HUMAN SCALP HAIR FOLLICLES EXPRESS PROSTAGLANDIN E_2 LIPID MEDIATOR AND RECEPTORS FOR PGE_2

Karzan **G**hafur **K**hidhir
Department of Biology, Faculty of Science, University of Sulaimani, Sulaimani, Kurdistan Region-Iraq.
(Accepted for publication: June 9, 2013)

ABSTRACT

The hair follicle, which is a unique characteristic of the mammals, plays a vital role in a personal appearance and self-image confidence throughout the life and hair growth disorders cause serious psychological distress. The common pathological abnormalities are abnormal hair loss (alopecia) and excessive hair growth (hirsutism), but they are poorly controlled. Therefore an improved treatment for these disorders requires a better understanding of the mechanisms regulating hair growth. Prostaglandin analogues such as latanoprost, which are used for glaucoma treatment, also makes eyelashes grow longer. The mechanism of action by which these drugs stimulate eyelash hair growth is poorly understood. To determine whether PGE_2 lipid mediator and receptors for PGE_2 (EP_2) are expressed in scalp hair follicle, electrospray tandem mass spectrometry coupled to liquid chromatography (LC/ESI-MS/MS), RT-PCR and Immunohistochemistry were carried out. Human scalp skin from non-balding areas (occipital and parietal) was obtained from healthy donors undergoing elective cosmetic surgery; with appropriate ethical approval. Isolated scalp hair follicle expresses PGE_2 lipid mediator genes and protein for EP_2. So isolated human scalp follicles contain PGE_2 lipid mediator and express genes and protein for EP_2 indicating that PGE_2 may play a vital role in regulating hair growth, which may lead to a new method for hair loss treatment.

KEYWORDS: *Alopecia, Hair Follicle, Immunohistochemistry, Lipidomics, Prostaglandin E_2 receptor, RT-PCR.*

INTRODUCTION

The most prominent skin appendage is the hair follicle, a special organ found only in the mammals which producing hair fiber. Hair follicles are found all over the body except in the glabrous skin of the lips, palms and soles. One of the most important roles of hair is thermal insulation. It's essential for them to be warm bloodedness and crucial for their evolutionary success. In human the thermoregulatory function is minor because of the reduction in large hairs, this is probably to enable cooling of their bodies by evaporating sweat, despite of remaining of hair erection in response to cold (Orentreich, 1969; Randall and Ebling, 1991).

Human hair plays essential roles in social and sexual communications in all cultures (Jansen and van Baalen 2006; Randall 2007). Hair loss disorders such as androgen-dependent male pattern baldness (androgenetic alopecia) (Hamilton 1951) or alopecia areata, a recognized autoimmune disease of both sexes (Randall 2001), although are not life threatening but they cause significant psychological distress (Girman, Rhodes, Lilly *et al.* 1998; Gulec, Tanriverdi, Duru *et al.* 2004) and has negative impact on the quality of life (Girman, Rhodes, Lilly *et al.* 1998). Unfortunately, hair loss disorders are currently poorly controlled; the existing treatments are either limited in their success rate or have unwanted side effects (Rogers and Avram 2008; Garg and Messenger 2009). Two of the main therapies for androgenetic alopecia were developed for other conditions. Minoxidil (Regaine), works by opening the ATP-sensitive potassium channels (Shorter, Farjo, Picksley *et al.* 2008), which was originally a treatment for hypertension, but this application was discontinued as it stimulated unacceptable hair growth in many areas as a side-effect (Messenger and Rundegren 2004). Finasteride (Propecia), is a hormonal treatment, which reduces androgen effects by blocking testosterone metabolism to more active 5α-dihydrotestosterone. This was initially designed for prostate disorders (Kaufman, Olsen, Whiting *et al.* 1998; Whiting, Olsen, Savin *et al.* 2003). The latest drugs reported to stimulate hair growth as an unexpected side-effect are prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) analogues, such as latanoprost, and a prostamide $F_{2\alpha}$ analogue, bimatoprost, used as eye drops to reduce intraocular pressure in glaucoma but they also stimulate eyelashes to grow longer, thicker and darker (Curran 2009). Prostaglandins are potent lipid mediators having a vast number of physiological effects (Samad, Sapirstein and Woolf 2002; Wise, Wong and Jones 2002). PGE_2 play a vital role in regulation of physiologic function but its role in human hair growth is not clear, therefore, it is important to

determine whether PGE_2 and its receptors are expressed within hair follicle or not.

Expression of PGE_2 lipid mediator in scalp hair follicle was investigated by lipidomic analysis using Electrospray tandem mass spectrometry coupled to liquid chromatography (ESI-LC-MS/MS). Expression of genes for PGE_2 receptors (EP_2) in scalp hair follicle was studied using Reverse Transcription Polymerase Chain Reaction (RT-PCR); and the expression for proteins for EP_2 receptors in the hair follicle was investigated by Immunohistochemistry.

