2013
대 한 모 발 학 회
제12차 Hair Forum

- 일시: 2013년 8월 17일(토) 15:00-18:30
- 장소: 대전 유성 호텔아드리아 3층 그랜드볼룸

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2013. 8. 17(토) **대전 유성 호텔아드리아**

일 정 표

오후

3:00-3:10 **개회사 및 일정소개** ····· 김도원 회장 / 이원수 총무이사

1부: 자유연제 발표

3:10-3:20 **How can we enhance follicular penetration? (*In vivo* preliminary study)**
····· 가톨릭의대 강 훈 교수 / 6

3:20-3:30 **Novel role of placental growth factor in hair growth**
····· 서울의대 윤선영 연구원 / 11

3:30-3:40 **Expression patterns of PHLDA-1, TGF-β1/β2, and p63 in follicular tumors**
····· 동아의대 전수영 전공의 / 29

3:40-3:50 **Klotho is an important regulatory factor for human hair growth and hair cycle change** ····· 원주의대 김성해 연구원 / 41

3:50-4:00 **Distribution and maturation of integral hair lipid based barrier in human hair follicle according to the hair keratinization** ····· 원주의대 피용천 연구원 / 51

4:00-4:10 **Therapeutic effect of 308nm excimer laser on alopecia induced C3H/HeJ mice**
····· 인하의대 문종혁 전공의 / 62

4:10-4:20 **Effects of home used microneedle divece on pattern hair loss**
····· 경북의대 채수열 전공의 / 64

4:20-4:30 **Pressure alopecia: Clinical presentation and prognosis**
····· 경희의대 노승희 전공의 / 73

4:30-4:50 **Coffee Break**

4:50-5:00 **대한모발학회 관련 주요 현안업무 소개** ····· 이원수 총무이사

2부: 7th World Congress for Hair Research Review

2013

대한모발학회

제12차 Hair Forum

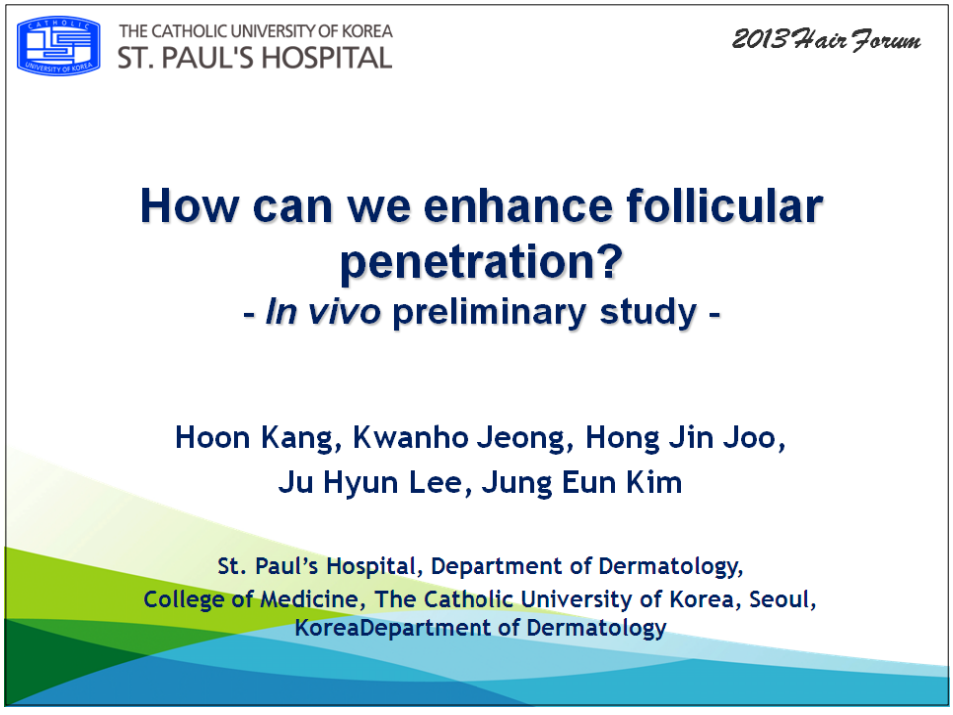
제 1 부 : 자유연제 발표

The Korean Hair Research Society

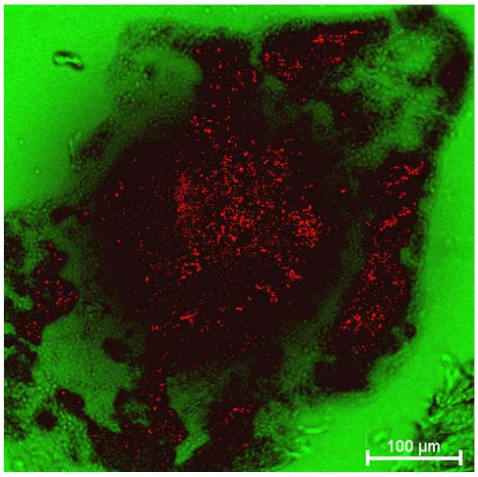
How can we enhance follicular penetration?
- *In vivo* preliminary study -

**Hoon Kang, Kwanho Jeong, Hong Jin Joo,
Ju Hyun Lee, Jung Eun Kim**

St. Paul's Hospital, Department of Dermatology,
College of Medicine, The Catholic University of Korea,
Seoul, KoreaDepartment of Dermatology



- **Titanium dioxide microparticles in the follicular orifices**



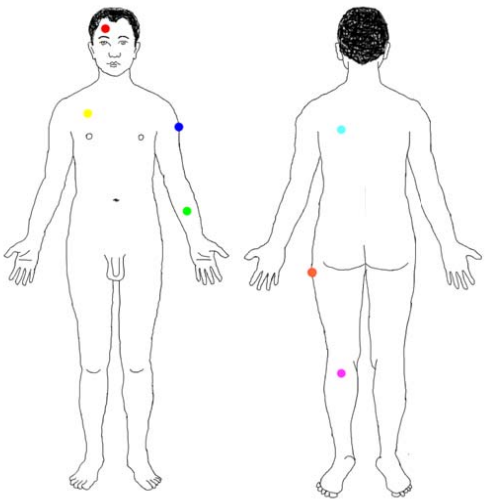
Osmium tetra oxide staining of a tape in combination with LSM measurement

Can vellus hair follicles form a relevant reservoir for topically applied substances ?

Study design

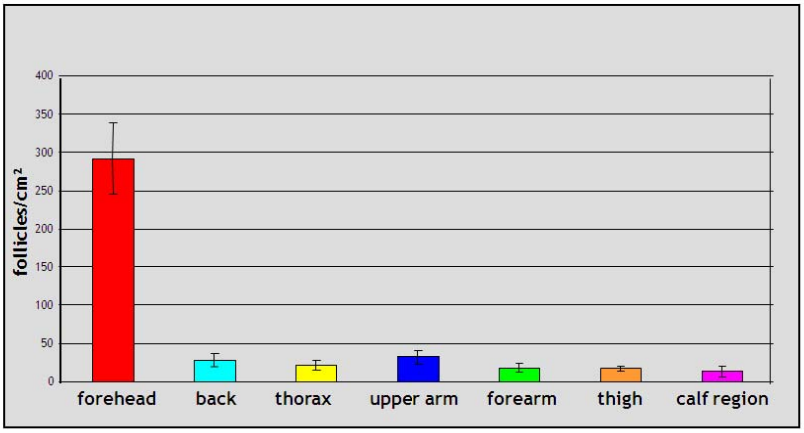
- 6 healthy volunteers with normal body mass indices
- Cyanoacrylate skin surface biopsies were taken from 7 different regions of the body, free of terminal hair and measured with light microscopy and a special software imaging system (analySIS®).

