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Defining the role of primary cilia on skin derived precursors

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Abstract

Isolated in 2001, Skin Derived Precursors (SKPs) represent a novel population of multipotent stem cells[1,2] residing at the base of hair follicle where they play a key role in defining the physiology and regeneration capacity of hair follicles and skin[3]. In order to understand how SKPs behavior is regulated in the skin, we asked whether primary cilia, microtubule bundles projected from the cell surface that transmit chemical signals between cells[4], are present in the dermal papilla and dermal sheath in-vivo and in the population of isolated SKPs. In our investigation, we performed immunohistochemistry for acetylated tubulin and showed that SKPs do have cilia. We then tested whether these cilia can be elongated following treatments of lithium chloride on these dermal precursors. We then asked whether elongation of cilia has an effect on the self-renewal capacity of SKPs and whether drugs elongating cilia can work synergistically with Platelet Derived Growth Factor (PDGF), a growth factor that we have previously shown to improve cell growth and cell division. Experiments assessing the self-renewal capacity of SKPs suggested significant increase in the diameter and the number of spherical presence when treated with lithium chloride and when lithium chloride is added in combination with PDGFβ when compared to PDGFβ alone. This suggests that signaling in cilia may influence PDGF signals causing an enhanced effect on SKP proliferation. Further experiments including knocking down primary cilia by blocking the transcription of ciliary protein using shRNA and in-vivo transplantations of lithium chloride and PDGF treated SKPs in a hair follicle formation assays will be executed to understand the key roles of primary cilia on SKPs. These studies will ultimately aim to answer whether drugs affecting cilia can function as potential therapeutic targets for autologous adult stem cell based therapies.

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