MATERIALS AND METHODS

Hair follicle samples

Samples of hairy skin from occipital scalp region were obtained from healthy male donors undergoing elective hair transplant at Farjo medical center after getting written consent and approval from ethical committee. For lipidomic analysis the samples (n=3) were immediately placed in normal saline solution and for molecular biological investigations, the samples (n=5) were placed into sterile universal tubes (10 ml) containing RNA stabilization solution, RNA*later* (Sigma-Aldrich Ltd.) to inhibit RNases; and for immunohistochemistry the samples (n=5) were placed in cryoprotectant

Sakura Tissue-Tek O.C.T^{TM} (Raymond A Lamb Ltd, Sussex, UK). The samples were transported on ice and kept at 4°C overnight to allow tissue penetration by the RNA*later* or O.C.T^{TM} and then stored at −20 °C for further experimentation.

Scalp hair follicles in the growing phase, anagen, were microdissected individually from each skin sample under a Leica MZ8 dissecting microscope with fiber optic cool illumination using sterile equipment and plastic ware. Each sample was transferred to a Petri dish containing sterile normal saline solution for lipidomic analysis and RNA*later* for the molecular biological investigations. Samples were then cut at the level of the dermal-subcutaneous fat interface using a scalpel blade and intact anagen lower follicles were then gently pulled from the subcutaneous fat with the help of microsurgery tweezers (Agar Scientific, Stansted, UK). Isolated follicles were pooled into a fresh dish of cold normal saline solution or RNA*later* and each follicle was gently cleaned of any attached dermis or subcutaneous fat using sterile syringe needles.

Lipidomic analysis

Lipid mediators were extracted from isolated scalp anagen hair follicles using a well reported method with little modification (Masoodi and Nicolaou 2006). The lipid extracts were investigated using a targeted approach for identification and quantification of prostanoids, by utilizing electrospray tandem mass spectrometry coupled to liquid chromatography (LC/ESI-MS/MS). A multiple reaction monitoring (MRM) transitions and optimum collision energy for PGE_2 (MRM 351>271 m/z & collision energy 17 eV) was used to generate the most abundant product ions (Kempen et al., 2001; Yang et al., 2002; Masoodi and Nicolaou, 2006; Taylor et al., 2006).

The prostanoids were obtained from Cayman Chemicals (Ann Arbor, Michigan, USA). HPLC-grade ethanol, methanol, hexane, hydrochloric acid and acetonitrile from Fisher Chemicals (Loughborough, UK), HPLC-grade glacial-acetic acid and methyl formate were from Sigma-Aldrich (Dorset, UK).

To extract lipid mediators, homogenisation of isolated hair follicles was carried out in 3 ml ice-cold Milli-Q water using a sonicator (Dawe Instruments Ltd., Middlesex, UK) at 60 Hz for 3 X 2 minute intervals with 1 minute cooling down on ice in between. Extraction of lipid mediators, preparation of standards and calibration lines and LC/ESI-MS/MS analysis was carried out as described previously (Masoodi and Nicolaou 2006).

PGE_2 was quantified using calibration lines of commercially available standards (Cayman Chemicals). The amount of protein in each sample was estimated with a BioRad protein assay kit (BioRad laboratories, Herts, UK) using the Lowry method (Noble and Bailey 2009); BSA at a range of 0-1.5 dilutions in NaOH (0.5M) was used as standard. Results expressed as pg/mg of follicle protein.

Molecular biological investigations: RT-PCR

Samples

RNA was isolated from scalp anagen follicles immediately after microdissection using RNeasy Mini Kit (Qiagen, Hilden, Germany) and RNA quality was checked by agarose gel electrophoresis (1.5%).

To remove any contaminating genomic DNA the mRNA samples were treated with DNase I (Invitrogen Ltd., Paisley, UK). Briefly RNA (8 µl) was mixed with 1 µl of 10X DNase reaction buffer [200 mM Tris-HCl (pH 8.4), 20 mM

MgCl2, and 500 mM KCI] and 1 U of DNase I amplification grade for 15 min. To inactivate the DNase, the samples were incubated with 2.5 mM EDTA at 65°C for 10 min. Samples were either placed on ice for immediate cDNA synthesis or stored at -20°C until utilized. The cDNAs were synthesized immediately using the avian myeloblastosis virus (AMV) reverse transcription system (Promega, Southampton, UK) (Shorter, Farjo, Picksley *et al.* 2008). PCR amplification was performed using 50 ng cDNA in a 50 µl reaction volume containing 0.3 µM of forward and reverse primers **F**: 5'-CTTTCGCCATGACCTTCTTC-3' and **R**: 5'-GTGAAAGGCAAGGAGCAGAC-3' (Sigma-Genosys Ltd., Pamisford, UK) which were designed from human EP_2 gene sequence using the NCBI primer blast tool.