Position of skin areas

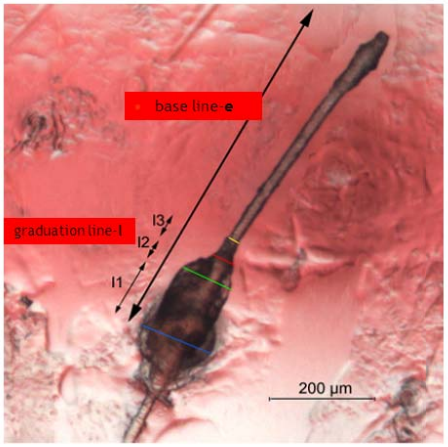


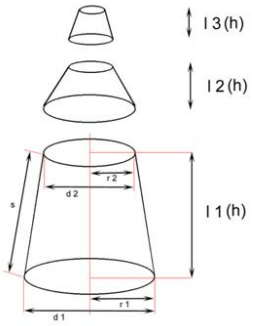
1. forehead
2. thorax
3. back
4. upper arm
5. forearm
6. thigh
7. calf region

Follicular density



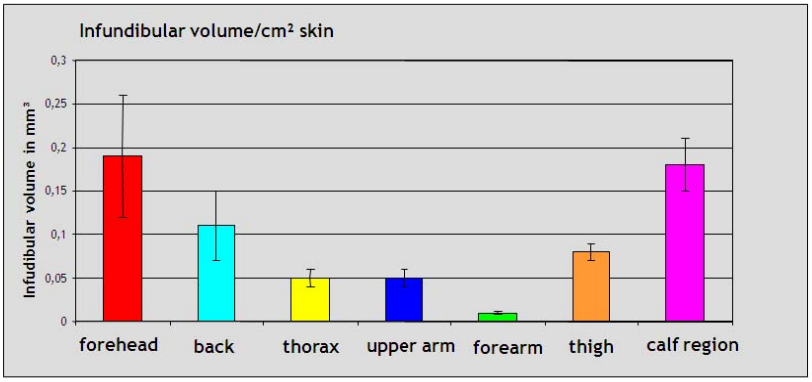
Measurement and calculation





- $V = \pi/12\ h(d_1^2 + d_2^2 + d_1d_2)$
- $A = \pi s(r_1 + r_2)$
- $s^2 = (r_1 + r_2)^2 + h^2$

Infundibular volume



Novel role of placental growth factor in hair growth

Sun-Young Yoon[1,2,3],Seong Jin Jo[1,2,3], Chang Yup Shin[1,2,3], Jong-Yeon Shin[4,5], Jong-Il Kim[4,5], Ohsang Kwon[1,2,3*], Kyu Han Kim[1,2,3*]

[1]Department of Dermatology, Seoul National University College of Medicine, Seoul, Korea; [2]Institute of Human-Environment Interface Biology, Seoul National University Medical Research Center, Seoul, Korea; [3]Laboratory of Cutaneous Aging and Hair Research, Biomedical Research Institute, Seoul National University Hospital, Seoul, Korea; [4]Genomic Medicine Institute (GMI), Medical Research Center, Seoul National University, Seoul, Korea; 5Department of Biochemistry and Molecular Biology, Seoul National University College of Medicine, Seoul, Korea.

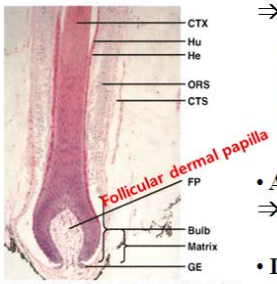
The dermal papilla (DP) comprises specialized mesenchymal cells at the bottom of the hair follicle and plays a pivotal role in hair formation, anagen induction and the hair cycle. In this study, DPs were isolated from human hair follicles and serially subcultured. From each subculture at passage 1, 3, and 5 (n = 4), we compared gene expression profiles using mRNA sequencing. Among the growth factors that were down-regulated in later passages of human DP cells (hDPCs), placental growth factor (PlGF) was selected. We confirmed that the mRNA and protein expression levels of PlGF significantly decreased following subculture of the cells. PlGF prevented cell death by increasing the levels of phosphorylated extracellular signal-regulated kinase (ERK) and cyclin D1 and promoted survival by up-regulation of phosphorylated Akt and Bcl2, as determined by Western blotting. We also found that PlGF enhanced hair shaft elongation in *ex vivo* hair organ culture. Furthermore, PlGF significantly accelerated hair follicle growth and markedly prolonged anagen hair growth in an *in vivo* model of depilation-induced hair regeneration. Our results suggest that PlGF plays a role in the promotion of hair growth and therefore may serve as an additional therapeutic target for the treatment of alopecia.

Novel role of placental growth factor in hair growth

모발성장에 미치는 태반성장인자의 새로운 역할

Sun-Young Yoon

❖ *Background and significance*



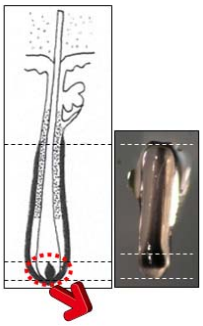
PHYSIOLOGICAL REVIEWS Vol. 81, No. 1, January 2001

- **Dermal papilla (DP)**
  ⇒ **specialised mesenchymal cells at the bottom of the hair follicle**
  carry nutrients to enhance new hair growth
  contain receptors for androgens and other diverse hormones
  play a pivotal role in hair formation, anagen induction, and hair cycle

- **Abnormalities in the functions of the DP**
  ⇒ **main causes of imbalanced follicle growth cycling and hair loss**

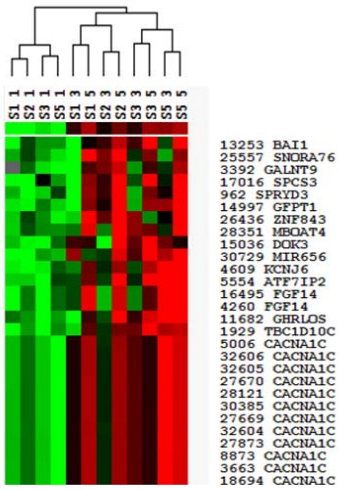
- **DP number dictates the size and shape of the hair**
- **Degeneration of the DP population in mice**
  ⇒ **leads to the types of hair thinning and loss**

❖ *In our study,*



- Cultured DP cells
  ⇒ significantly lost hair inductive activity following subculture of the cells
- Studies of specific genes related to the function of DP in the HF
  ⇒ necessary to further our knowledge of human hair growth
- In this study, DP
  ⇒ isolated from human hair follicles
  ⇒ subcultured at passages 1, 3, and 5 (n=4)
- In each subculture at passages 1, 3, and 5 (n=4), we compared the gene expression profiles of the cells using mRNA sequencing.

❖ From gene expression analysis, in later passages of the cells



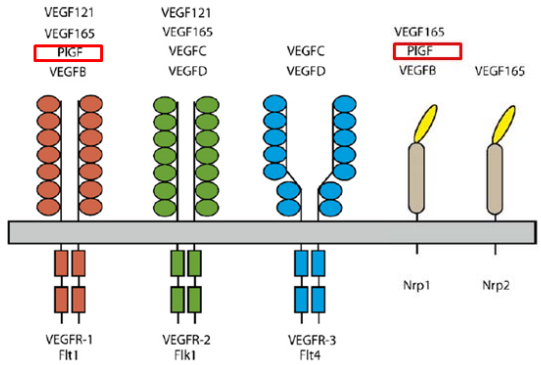
- Hierarchical Clustering
  : In each subculture at passages 1, 3, and 5 (n=4)
- Statistical test : F-test
- P-value < 0.01
  : 232 up-regulated genes
  : 2,249 down-regulated genes

Table 1. Downregulated growth factors following subculture of hDPCs (passages 1,3, and 5)

Gene	Definition	P-Value	Gene ontology-biological function	Accession
PlGF	placental growth factor	0.0037	regulation of cell division	NM_002632
HDGF	hepatoma-derived growth factor	0.0002	cell proliferation	NM_004494
PDGFRA	platelet-derived growth factor receptor	0.0034	reproductive developmental process	NM_006206
FGFR1	fibroblast growth factor receptor 1	0.0072	skeletal system development	NM_015850
TGFB3	transforming growth factor, beta 3	0.0016	tube development	NM_003239
IGF2	insulin-like growth factor 2	0.0013	regulation of cell growth	NM_001127598

● **PlGF (placental growth factor)**

• member of VEGF(vascular endothelial growth factor) subfamily (42% homology)
• a key molecule in angiogenesis during embryogenesis.
• potent angiogenic/permeability factor in neoangiogenesis during wound healing
• binds to VEGF receptor-1 (Flt-1), or neuropilin-1
• functions in survival, proliferation and migration in endothelial cells, smooth muscle cells and hematopoietic myeloid cells and etc.
• cellular location : cell membrane, cytosol, secreted



Biochimica et Biophysica Acta 1762 (2006) 1109–1121

Angiogenesis takes place during anagen phase to support hair growth whereas inhibiting angiogenesis leads to a retardation of anagen development.

Mecklenburg L, Tobin DJ, Müller-Röver S, *et al*. (2000) Active hair growth (anagen) is associated with angiogenesis. J Invest Dermatol 114:909-16.
Odorisio T, Cianfarani F, Failla CM, *et al*. (2006) The placenta growth factor in skin angiogenesis. J Dermatol Sci 41:11-9.
Yano K, Brown LF, Detmar M (2001) Control of hair growth and follicle size by VEGF-mediated angiogenesis. J Clin Invest 107:409-18.

In adult skin, PlGF expression is up-regulated in association with both physiological and pathological neoangiogenesis, such as hair follicle cycles, wound healing and ischemia.

