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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 most promising approaches for treatment. Multipotent stem cells residing in the hair follicle papilla are highly plastic and are reprogrammable to bone, cartilage, fat, 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 has up-regulated the muscle marker myogenin in co-culture with human myoblasts, suggesting that DPC fully underwent myogenic differentiation in these co-cultures. We showed that DPC incorporation efficiency was low in all co-cultures and differed significantly between various types of myoblasts. 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 were 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

Maral Rashidi is a student at School of Pharmacy at Shiraz University of Medical Sciences, Iran. She has finished her BSc degree in Biochemistry. She is currently undertaking pre-registration clinical trainings at designated pharmacies affiliated to Shiraz University. She is also conducting research on stem cells in collaboration with colleagues from other universities. Her work is focused on evaluating skin stem cells for cell-based therapies in muscular dystrophies. In her work, the effects of varoius dosages of several drugs/treatments on the stem cells differentiation is evaluated. She is also conducting research in the fields of Clinical and Herbal Pharmacology and has gathered data on 100 rare herbal medicines merely found in Iran along with their therapeutic applications. Considerable part of her work is devoted to approach the extrapolation of experimental data to the clinical trials.

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