A negative control in which the cDNA was replaced with nuclease-free water was used in parallel with each PCR reaction. Amplification conditions were as follow: initial denaturation at 95°C for 7 min, followed by 35 cycles of 95°C for 30 sec, 53°C for 30 sec and 72°C for 30 sec and a final extension at 72°C for 10 min. PCR products were analyzed by gel electrophoresis on a 1.5% Tris-acetate-EDTA (TAE) agarose gel (Invitrogen Ltd.) containing 0.25 µg/ml ethidium bromide run in TAE buffer containing 0.5 µg/ml ethidium bromide at 100 V. PCR gene products were visualized and photographed using the UVitec gel documentation system (UVitec Limited, Cambridge, UK) at 312 nm wavelength using the DNA ladder to estimate gene product size.

To confirm the identity of the base pair products, the PCR process was repeated with thin-walled PCR tubes (VWR International Ltd., Poole, UK) using the thermocycler with the hot lid. The products were separated on a low-melting point 1.5% agarose gel (Invitrogen Ltd.), excised, and purified using the MinElute Gel Extraction kit (Qiagen, Crawley, UK) following the manufacturer's instructions and sequenced by Geneblitz (Sunderland, UK). Sequencing results were compared with the known published sequences using the National Center for Biotechno-logy Information (NCBI) BLAST program (http://www.ncbi.nlm.nih.gov/blast/bl2seq/wblast2.cgi).

Immunohistochemistry

To confirm EP_2 protein expression and localization of EP_2 in the hair bulb immunohistochemistry was performed. Vertical frozen sections of human occipital scalp (5 µm thick) were cut using a Leica cryostat (CM 1800) and were collected on poly-L-lysine coated slides to increase adherence. The sections were air-dried at room temperature for 1 hour and then fixed in ice-cold acetone for 10 min followed by rehydration in PBS for 10 min. The sections were incubated in 3% hydrogen peroxide in methanol for 30 min to block the endogenous peroxidase activity, accompanied by a brief rinse in PBS. The sections were incubated in 5% normal mouse serum (Sigma-Aldridge Ltd.) in PBS for 20 min to block any potential nonspecific binding. Sections were also incubated with polyclonal goat antibodies to EP_2 (Santa Cruz Biotechnology, Santa Cruz, CA, USA), at dilution 1:100 at 4°C for 18 h in a moist chamber to avoid dehydration. Antibodies were diluted in 1.5% normal mouse serum in PBS. Slides were rinsed twice in PBS for 20 min to remove any unbound primary antibody before incubation with a mouse monoclonal anti-goat biotin-conjugated secondary antibody (Sigma-Aldrich Ltd.) at 1:20 dilution with 5% normal mouse serum in PBS for 30 min. Then sections were washed twice in PBS followed by application of Extra Avidin horseradish peroxidase (Sigma-Aldridge Ltd.) diluted 1:20 with PBS for 30 min. After two further PBS washing, the antibody binding was visualized by the addition of the peroxidase substrate, 3-amino-9-ethylcarbazole (Vector Laboratories Ltd., Peterborough, UK). Formation of chromogen staining was observed under a light microscope, and the reaction was stopped by placing the slides in distilled water when sufficient color was observed. Negative controls were done by replacing the primary antibodies with PBS. Sections were counterstained in Mayer's hematoxylin, blued in Scott's tap water, and rinsed in tap water before being mounted with Aquamount (VWR International, Leicester, UK). The final stain was examined and photographed using a Nikon Eclipse 80i light microscope with a Nikon ACT-2U photographic system.

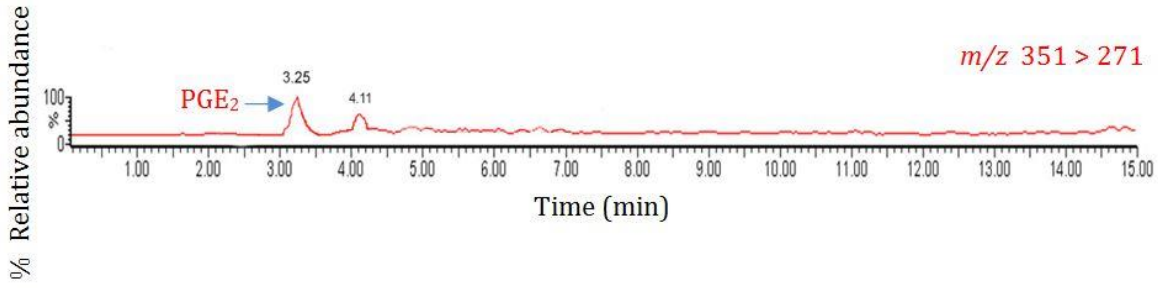
RESULTS

Prostaglandin E_2 lipid mediator expressed in human scalp hair follicle

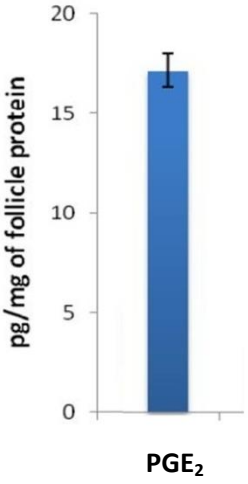
To find out whether prostaglandin E_2 (PGE_2) is present in human anagen scalp hair follicles, the expression of PGE_2 lipid mediator was

investigated in isolated anagen scalp hair follicles using LC/ESI-MS/MS. Prostanoid profiles are tissue-dependent and quantitative methodologies which need a high sensitivity because of the short half-lives and low concentrations of these compounds. The LC/ESI-MS/MS is a sensitive and quick assay appropriate to lipidomic analyses.