Cianfarani F, Zambruno G, Brogelli L, *et al*. (2006) Placenta growth factor in diabetic wound healing: altered expression and therapeutic potential. The American journal of pathology 169:1167-82.
De Falco S (2012) The discovery of placenta growth factor and its biological activity. Exp Mol Med 44:1-9.
Failla CM, Odorisio T, Cianfarani F, *et al*. (2000) Placenta growth factor is induced in human keratinocytes during wound healing. J Invest Dermatol 115:388-95.
Odorisio T, Cianfarani F, Failla CM, *et al*. (2006) The placenta growth factor in skin angiogenesis. J Dermatol Sci 41:11-9.

Overexpressed PlGF strongly increased vascularization and enhanced vessel permeability.

Odorisio T, Schietroma C, Zaccaria ML, *et al*. (2002) Mice overexpressing placenta growth factor exhibit increased vascularization and vessel permeability. J Cell Sci 115:2559-67.
Oura H, Bertoncini J, Velasco P, *et al*. (2003) A critical role of placental growth factor in the induction of inflammation and edema formation. Blood 101:560-7.

PlGF is expressed in the outer root sheath keratinocytes during anagen phase of the hair follicle cycle, whereas expression of PlGF was not observed in catagen and telogen phase.

Cianfarani E, Zaccaria M, Odorisio T, *et al*. (2005) Expression of placenta growth factor in mouse hair follicle cycle. G Ital Dermatol Venereol 140:497-504.

Perifollicular angiogenesis was correlated with up-regulation of VEGF expression in follicular keratinocytes of the outer root sheath during anagen phase They suggested that transgenic overexpression of VEGF improved perifollicular vascularization and accelerated murine hair re-growth.

Yano K, Brown LF, Detmar M (2001) Control of hair growth and follicle size by VEGF-mediated angiogenesis. J Clin Invest 107:409-18.

❖ *Research goals,*

✓ **PlGF**
⇒ **increased cutaneous vascularization and vascular permeability**

✓ **Effect of PlGF on human hair growh**
⇒ **has not been investigated**

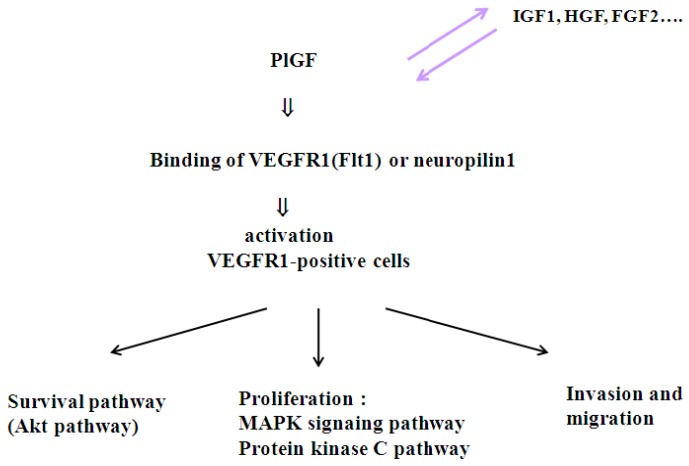
Our purpose,

1) Elucidate unknown function of PlGF in hair follicle cells

2) Evaluate the biological role of PlGF

3) be used as additional therapeutic target for treatment of alopecia

in hair follicle cells,



◆ PlGF mRNA and protein levels were significantly decreased in later passages of hDPCs.

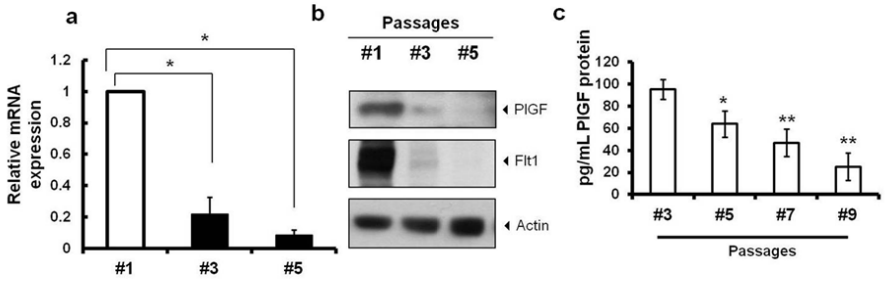


Figure 1. PlGF mRNA and protein levels were significantly decreased in later passages of hDPCs. DPs were isolated from human HFs and subcultured (passages 1, 3, and 5). (**a**) Total RNA from hDPCs was isolated, and mRNA expression levels were measured by quantitative real-time PCR. (**b**) hDPCs were lysed and analyzed by Western blotting. (**c**) Supernatants of the different passages of hDPCs were collected, and the amount of PlGF secretion was measured by ELISA. Results are expressed as the mean ± standard error (SE). $^{**}P < 0.01$, $^{*}P < 0.05$ versus passage 1.

◆ Expression of PlGF and Flt1.

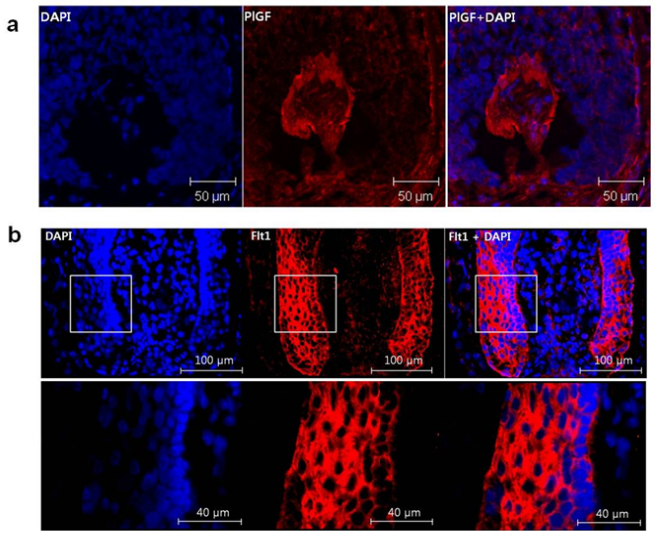


Figure 2. Expression of PlGF and Flt1. Immunofluorescent staining of PlGF (**a**, red fluorescence) and Flt1 (**b**, red fluorescence) was performed in hHFs. Nuclei were stained by DAPI (blue fluorescence). Original magnification ×400, ×1000

◆ Expression of PlGF and Flt1.

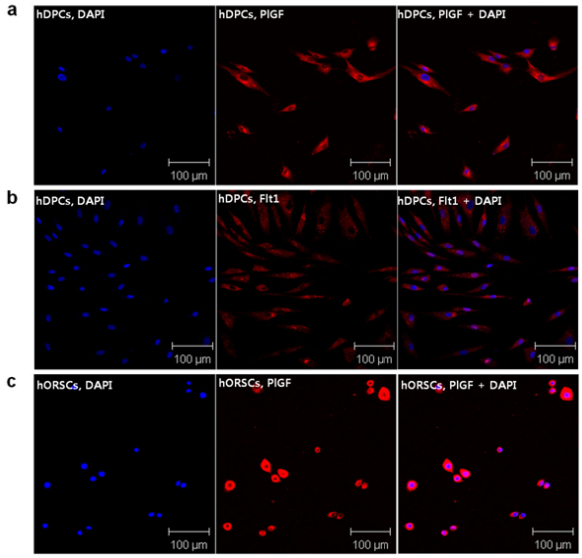


Figure 3. Expression of PlGF and Flt1. Immunofluorescent staining of PlGF (**a** and **c** red fluorescence) and Flt1 (**b**, red fluorescence) was performed in hDPCs (**a** and **b**), or hORSCs (**c**). Nuclei were stained by DAPI (blue fluorescence). Scale bar = 100 μm; Original magnification ×200

◆ PlGF enhanced hair shaft elongation in *ex vivo* hair organ culture.

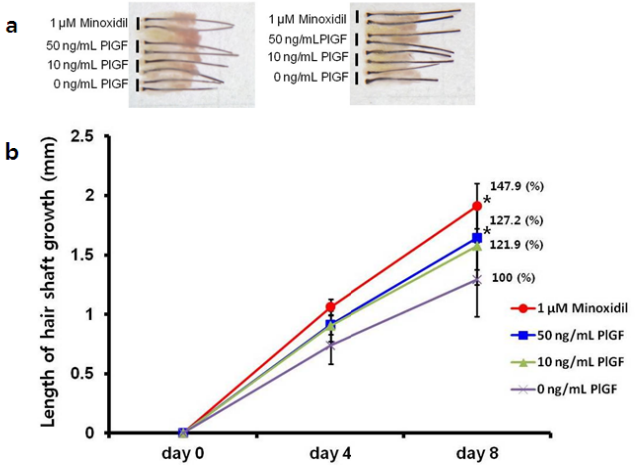


Figure 4. PlGF enhanced hair shaft elongation in *ex vivo* hair organ culture. (**a** and **b**) HF elongation was measured directly at 4 and 8 days of culture using a stereo microscope. Results are expressed as the mean ± SE. **P* < 0.05 versus the control. Numbers beside next to the lines are percentage ratios compared to the control.

