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Original article

Human platelet lysate versus minoxidil stimulates hair growth by activating anagen promoting signaling pathways

Maryam Dastan, M.S.c[a,b], Nowruz Najafzadeh, Ph.D[b,*], Ali Abedelahi, Ph.D[c], Mohammadreza Sarvi, M.S.c[d], Ali Niapour, Ph.D[b]

[a] Department of Biology, Urmia University, Urmia, Iran
[b] Research Laboratory for Embryology and Stem Cells, Department of Anatomy and Pathology, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran
[c] Department of Anatomy, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
[d] Department of Medical Mycology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Minoxidil and human platelet lysate (HPL) are commonly used to treat patients with hair loss. However, the roles of HPL versus minoxidil in hair follicle biology largely remain unknown. Here, we hypothesized that bulge and dermal papilla (DP) cells may express specific genes, including *Kras, Erk, Akt, Shh* and *β-catenin* after exposure to minoxidil or HPL. The mouse hair follicles were isolated on day 10 after depilation and bulge or DP regions were dissected. The bulge and DP cells were cultured for 14 days in DMEM/F12 medium. Then, the cells were treated with 100 μM minoxidil and 10% HPL for 10 days. Nuclear morphology was identified using DAPi staining. Reverse transcriptase and real-time polymerase chain reaction (PCR) analysis were also performed to examine the expression of *Kras, Erk, Akt, Shh* and *β-catenin* mRNA levels in the treated bulge and DP regions after organ culture. Here, we found that minoxidil influences bulge and DP cell survival ($P < 0.05$). Apoptosis in DP cells was also meaningfully decreased by HPL treatment ($P = 0.014$). In addition, *Kras, Akt, Erk, Shh* and *β-catenin* mRNA levels were changed in response to minoxidil treatment in both bulge and DP cells. HPL mediated *Erk* upregulation in both bulge and DP cells ($P < 0.05$), but *Kras* and *Akt* mRNA levels were not considerably different in the HPL-treated cells. *β-catenin* mRNA level was also significantly increased in the bulge region by HPL. We also found that *Shh* mRNA level was considerably higher in HPL-treated bulge cells than in minoxidil-treated bulge cells. In contrast, the expression of *β-catenin* and *Shh* in the DP cells was not meaningfully increased after treatment with HPL. Our results suggest that minoxidil and HPL can promote hair growth by activating the main anagen inducing signaling pathways.

1. Introduction

The hair follicle undergoes cycles of rapid growth (anagen), involution (catagen) and rest (telogen). Each hair follicle is composed of epithelial and mesenchymal compartments. The hair follicle contains a reservoir of stem cells in the bulge region of outer root sheath (ORS) [1–3]. In addition, the lower end of the anagen hair follicle is composed of transient amplifying cells and dermal papilla (DP). There are some signaling interactions between keratinocytes of the hair matrix and fibroblasts of DP. Their interactions play a critical role in development and cycling of the hair follicle. Throughout the anagen phase, the DP cells act as a signaling center to guide the surrounding epithelial cells to proliferate and migrate [4]. Hair matrix keratinocytes express β-catenin/Lef1, c-kit, c-met, FGFR2 and IGF-IR during anagen while the corresponding ligands, including Wnt5a, SCF, HGF, FGF7, and IGF-1 are expressed in the DP cells [5].

It is well-known that matrix cells stop proliferating during catagen, and catagen-inducing factors stimulate apoptosis in the hair matrix cells. In telogen, the hair follicle enters a quiescent state that can last several months [5]. It seems that initiation of new anagen depends on the activating hair follicle stem cells [6]. Major signaling pathways such as Wnt/β-catenin, and Sonic hedgehog (Shh) control hair follicle morphogenesis and are required for telogen-anagen transition [4,7].

* Corresponding author.
E-mail addresses: nowruz30@gmail.com, n.najafzade@arums.ac.ir (N. Najafzadeh).

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