The LC/ESI-MS/MS analysis identified PGE_2 in scalp hair follicle (n= 3) using multiple reaction monitoring (MRM) transitions and optimum collision energy to generate the most abundant product ion for PGE_2 (Kempen, Yang, Felix *et al.* 2001; Yang, Felix, Madden *et al.* 2002; Masoodi and Nicolaou 2006; Taylor, Bruno, Frei *et al.* 2006). The limit of detection was in the range of 0.1-10 pg/µl and the limit of quantification was in the range of 0.5-20 pg/µl. The ESI-MS/MS product ion spectra revealed several prostanoids and the LC/ESI-MS/MS chromatographic separation of the compounds on a C18 column using a gradient of two acetonitrile-based solvents confirmed the PGE_2 presence (Figure 1a). The quantity of the identified PGE_2 was worked out as concentration per mg of protein in the sample as the mean ± SEM from three different experiments each analyzed in duplicate. The amount of PGE_2 lipid mediator identified was (17.1920 ± 2.2 pg/mg of follicle protein) (Figure 1b).



(a)



(b)

Figure 1 Prostaglandin E_2 lipid mediators exist in human hair follicles
(a) The chromatogram of PGE_2 lipid mediators. The run time of the assay was 30 min including a 10 min wash cycle programmed to run before the next injection into the electrospray tandem mass spectrometry.
(b) Profile of the PGE_2 naturally present in human scalp anagen hair follicles using LC/ESI-MS/MS. Value is the mean ± SEM of 3 samples of human scalp hair follicles from adult men; each sample was analyzed in duplicate.

Human scalp hair follicles express the genes for PGE_2 receptor (EP_2)

To identify the expression of genes for the EP_2 in human scalp hair follicles, RT-PCR was carried out using cDNA from scalp skin samples. Total RNA was successfully extracted from the lower follicles of individually microdissected anagen scalp follicles (n=5), and the quality of each individual's cDNA was confirmed by PCR using primers for β-actin

(Figure 2a). RT-PCR reactions using specific primers for EP_2 developed precise product band for EP_2: 505 bp (Figure 2b); sequence analysis confirmed these genes when compared against the relevant human sequence in GenBank.

