Laminin-α2 Chain-Deficient Congenital Muscular Dystrophy: Pathophysiology and Development of Treatment.

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Abstract
Laminin-211 is a major constituent of the skeletal muscle basement membrane. It stabilizes skeletal muscle and influences signal transduction events from the myomatrix to the muscle cell. Mutations in the gene encoding the α2 chain of laminin-211 lead to congenital muscular dystrophy type 1A (MDC1A), a life-threatening disease characterized by severe hypotonia, progressive muscle weakness, and joint contractures. Common complications include severely impaired motor ability, respiratory failure, and feeding difficulties. Several adequate animal models for laminin-α2 chain deficiency exist and analyses of different MDC1A mouse models have led to a significant improvement in our understanding of MDC1A pathogenesis. Importantly, the animal models have been indispensable tools for the preclinical development of new therapeutic approaches for laminin-α2 chain deficiency, highlighting a number of important disease driving mechanisms that can be targeted by pharmacological approaches. In this chapter, I will describe laminin-211 and discuss the cellular and molecular pathophysiology of MDC1A as well as progression toward development of treatment.

KEYWORDS: Apoptosis; Autophagy; Dystroglycan; Fibrosis; Integrin; Laminin; Muscular dystrophy; Proteasome

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