◆ PlGF induced proliferation in hair matrix keratinocytes.

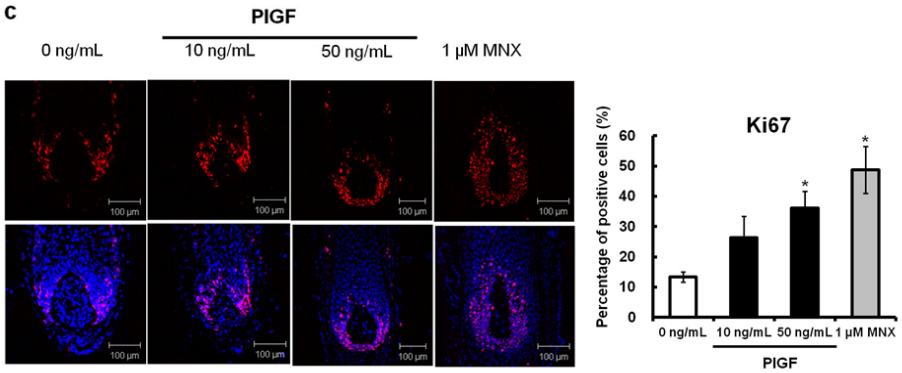


Figure 4. PlGF induced proliferation in hair matrix keratinocytes. (**c**) 5-μm frozen sections of hHFs from 3 different individuals were analyzed for proliferation (Ki67-positive, red fluorescence) in the keratinocytes of hair bulb. Nuclei were counterstained with DAPI (blue fluorescence). For quantitative analyses, the number of Ki67-positive cells was counted and normalized to the number of DAPI-stained cells. Results are expressed as the mean ± SE. **P* < 0.05 versus the control. Numbers beside next to the lines are percentage ratios compared to the control. Scale bar = 100μm; Original magnification ×200

◆ Anti-Flt1 decreased hair shaft elongation in *ex vivo* hair organ culture.

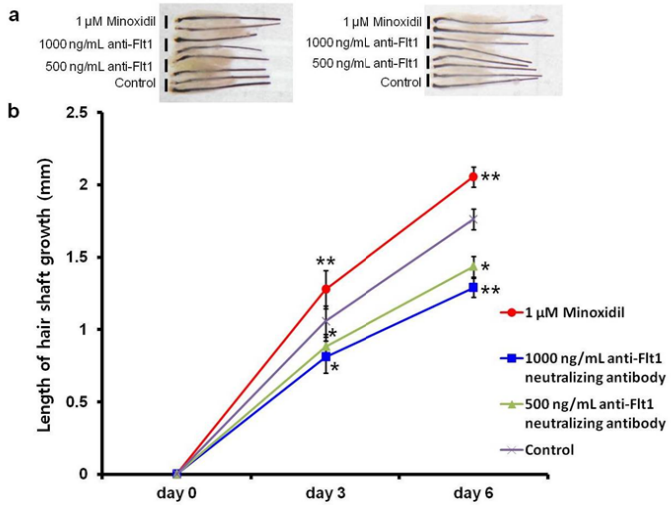


Figure 5. Anti-Flt1 decreased hair shaft elongation in *ex vivo* hair organ culture. (**a** and **b**) HF elongation was measured directly at 3 and 6 days of culture using a stereo microscope. Results are expressed as the mean ± SE. ***P* < 0.01, **P* < 0.05 versus the control.

Hair matrix keratinocytes are important for hair growth and DP regulates the activity of matrix keratinocytes

Botchkarev VA, Kishimoto J (2003) Molecular control of epithelial-mesenchymal interactions during hair follicle cycling. J Investig Dermatol Symp Proc 8:46-55

In this study, PlGF increased the proliferation of human hair matrix keratinocytes, as determined by immunofluorescence staining for Ki-67, a proliferation marker.

We also confirmed that in human HFs, Flt-1, a PlGF receptor was highly expressed in hair matrix keratinocytes.

Interestingly, we found that PlGF enhanced hair shaft elongation in *ex vivo* hair organ culture, whereas hair growth was inhibited by blockade of Flt-1

These results suggest the possibility that PlGF, a paracrine factor secreted from DPCs, acts on neighboring follicular matrix keratinocytes and has a direct stimulatory effect on hair growth by binding Flt-1

◆ PlGF induced proliferation of hDPCs.

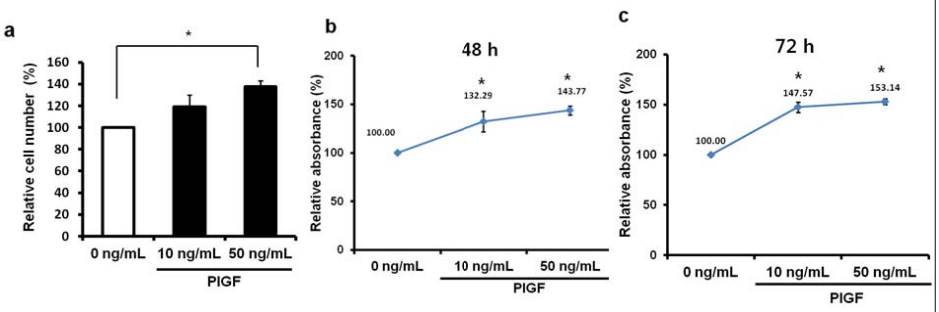


Figure 6. PlGF induced proliferation of hDPCs. (**a**) hDPCs were incubated with the indicated concentrations of PlGF. After 72 h, the cell number was measured using a hemocytometer and expressed as cell number of the treated samples relative to that of untreated controls. (**b** and **c**) For the quantification of cell proliferation, a BrdU-ELISA assay was used. hDPCs were incubated with the indicated concentrations of PlGF. After 48 h (**b**) or 72 h (**c**), incorporated BrdU levels were measured by ELISA and expressed as the absorbance of the treated samples relative to that of the untreated control. Results are expressed as the mean ± SE. Numbers on the lines are percentages compared to control. *$P < 0.05$ versus the control.

◆ PlGF enhanced mRNA expression of genes related to hair induction and proliferation of hDPCs.

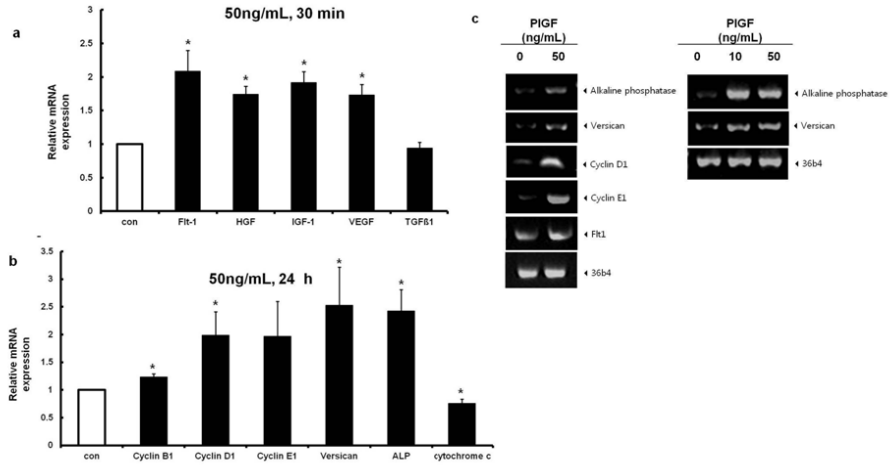


Figure 7. PlGF enhanced mRNA expression of genes related to hair induction and proliferation of hDPCs. (**a** and **b**) Cells were treated with 50 ng/mL PlGF (**a** and **b**) for 30 min (**a**) or 24 h (**b**), total RNA was isolated, and mRNA expression was analyzed by quantitative real-time PCR. (**c**) hDPCs were treated with the indicated concentrations of PlGF for 24 h and total RNA was isolated, and mRNA expression was analyzed by RT-PCR. Results are expressed as the mean ± SE. **P* < 0.05 versus the control. ALP, alkaline phosphatase.

◆ PlGF siRNA down-regulated the expression of genes related to the stimulation of hair growth.