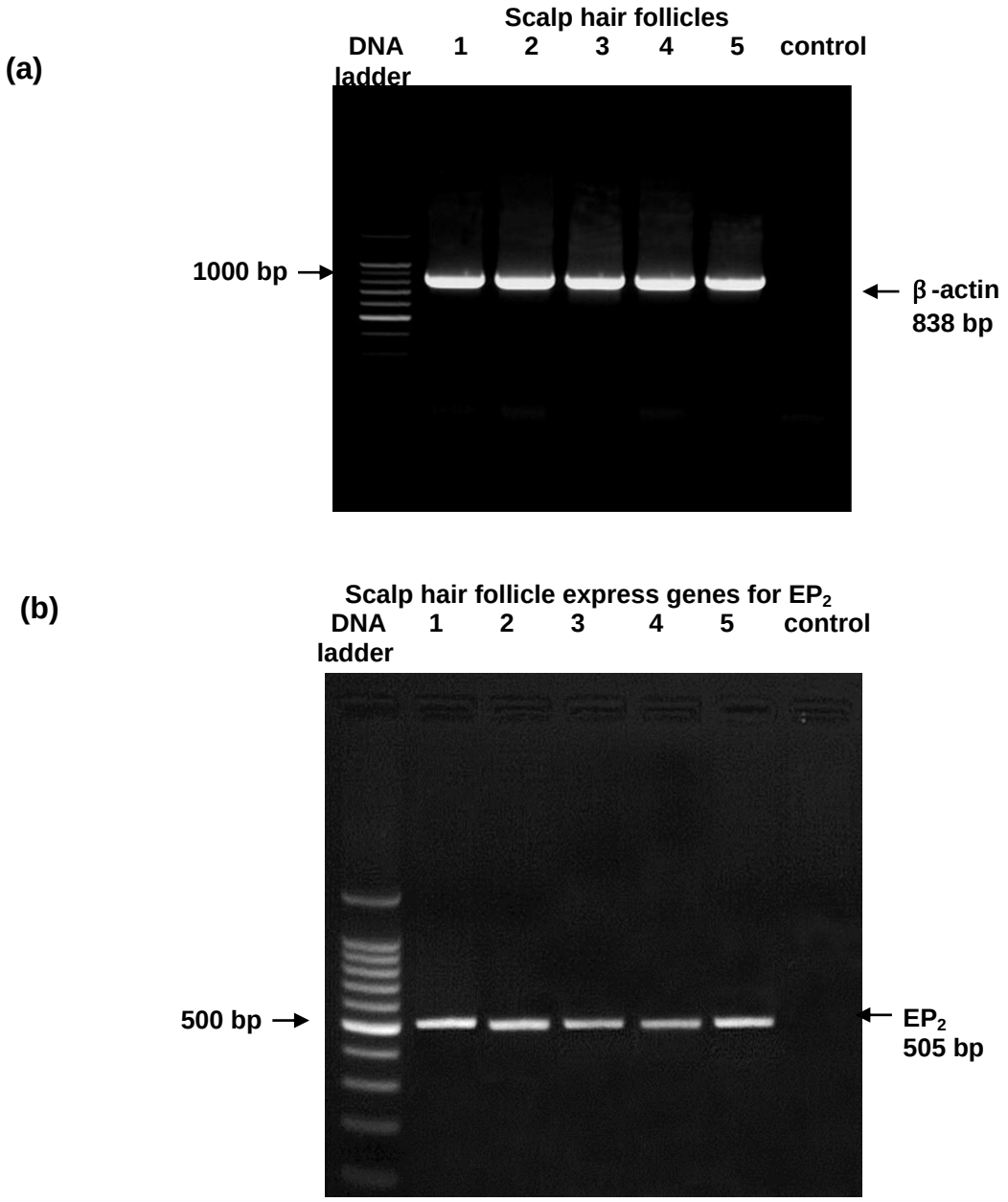


Figure 2: PGE_2 receptor (EP_2) genes are expressed in human scalp hair follicles
The PCR products (30 µl) of hair follicle cDNAs (n=5) were analysed by agarose gel electrophoresis. To check the quality of each individual's cDNA, PCR was carried out using primers for the positive control, housekeeping gene, β-actin. All cDNAs showed bands of expected size for β-actin 838 bp (a). The EP_2 PCR products showed bands corresponding to the PGE_2 receptor (505 bp) (b).

Localization of PGE_2 receptor protein in scalp hair follicles by immunohistochemistry

Frozen scalp skin sections were stained by an antibody to EP_2 which displayed strong staining in the dermal papillae and the connective tissue sheath surrounding the hair bulb (Figure 3b), but there was no staining in the epithelial keratinocytes or the melanocytes (Figure 3a) indicating the expression of EP_2 protein only in the dermal fibroblast tissue.

