromuscular junctions.

The study will appear online on Monday, January 5, 2009 (www.jcb.org) and in the January 12, 2009 print issue of the *Journal of Cell Biology*.

Muscle fiber cells contain hundreds of nuclei. In normal fibers, several nuclei cluster together under the cell membrane at sites of neuronal contact. These postsynaptic nuclei synthesize the components of the neuromuscular junction that specify the overlying membrane as the target site for innervation. The authors found that LMNA-deficient

animals (including those with a point mutation in LMNA that in humans can cause Emery-Dreifuss disease) failed to position nuclei into these postsynaptic clusters. This prevented the proper organization of the neuromuscular junction and disrupted muscle fiber innervation, says author Alexandre Méjat.

The authors showed that either loss or mutation of LMNA disrupted nuclear positioning by causing the mislocalization of two other proteins: Nesprin-1, which spans the outer nuclear membrane and anchors nuclei to the actin cytoskeleton, and SUN2, which spans the inner nuclear membrane, linking Nesprin to lamin A/C. Although lamin A/C is ubiquitously expressed, LMNA defects specifically affected striated and skeletal muscle because Nesprin-1 and SUN2 are highly expressed in these tissues. Samples from Emery-Dreifuss muscular dystrophy patients exhibit similar hallmarks of skeletal muscle functional denervation, suggesting the authors are on the right track.

Paper: Méjat, A., et al. 2008. J. Cell Biol. doi:10.1083/jcb.200811035.

Source: Rockefeller University