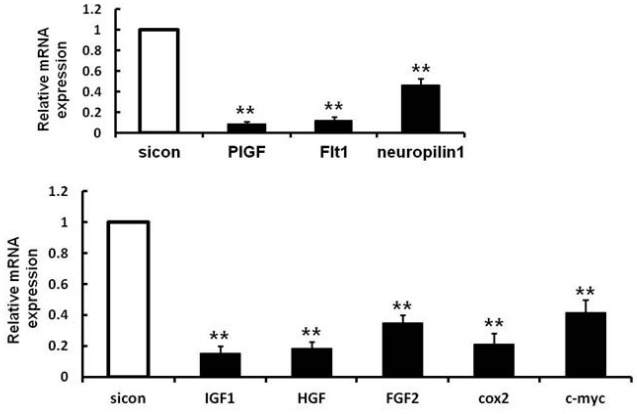


Figure 8. PlGF siRNA down-regulated the expression of genes related to the stimulation of hair growth. hDPCs were transfected with PlGF siRNA. After 24 h, total RNA was isolated, and mRNA expression was analyzed by quantitative real-time PCR. Results are expressed as the mean ± SE. ***P* < 0.01 versus control siRNA.

◆ PlGF promoted the survival of hDPCs.

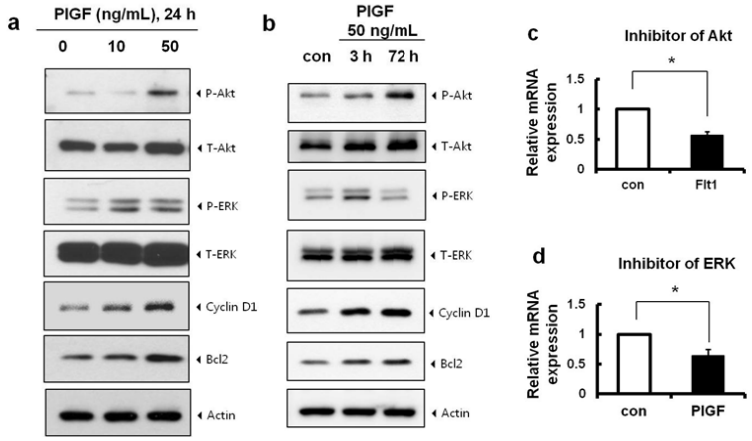


Figure 9. PlGF promoted the survival of hDPCs. (**a** and **b**) hDPCs were incubated with the indicated concentrations of PlGF. After 24 h (**a**) or 72 h (**b**), cells were lysed and analyzed by Western blotting. (**c** and **d**) hDPCs were treated with 1μM LY294002 (an inhibitor of Akt, **c**) or PD98059 (an inhibitor of ERK, **d**) for 48 h (**c**) or 24 h (**d**). Total RNA was isolated and mRNA expression was analyzed by quantitative real-time PCR. Results are expressed as the mean ± SE. **P* < 0.05 versus the control.

◆ PlGF siRNA suppressed the survival of hDPCs.

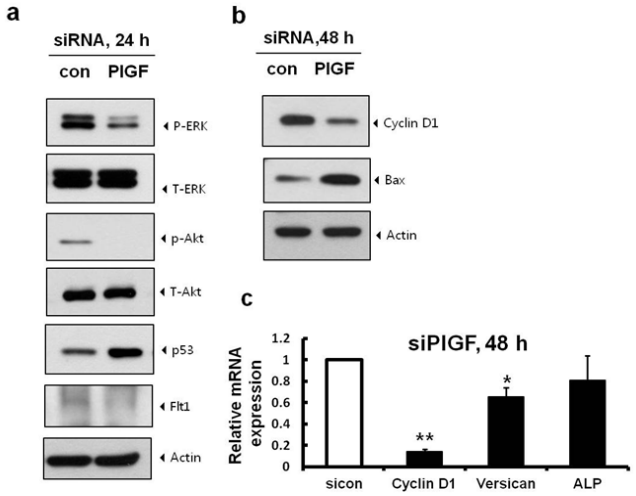
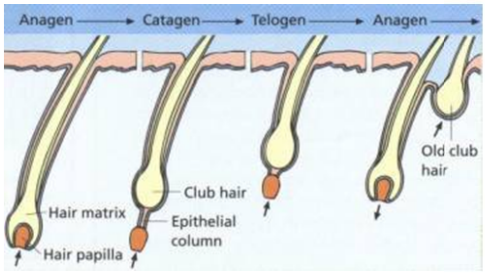


Figure 10. PlGF siRNA suppressed the survival of hDPCs. hDPCs were transfected with PlGF siRNA. After 24 h (**a**) or 48 h (**b**), cells were lysed and analyzed by western blotting. (**c**) hDPCs were transfected with PlGF siRNA. After 48 h, total RNA was isolated, and mRNA expression was analyzed by quantitative real-time PCR. ***P* < 0.01, **P* < 0.05 versus control siRNA. Results are expressed as the mean ± SE.

In vivo study,

whether PlGF accelerates hair regrowth and prolongs the anagen phase.

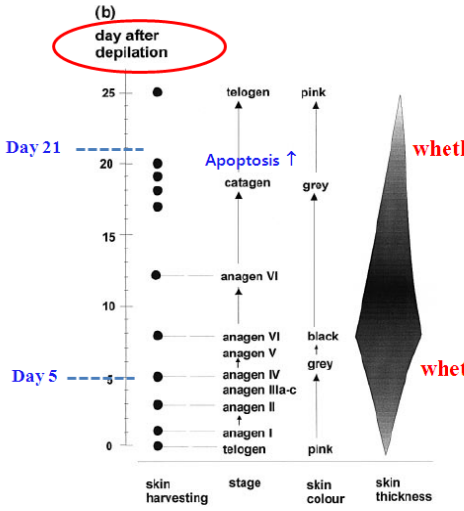
The back skin of 8-week-old C57BL/6 female mice in the telogen phase
⇒ depilated using wax in order to induce synchronized anagen stage.
Treatment with vehicle, PlGF, MNX via ID injection twice a day.



Anagen : rapid growth
Catagen : apoptosis-driven regression
Telogen : relative quiescence

http://www.pgbeautygroomingscience.com/the-hair-growth-cycle.php

A Comprehensive Guide for the Accurate Classification of Murine Hair Follicles in Distinct Hair Cycle Stages THE JOURNAL OF INVESTIGATIVE DERMATOLOGY



whether PlGF prolongs anagen phase

whether PlGF accelerates hair re-growth

Figure 2. (*a*) Time-scale for the hair cycle in female C57BL/6 mice during the first 14 wk after birth. (*b*) Time-scale for the hair cycle in female C57BL/6 mice and changes of skin pigmentation and skin thickness after depilation.

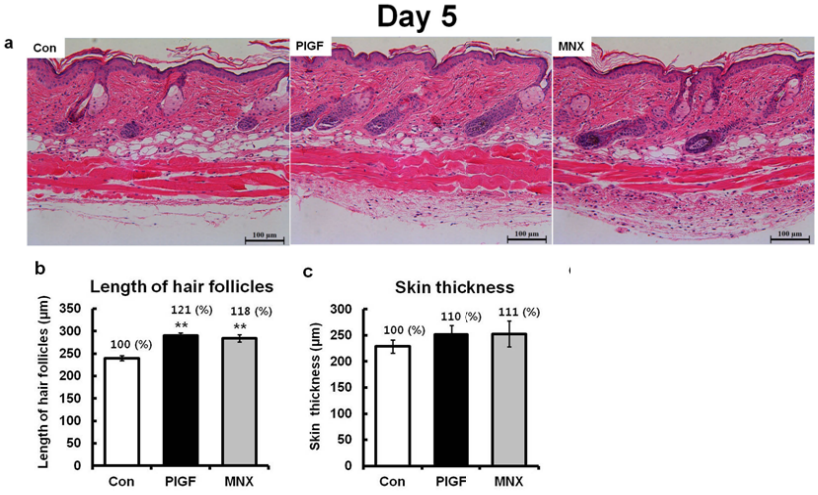


Figure 11. PlGF accelerated hair follicle growth and prolonged anagen hair growth. (a and d) At day 5 (a) or day 21 (d), skin samples were obtained for histological analysis of H&E-stained paraffin sections. (b and c) At day 5, the length of the hair follicles skin thickness was measured in H&E-stained sections. (e) Bulb diameter was measured at the level of the largest diameter ("Auber's line") of hair bulbs. (f) Apoptosis (TUNEL-positive, green fluorescence) was analyzed in the keratinocytes of the hair bulb. Numbers on the bars are percent ratios compared to the control. Results are expressed as the mean ± SE. $^{**}P < 0.01$ versus the control group. Scale bar = 100μm; Original magnification ×200