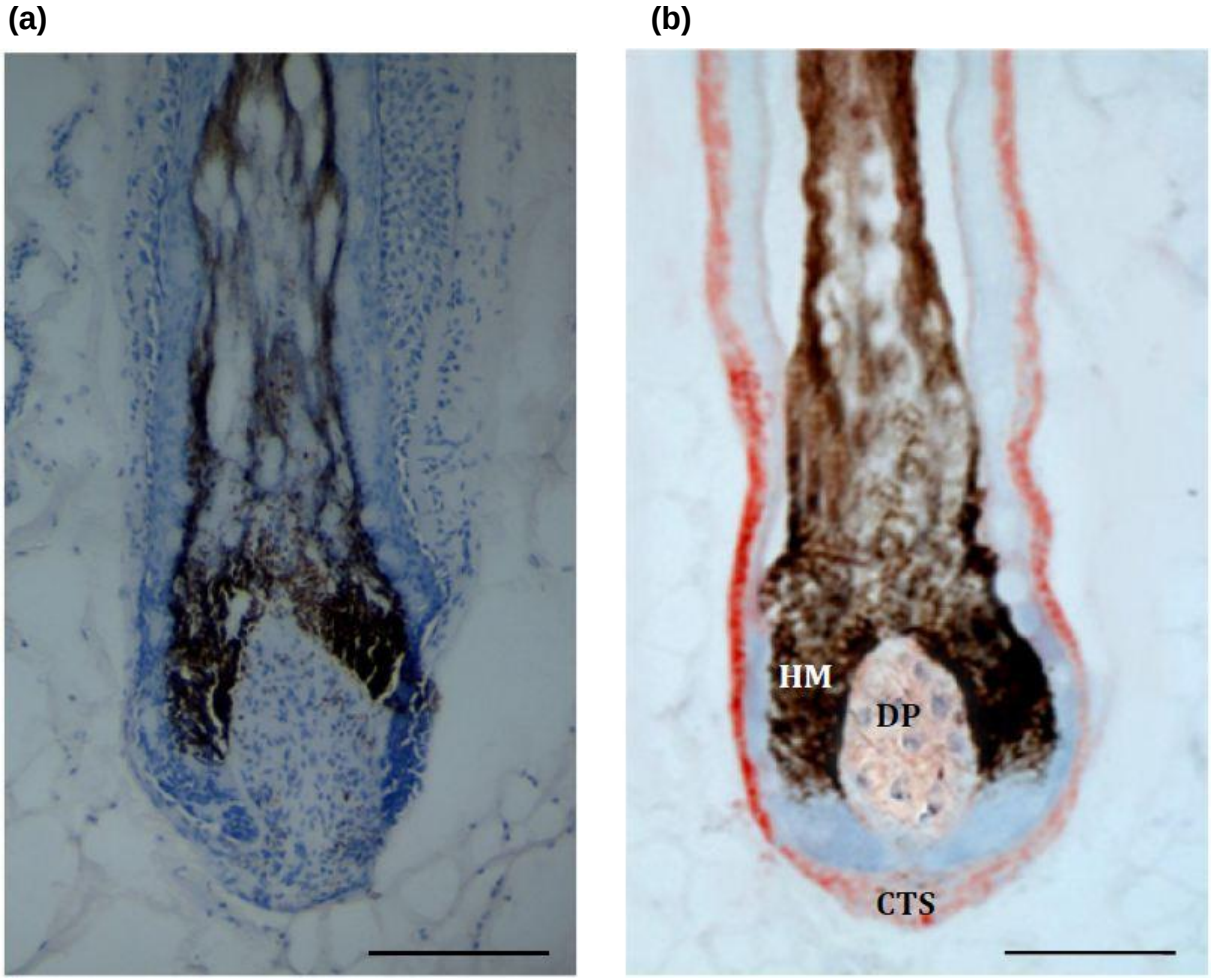


Figure 3 Localization of EP_2 in human hair follicle by Immunohistochemistry
Immunohistochemistry was performed using a goat polyclonal antibody to EP_2 (at 1:100 dilution).
Absence of staining in the negative control where the primary antibody was replaced with 1.5% normal mouse serum
(a). EP_2 protein was localized in the cells of the dermal papilla (DP) and connective tissue sheath (CTS) surrounding the hair bulb and lower follicle but not in the epithelial cells or melanocytes of the hair bulb matrix
(b). DP: dermal papilla, CTS: connective tissue sheath; HM: hair matrix. Red: positive staining; blue: hematoxylin counterstain. Scale bar = 150μm

DISCUSSION

Lipidomic approaches was conducted to study the *in vivo* presence of PGE_2 lipid mediator in hair follicles isolated from human scalp skin from 3 persons. Liquid chromatography electrospray tandem mass spectrometry (LC/ESI-MS/MS) of follicle lipid extracts identified PGE_2 (Figure 1a). The amount of naturally occurring PGE_2 lipid mediator detected in scalp hair follicle was (17.1920 ± 2.2 pg/mg protein) (Figure 1b). The levels of the PGE_2 were lower than those previously reported in human myometrium tissue at term gestation (Durn, Marshall, Farrar *et al.* 2010). The eicosanoids are known to have significant physiological roles in the skin including repairs of cutaneous integrity and the restoration of skin function after injury (Ziboh, Miller and Cho 2000).

The identification of EP_2 gene and protein in the dermal papilla and connective tissue sheath of hair follicle, plus the identification of other prostanoid receptor genes expression in the dermal papilla by Colombe (Colombe, Michelet and Bernard 2008) strongly support the hypothesis that PGE_2 act directly on hair follicles via intracellular receptors. The dermal papilla determines the type of hair formed by a follicle by making paracrine factors to control other follicular functions (Jahoda, Horne and Oliver 1984; Jahoda 1992) and the lower follicular connective tissue sheath can substitute this function (Reynolds, Lawrence, Cserhalmi-Friedman *et al.* 1999). Reports of prostaglandin metabolizing enzymes in human scalp dermal

papilla cells (Colombe, Vindrios, Michelet *et al.* 2007; Colombe, Michelet and Bernard 2008) support this localization in the dermal papilla. The absence of any relevant prostanoid receptors from the bulb keratinocytes which form the hair or the melanocytes which produce the pigment and from the bulge region which is the site of epithelial stem cells (Sotiropoulou, Candi, Mascre *et al.*) and melanocyte stem cells (Nishimura, Granter and Fisher 2005), strongly suggests that the dermal papilla is coordinating follicular responses of increased pigmentation and growth. This is probably via altering its production of paracrine factors which influence the activity of the bulb keratinocytes and melanocytes.

Overall, these experiments showed that human scalp hair follicle contain PGE_2 lipid mediator and receptors for PGE_2, supporting the paracrine mode of action of prostanoids. Since the development of new treatments for distressing hair growth disorders, such as alopecia, is hampered by our lack of understanding of hair follicle biology, the specific effects of PGE_2 on hair follicles require further analysis. Interestingly, the present treatment for alopecia, minoxidil, has been reported to increase prostaglandin synthesis in cultured dermal papilla cells (Michelet, Commo, Billoni *et al.* 1997). Overall, our conclusion is that prostaglandin related drugs seem to offer a new method for treating alopecia.

REFERENCES

Colombe, L., J. F. Michelet, et al. (2008). "Prostanoid receptors in anagen human hair follicles." Exp Dermatol **17**(1): 63-72.

Colombe, L., A. Vindrios, et al. (2007). "Prostaglandin metabolism in human hair follicle." Exp Dermatol **16**(9): 762-769.

Curran, M. P. (2009). "Bimatoprost: a review of its use in open-angle glaucoma and ocular hypertension." Drugs Aging **26**(12): 1049-1071.

