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Satellite cells deficiency and defective regeneration in dynamin 2-related centronuclear myopathy

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Abstract

Dynamin 2 (DNM2) is a ubiquitously expressed protein involved in many functions related to trafficking and remodeling of membranes and cytoskeleton dynamics. Mutations in the DNM2 gene cause the autosomal dominant centronuclear myopathy (AD-CNM), characterized mainly by muscle weakness and central nuclei. Several defects have been identified in the KI-Dnm2$^{R465W/+}$ mouse model of the disease to explain the muscle phenotype, including reduction of the satellite cell pool in muscle, but the functional consequences of this depletion have not been characterized until now. Satellite cells (SC) are the main source for muscle growth and regeneration of mature tissue. Here, we investigated muscle regeneration in the KI-Dnm2$^{R465W/+}$ mouse model for AD-CNM. We found a reduced number of Pax7-positive SCs, which were also less activated after induced muscle injury. The muscles of the KI-Dnm2$^{R465W/+}$ mouse regenerated more slowly and less efficiently than wild-type ones, formed fewer new myofibers, and did not recover its normal mass 15 days after injury. Altogether, our data provide evidence that the muscle regeneration is impaired in the KI-Dnm2$^{R465W/+}$ mouse and contribute with one more layer to the comprehension of the disease, by identifying a new pathomechanism linked to DNM2 mutations which may be involved in the muscle-specific impact occurring in AD-CNM.

Keywords: GTPase; congenital; injury; muscle; stem cell.