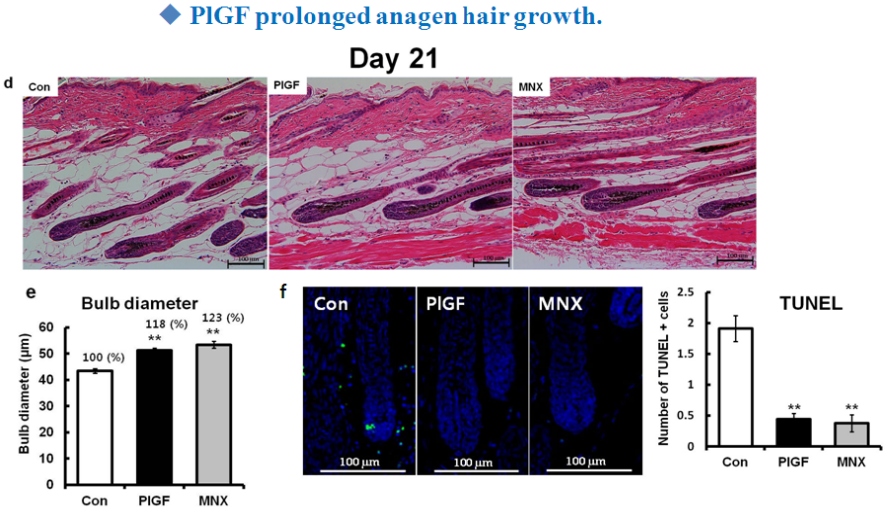


Figure 11. PlGF accelerated hair follicle growth and prolonged anagen hair growth. (a and d) At day 5 (a) or day 21 (d), skin samples were obtained for histological analysis of H&E-stained paraffin sections. (b and c) At day 5, the length of the hair follicles skin thickness was measured in H&E-stained sections. (e) Bulb diameter was measured at the level of the largest diameter ("Auber's line") of hair bulbs. (f) Apoptosis (TUNEL-positive, green fluorescence) was analyzed in the keratinocytes of the hair bulb. Numbers on the bars are percent ratios compared to the control. Results are expressed as the mean ± SE. $^{**}P < 0.01$ versus the control group. Scale bar = 100μm; Original magnification ×200

◆ PlGF increase the average area of vessels.

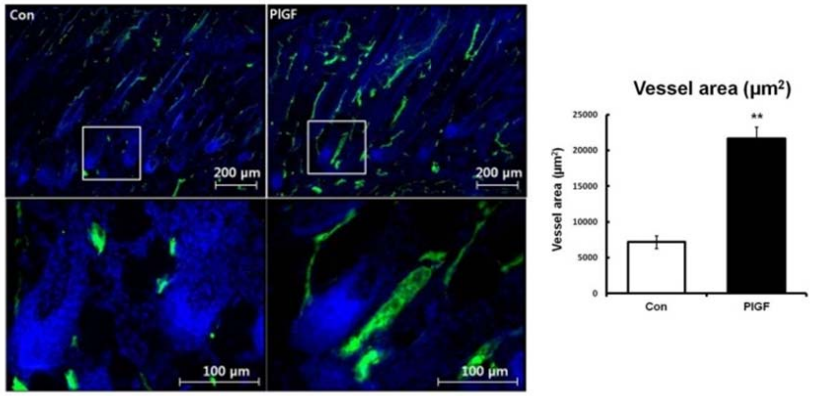


Figure 12. PlGF increase the average area of vessels. At day 21, skin samples were obtained for immunofluorescent staining of CD31 (blood vessel marker, green fluorescence). Nuclei were stained by DAPI (blue fluorescence). Results are expressed as the mean ± SE. $^{**}P < 0.01$ versus the control group. Original magnification ×100, ×400

◆ PlGF induced the recruitment of macrophages.

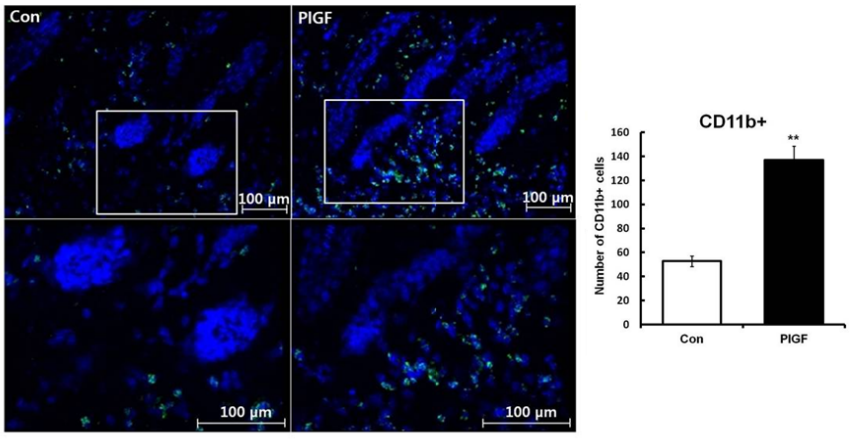


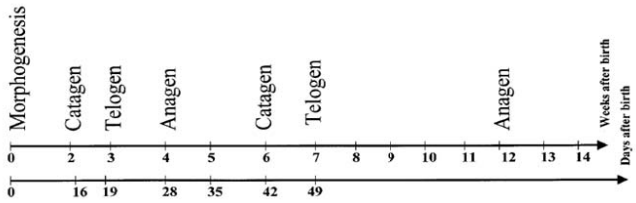
Figure 13. PlGF induced the recruitment of macrophages. At day 21, skin samples were obtained for immunofluorescent staining of CD11b (macrophage marker, green fluorescence). Nuclei were stained by DAPI (blue fluorescence). Results are expressed as the mean ± SE. $^{**}P < 0.01$ versus the control group. Original magnification ×200, ×400

In vivo study ; anagen induction test

whether PlGF induces anagen hair growth in telogen mouse skin

The back skin of 8-week-old C57BL/6 female mice in the telogen phase
⇒ was shaved with clipper
Treatment with vehicle, PlGF, MNX via ID injection twice a day.

● Time-scale for the hair cycle in C57BL/6 mice



THE JOURNAL OF INVESTIGATIVE DERMATOLOGY, VOL. 117, NO. 1 JULY 2001

◆ PlGF induced anagen hair growth in telogen mouse skin.

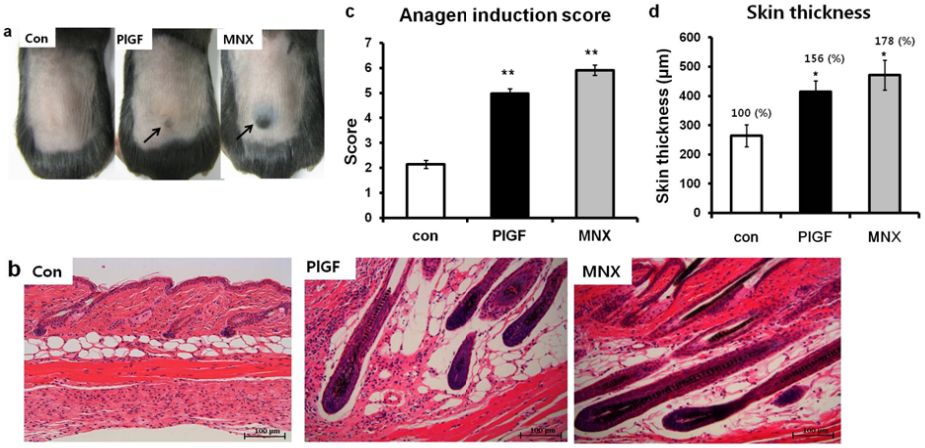


Figure 14. PlGF induced anagen hair growth in telogen mouse skin. (**a**) At day 41, we observed that hair growth was restricted to the site of intradermal injection in PlGF- and MNX-treated C57BL/6 mice. (**b** and **c**) At day 41, skin was obtained for histological analysis of H&E-stained paraffin sections. Hair cycle scores (HCSs) were calculated and by using assigned score values (telogen = 1, anagen I to VI = 2 to 7). (**d**) Skin thickness was measured as the distance from the epidermis to the subcutaneous fat. Numbers on the bars are relative percentages compared to control. Results are expressed as the mean ± SE. $^{**}P < 0.01$, $^{*}P < 0.05$ versus the control group. Scale = 100 μm; Original magnification ×200

❖ Summary and Conclusion

1) PlGF mRNA expression and protein levels were significantly decreased in later passages of hDPCs: Q-PCR, western, Elisa

2) Expression of PlGF and Flt1 in hDPCs and HF was confirmed.
: immunofluorescence staining

3) PlGF enhanced hair shaft elongation in *ex vivo* hair organ culture.

4) Anti-Flt1 decreased hair shaft elongation in *ex vivo* hair organ culture.