Durn, J. H., K. M. Marshall, et al. (2010). "Lipidomic analysis reveals prostanoid profiles in human term pregnant myometrium." Prostaglandins Leukot Essent Fatty Acids **82**(1): 21-26.

Garg, S. and A. G. Messenger (2009). "Alopecia areata: evidence-based treatments." Semin Cutan Med Surg **28**(1): 15-18.

Girman, C. J., T. Rhodes, et al. (1998). "Effects of self-perceived hair loss in a community sample of men." Dermatology **197**(3): 223-229.

Gulec, A. T., N. Tanriverdi, et al. (2004). "The role of psychological factors in alopecia areata and the impact of the disease on the quality of life." Int J Dermatol **43**(5): 352-356.

Hamilton, J. B. (1951). "Patterned loss of hair in man; types and incidence." Ann N Y Acad Sci **53**(3): 708-728.

Jahoda, C. A. (1992). "Induction of follicle formation and hair growth by vibrissa dermal papillae implanted into rat ear wounds: vibrissa-type fibres are specified." Development **115**(4): 1103-1109.

Jahoda, C. A., K. A. Horne, et al. (1984). "Induction of hair growth by implantation of cultured dermal papilla cells." Nature **311**(5986): 560-562.

Jansen, V. A. and M. van Baalen (2006). "Altruism through beard chromodynamics." Nature **440**(7084): 663-666.

Kaufman, K. D., E. A. Olsen, et al. (1998). "Finasteride in the treatment of men with androgenetic alopecia. Finasteride Male Pattern Hair Loss Study Group." J Am Acad Dermatol **39**(4 Pt 1): 578-589.

Kempen, E. C., P. Yang, et al. (2001). "Simultaneous quantification of arachidonic acid metabolites in cultured tumor cells using high-performance liquid chromatography/electrospray ionization tandem mass spectrometry." Anal Biochem **297**(2): 183-190.

Masoodi, M. and A. Nicolaou (2006). "Lipidomic analysis of twenty-seven prostanoids and isoprostanes by liquid chromatography/electrospray tandem

mass spectrometry." Rapid Commun Mass Spectrom **20**(20): 3023-3029.

Messenger, A. G. and J. Rundegren (2004). "Minoxidil: mechanisms of action on hair growth." Br J Dermatol **150**(2): 186-194.

Michelet, J. F., S. Commo, et al. (1997). "Activation of cytoprotective prostaglandin synthase-1 by minoxidil as a possible explanation for its hair growth-stimulating effect." J Invest Dermatol **108**(2): 205-209.

Nishimura, E. K., S. R. Granter, et al. (2005). "Mechanisms of hair graying: incomplete melanocyte stem cell maintenance in the niche." Science **307**(5710): 720-724.

Noble, J. E. and M. J. Bailey (2009). "Quantitation of protein." Methods Enzymol **463**: 73-95.

Randall, V. A. (2001). "Is alopecia areata an autoimmune disease?" Lancet **358**(9297): 1922-1924.

Randall, V. A. (2007). "Hormonal regulation of hair follicles exhibits a biological paradox." Semin Cell Dev Biol **18**(2): 274-285.

Reynolds, A. J., C. Lawrence, et al. (1999). "Trans-gender induction of hair follicles." Nature **402**(6757): 33-34.

Rogers, N. E. and M. R. Avram (2008). "Medical treatments for male and female pattern hair loss." J Am Acad Dermatol **59**(4): 547-566; quiz 567-548.

Samad, T. A., A. Sapirstein, et al. (2002). "Prostanoids and pain: unraveling mechanisms and revealing therapeutic targets." Trends Mol Med **8**(8): 390-396.

Shorter, K., N. P. Farjo, et al. (2008). "Human hair follicles contain two forms of ATP-sensitive potassium channels, only one of which is sensitive to minoxidil." FASEB J **22**(6): 1725-1736.

Sotiropoulou, P. A., A. Candi, et al. "Bcl-2 and accelerated DNA repair mediates resistance of hair follicle bulge stem cells to DNA-damage-induced cell death." Nat Cell Biol **12**(6): 572-582.

Taylor, A. W., R. S. Bruno, et al. (2006). "Benefits of prolonged gradient separation for high-performance liquid chromatography-tandem mass spectrometry quantitation of plasma total 15-series F-isoprostanes." Anal Biochem **350**(1): 41-51.

Whiting, D. A., E. A. Olsen, et al. (2003). "Efficacy and tolerability of finasteride 1 mg in men aged 41 to 60 years with male pattern hair loss." Eur J Dermatol **13**(2): 150-160.

Wise, H., Y. H. Wong, et al. (2002). "Prostanoid signal integration and cross talk." Neurosignals **11**(1): 20-28.

Yang, P., E. Felix, et al. (2002). "Quantitative high-performance liquid chromatography/electrospray ionization tandem mass spectrometric analysis of 2- and 3-series prostaglandins in cultured tumor cells." Anal Biochem **308**(1): 168-177.

