Differentiation of murine dermal papilla cells into myogenic lineage for cell-based therapies in Duchenne muscular dystrophy

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Duchenne muscular dystrophy (DMD) is the commonest muscular dystrophy caused by the absence of dystrophin. Stem-cell-therapy in DMD is one of the more promising approaches for treatment. Multipotent stem-cells residing in the hair follicle papilla are highly plastic and are reprogrammable to bone, cartilage, haematopoietic and muscle. Dermal papilla cells (DPC) from the hair follicles of mouse whisker pad were microdissected and cultured. We showed that DPC undergo myogenic differentiation when co-cultured with different types of myoblasts including normal and dystrophic human-myoblasts. Lamin A/C staining was used to distinguish DPC and myoblast-derived myonuclei inside myotubes. DPC incorporated into myotubes and up-regulated the muscle marker myogenin in co-culture with human-myoblasts, suggesting that DPC fully underwent myogenic differentiation in these co-cultures. DPC incorporation efficiency was low in all co-cultures and differed significantly between various types of myoblast; however, no significant difference was observed between normal and dystrophic human-myoblasts. These encouraging findings suggested that the altered properties of dystrophic myoblasts did not compromise the myogenic differentiation of DPC in vitro, supporting their in vivo application and possible therapeutic potential. The in vitro effects of galectin-1, reversine and activation of the Shh signaling pathway via recombinant Shh and purmorphamine, on DPC myogenic differentiation was also evaluated. None of the treatments increased myogenin expression in DPC; but, triggering Shh signaling produced a dose-dependent pattern, whereby lower levels of signaling promoted myogenic differentiation while higher levels inhibited it. Activating Shh signaling upstream of Smo via. purmorphamine, induced a biphasic differentiative response; however, the application of rShh hindered the differentiation of both cell types. Thus, murine DPC are a readily accessible source of stem cells that can undergo myogenic differentiation in vitro. We aim to improve their differentiation efficacy to make them suitable candidates for therapeutic applications in muscle wasting disorders.

Biography

Mahsa Rashidi is MD, PhD at Children’s National Hospital, DC, affiliated to George Washington University of Medical Sciences, USA. She has finished her Medical degree at Shahid Beheshti University of Medical Sciences, Tehran, Iran. Her PhD is a joint program between George Washington University, USA and the University of Melbourne, Australia. This abstract is based on her PhD thesis, submitted to the University of Melbourne, Faculty of Medicine, Australia. Her work is focused on evaluating skin stem cells for cell-based therapies in muscular dystrophies. In her work, the effects of various dosages of several drugs/treatments on the stem cells differentiation is evaluated.

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