IJAE
Vol. 121, n. 1 (Supplement): 85, 2016
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

The role of MICAL2 gene in myogenic differentiation

[1] Nefele Giarratana - [2] Onofrio Tamburro - [2] Laura Benedetti - [3] Debora Angeloni - [2] Maria Gabriella Cusella De Angelis - [2] Gabriele Ceccarelli - [2] Maurilio Sampaolesi

[1] Translational Cardiomyology Laboratory/Stem Cell Biology and Embryology Unit, University of Leuven/Dept of Development and Regeneration, Leuven, Belgio - [2] Human Anatomy Institute, University of Pavia/Dept of Public Health, Experimental and Forensic Medicine, Pavia, Italia - [3] Institute of Life Sciences, Scuola Superiore Sant'Anna, Pisa, Italia

The dystrophin-glycoprotein complex (DGC) is composed of several transmembrane and peripheral components localized in the sarcolemma of skeletal muscle. Mutations in genes that encode DGC components lead to the loss of either expression and/or function of the DGC in muscle. As DGC complex interacts with F-actin it is reasonable that the multidomain F-actin binding protein MICAL2 that transduces semaphorin/plexin external signaling into cytoskeletal modifications, might interact either directly or indirectly with the DGC complex. MICAL2 is indeed expressed in skeletal and cardiac muscles and drosophila Mical mutants reveal that the architecture of contractile muscle filaments is negatively affected. We focus here on the role of MICALs in myogenic differentiation. The rationale to investigate MICAL2 in muscle differentiation is also highlighted in a paper regarding a complex muscle genome-wide expression profiling during the disease evolution in mdx mice, a mouse model of Duchenne muscular dystrophy (1). In this study the authors found MICAL2 among a set of totally ten functionally linked genes involved in the decline of muscle necrosis in mdx mice. For this purpose MICAL2 gain and loss of function studies have been performed in myogenic cell line and compared to in vivo analysis of MICAL2 expressions in acute and chronic muscle degeneration. Recently we showed that that differential myogenic propensity influences the commitment of isogenic induce pluripotent stem cells and a specifically isolated pool of mesodermal iPSC-derived progenitors (MiPs) toward the striated muscle lineages (2). Analysis of MICAL2 expression in MiPs is currently under investigation. Taken together modulation of MICAL2 has an impact on skeletal muscle commitment and could be considered a potential therapeutic target for Duchenne patients.

This work was supported with the contribution of "Opening The Future" Campaign [EJJ-OPTFUT-02010] CARIPLO 2015_0634, FWO (#G088715N, #G060612N, #G0A8813N), and IUAP-VII/07 (EJJ-C4851-17/07-P) grants.

References

[1] Marotta et al. (2009) Muscle genome-wide expression profiling during disease evolution in mdx mice. Physiol Genomics. 137(2): 119; doi: 10.1152/physiolgenomics.90370.2008.

[2] Quattrocelli et al. (2015) Mesodermal iPSC-derived progenitor cells functionally regenerate cardiac and skeletal muscle. J Clin Invest. 125(12):4463; doi: 10.1172/JCI82735.

Keywords

Myogenic differentiation; MICAL2; stem cells; muscular dystrophies.