Ziboh, V. A., C. C. Miller, et al. (2000). "Significance of lipoxygenase-derived monohydroxy fatty acids in cutaneous biology." Prostaglandins Other Lipid Mediat **63**(1-2): 3-13.

HUMAN SCALP HAIR FOLLICLES EXPRESS PROSTAGLANDIN E_2 LIPID MEDIATOR AND RECEPTORS FOR PGE_2

Summary

Human hair has a vital role in a people's appearance and hair growth disorders cause serious psychological distress. The common abnormalities such as abnormal hair loss (alopecia) and excessive hair growth (hirsutism) are poorly controlled. Therefore a better treatment for hair disorders requires a better understanding of the mechanisms regulating hair growth. Prostaglandin analogues such as latanoprost, which are used for glaucoma treatment, also make eyelashes grow longer as a side effect. To determine whether PGE_2 lipid mediator and the receptors for PGE_2 (EP_2) are expressed in scalp hair follicle, electrospray tandem mass spectrometry coupled to liquid chromatography (LC/ESI-MS/MS), RT-PCR and Immunohistochemistry were carried out. Isolated scalp hair follicle expresses PGE_2 lipid mediator and the genes and protein for EP_2. So isolated human scalp follicles contain PGE_2 lipid mediator and receptors for PGE_2 indicating that PGE_2 may play role in regulating hair growth, therefore, PGE_2-related drugs may lead to a new method for hair loss treatment.

ڕەگی مووی سەر پرۆستاگلاندین E2 وە پرۆتینی وەرگری بۆ پرۆستاگرندین E2 ی تێدایە

پوختە

موو خاسیەتێکی تایبەتە بە زیندەوەرە شیردەرەکان وە دەورێکی کارگەری هەیە لە دەرکەوتنی ڕووخسار و باوەر بەخۆبوونی مرۆڤ لە ژیانیدا، وە ئەم نەخۆشیانەی کە ڕوو ئەدات لە گەشەی موودا کاریگەری دەروونی هەیە لەسەر کەسەکان .

باوترینی حاڵەتە ناسروشتییانەی کە ڕووئەدات بریتیە لە وەرینی مووی سەر و زیاد بوونی لە خانماندا ، کە تائێستا چارەسەری تەواوەتی بۆ نەدۆزراوەتەوە. بۆیە دۆزینەوە چارەسەرێکی کاریگەر بۆ ئەم حاڵەتانەپێویستی بە باشتر تێگەیشتنە لە میکانیزمی ڕێکخستنی گەشەی موو.

داڕێژراوەکانی پرۆستاگلاندینەکانی وەکو لاتانۆ پرۆست کە بۆ چارەسەری بەرزی پەستانی چاو بەکاردێت، ئەبێتە هۆی زیادکردنی گەشەی برژانگی چاو وەکو کاریگەی لاوەکی.

میکانیزمی ئیش کردنی ئەم پێکهاتە کیمیاییانە لەسەر موو بە تەواوەتی نەزانراوە .

بۆ دۆزینەوەی بوونی PGE_2 وە وەرگرەکانی لە مووی سەری مرۆڤ دا RT-PCR و IHS وە LC/ ESI-MS/NS بەکار هێنرا وە مووی سەر لەو کەسانەوە وەرگیرا کە نەشتەرگەری ڕووانەوەی مووی سەریان بۆ ئەنجام دەدرا.

ئەم تویژینەوەیە دەریخست کە مووی سەری مرۆڤ چەوری PGE_2 ی تێدایە لەگەڵ جین و پرۆتین بۆ وەرگری PGE_2 کە بریتییە لە EP_2 کە ئەوە دەردەخات PGE_2 ڕۆڵی هەیە لە ڕێکخستنی گەشەی مووی سەردا.

محتوى دهون البروستوكلاندينز ومستقبلات PGE2 في بصيلات الشعر في راس الانسان

الخلاصة:

ان بصيلات الشعر تعتبر خاصية بحتة للثدييانت تلعب دورا مهما في مظهر الشخص وصورته خلال حياته حيث ان الخلل في نمو بصيلات الشعر تسبب مشاكل نفسية . واكثر انواع امرضية الغير طبيعية هي الصلع في الرجال ونمو الشعر الزائد في النساء والتي لم يتم السيطرة عليها بصورة تامة عليها . وعليه فان العلاج المثالي للموضوع يتطلب معرفة كاملة بميكانيكية تنظيم نمو الشعر. ان مشتقات البروستوكلاندين والتي تستعمل لعلاج داء الزرقاء، يعتبر كمصدر لزيادة طول الرموش . ولتحديد امكانية وجود دهون PEG2 ومستقبلاتها في بصيلات الشعر في الراس، تم استخدام جهاز (LC/ESI-MS/MS) و RT-PCR وكيمياء الانسجة المناعية (IHC). اظهرت النتائج احتواء بصيلات الشعر على هذه الدهون وجينات مستقبلات PGE2 والتي تدل عليها، قد تلعب دورا مهما في تنظيم نمو الشعر والتي تؤدي الى ظهور طرق جديدة لعلاج فقدان وتساقط الشعر.