Overexpression of miR-29 Leads to Myopathy that Resemble Pathology of Ullrich Congenital Muscular Dystrophy.


Abstract

Ullrich congenital muscular dystrophy (UCMD) bring heavy burden to patients' families and society. Because the incidence of this disease is very low, studies in patients are extremely limited. Animal models of this disease are indispensable. UCMD belongs to extracellular matrix-related diseases. However, the disease models constructed by knocking out some pathogenic genes of human, such as the Col6a1, Col6a2, or Col6a3 gene, of mice could not mimic UCMD. The purpose of this study is to construct a mouse model which can resemble the pathology of UCMD. miR-29 is closely related to extracellular matrix deposition of tissues and organs. To address this issue, we developed a mouse model for overexpression miR-29 using Tet-on system. In the muscle-specific miR-29ab1 cluster transgenic mice model, we found that mice exhibited dyskinesia, dyspnea, and spinal anomaly. The skeletal muscle was damaged and regenerated. At the same time, we clarify the molecular mechanism of the role of miR-29 in this process. Different from human, Col4a1 and Col4a2, target genes of miR-29, are the key pathogenic genes associating with these phenotypes. This mouse model simulates the human clinical and pathological characteristics of UCMD patients and is helpful for the subsequent research and treatment of UCMD.

KEYWORDS: UCMD; collagen; disease model; dysplasia; miR-29

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