5) PlGF induced proliferation in hair matrix keratinocytes.
: immunflurorescent staining of Ki-67

6) PlGF induced proliferation. : measurement of cell number, Brdu-ELISA assay

7) PlGF enhanced mRNA expression of genes related to hair induction and proliferation of hDPCs : Q-PCR (IGF1, HGF, VEGF, Versican, Alkaline phosphatase, cyclinD1 and etc.)

❖ Summary and Conclusion

8) PlGF siRNA down-regulated the expression of genes related to the stimulation of hair growth. : Q-PCR (IGF1, HGF, FGF2, Cox2, c-myc)

9) PlGF promoted the survival of hDPCs.
: western (P-Akt, P-Erk, cyclinD1, Bcl2)

10) PlGF siRNA suppressed the survival of hDPCs.
: western (P-Akt, P-Erk, P53, cyclinD1, Bax)

11) PlGF accelerated hair follicle growth and prolonged anagen hair growth.
: Histological analysis *in vivo*, immunflurorescent staining of TUNEL

12) PlGF increase the average area of vessels. : immunflurorescent staining of CD31

13) PlGF induced the recruitment of macrophages. : immunflurorescent staining of CD11b

14) PlGF induced anagen hair growth in telogen mouse skin. : Histological analysis *in vivo*

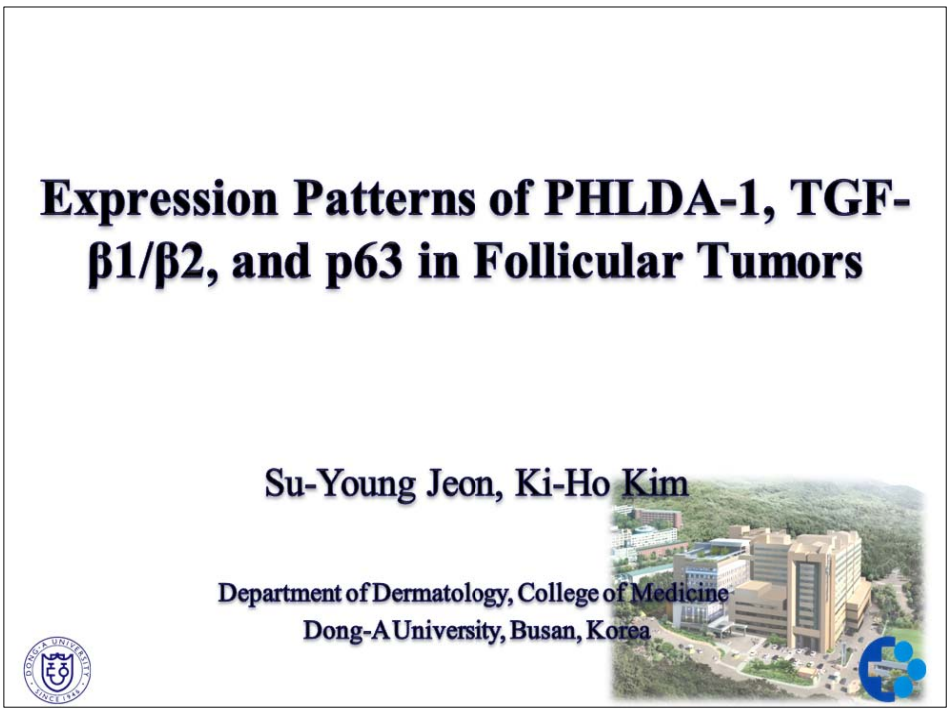
Although additional studies are necessary, from our results, we demonstrated for the first time that PlGF significantly stimulated hair growth in both *in vitro* and *in vivo* models. We propose that PlGF has a certain role as new inducer of hair growth and therefore may serve as an additional therapeutic target for the treatment of alopecia.

Thank You For your time

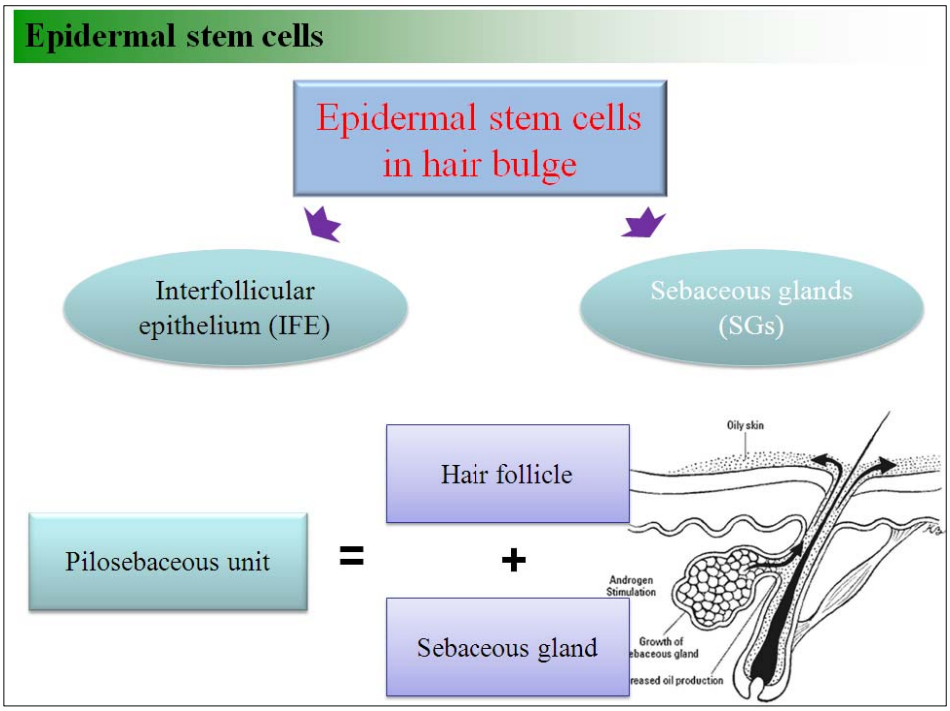
Expression patterns of PHLDA-1, TGF-β1/β2, and p63 in follicular tumors

Su-Young Jeon, Ki-Ho Kim

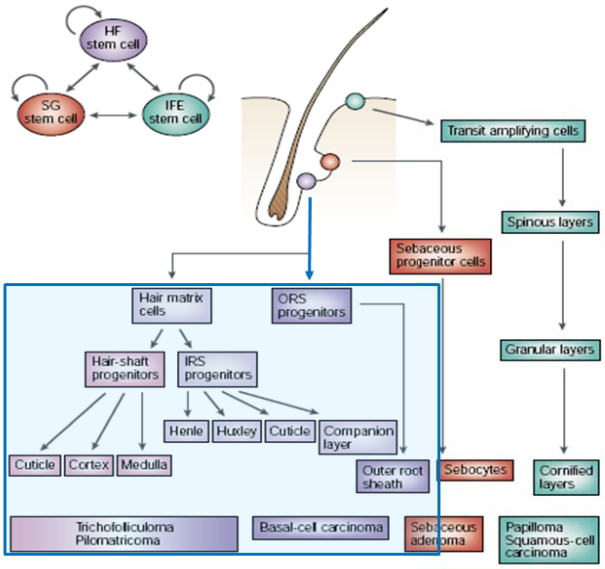
Department of Dermatology, College of Medicine
Dong-A University, Busan, Korea



Epidermal stem cells



Tumorigenesis of follicular tumors

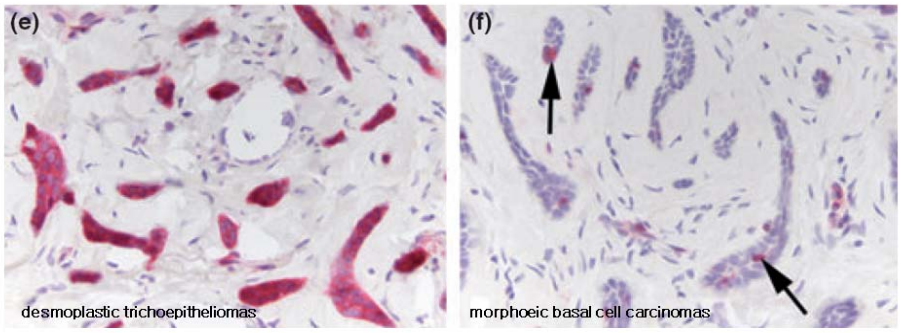


Niemann C, Watt FM.Designer skin: lineage commitment in postnatal epidermis. Trends Cell Biol 2002;12:185-192.

