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Differentiation of murine dermal papilla cells into myogenic linage 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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