PHLDA-1

i) PHLDA-1

- a marker for hair bulge stem cells
- prominently expressed in the hair follicle bulge of terminal and vellus hair follicles
- differentiates between desmoplastic trichoepitheliomas and nonulcerated morphoeic basal cell carcinomas



Sellheyer K, Krahl D. PHLDA1 (TDAG51) is a follicular stem cell marker and differentiates between morphoeic basal cell carcinoma and desmoplastic trichoepithelioma. Br J Dermatol 2011;164:141-147.

p63

ii) p63

- a member of the p53 gene family
- has complex functions in the epithelial morphogenesis
- the expression level correlates with tumor grading and/or aggressive behavior in epithelial tumors such as squamous cell carcinoma
- can be useful in distinguishing primary cutaneous adnexal tumor from metastatic adenocarcinoma to the skin

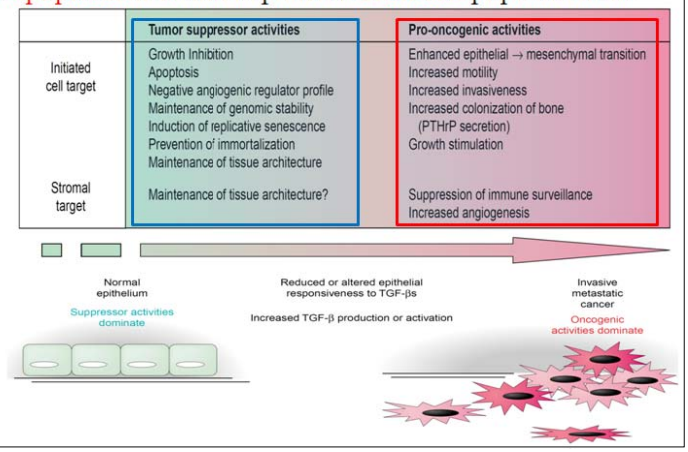
Gu X, Coates PJ, Boldrup L, Nylander K. p63 contributes to cell invasion and migration in squamous cell carcinoma of the head and neck. Cancer Lett 2008;263:26-34.

TGF-βs

iii) TGF-βs

- acts pro-oncogenic effects and also as a tumor suppressor

- TGF-β signaling plays an important role in regulating proliferation, differentiation, and apoptosis of distinct epithelial stem cell populations in hair follicles



Objectives of Study

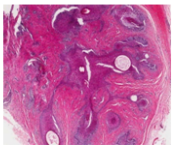
• To date, it remains unclear whether the expression levels of these a fore mentioned molecules correlate with tumor grading in follicular lineage tumors

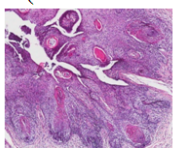
• In addition, the relationships between follicular tumors of these molecules in tumorigenesis are not fully understood.

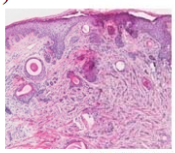
→ To elucidate the expression of PHLDA-1, TGF-β1/β2 and p63 in benign and malignant tumors of the hair lineage and their importance in the degree of differentiation of the corresponding tumors.

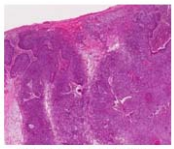
Materials & Methods

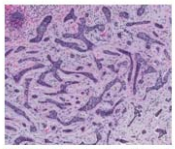
- Materials : 16 cases in total
  - Follicular tumors (total: 16 cases)


Trichofolliculoma (n = 2)


Pilar sheath acanthoma (n = 3)


Desmoplastic trichoepithelioma (n = 3)


Trichilemmal carcinoma (n = 4)


Moepheic basal cell carcinoma (n = 4)

- All slides of sebaceous and follicular tumors were reviewed and then the confirmed samples were included into this study

Tumors	*Classification*	*Number of cases*
Trichofolliculoma	Benign	2
Pilar sheath acanthoma	Benign	3
Desmoplastic trichoepithelioma	Benign	3
Trichilemmal carcinoma	Malignant	4
Morpheic basal cell carcinoma	Malignant	4
Total		16

Immunohistochemistry

- Primary antibodies

Name	*Clone*	*Dilution*	*Source*
Rabbit polyclonal anti-PHLDA-1 antibody	HPA019000	1:10	Atlas Antibodies AB, Stockholm, Sweden
Mouse monoclonal anti-TGF-β1 antibody	sc-52893	1:200	Santa Cruz Biotechnology Inc., Santa Cruz, CA, USA
Mouse monoclonal anti-TGF-β2 antibody	sc-80347	1:100	Santa Cruz Biotechnology Inc., Santa Cruz, CA, USA
Mouse monoclonal anti-p63 (A4A) antibody	790-4509	prediluted	BenchMark XT, Ventana Medical System, Inc., Tucson, AZ, USA

- PHLDA-1, TGF-β1, and TGF-β2 stains were performed manually as described by the manufacturer

- p63 stain were performed using an automatic immunohistochemical stainer (BenchMark XT, Ventana Medical System, Inc., Tucson, AZ, USA)

Evaluation of the immunohistochemical staining results

- The staining intensity

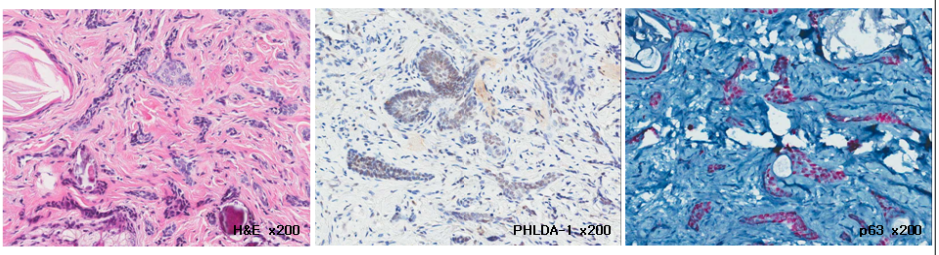
Intensity	Definition	
0	absence of any staining	
1	minimal intensity	
2	mild intensity	
3	moderate intensity	
4	maximal intensity	

- Localization patterns

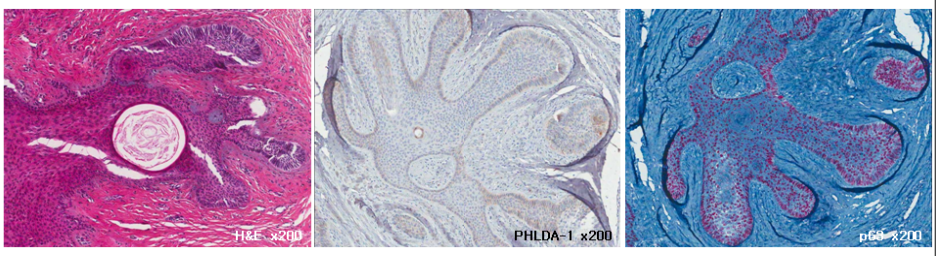
Localization pattern	Definition	
Nuclear (**N**)	stained in nucleus only	
Cytoplasmic (**C**)	stained in cytoplasm only	
Nuclear and cytoplasmic (**N&C**)	stained in both nucleus and cytoplasm	

The H & E and IHC of follicular tumors

Desmoplastic trichoepithelioma

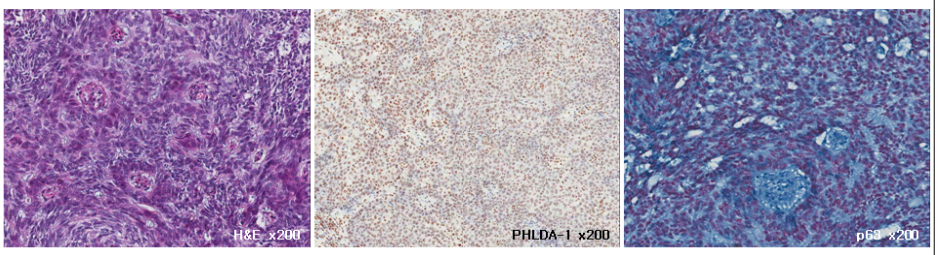


Trichofolliculoma

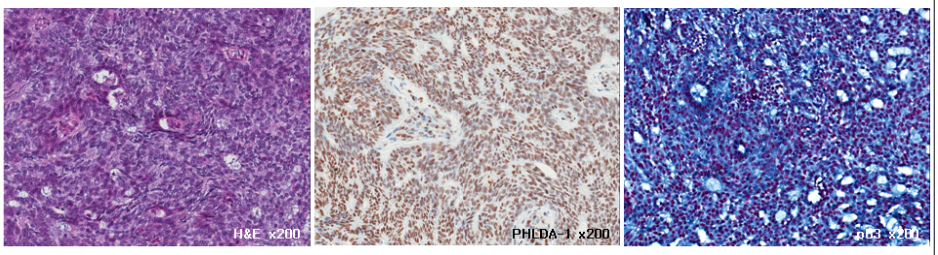


The H & E and IHC of follicular tumors

Trichilemmal carcinoma (well trichilemmal differentiation)

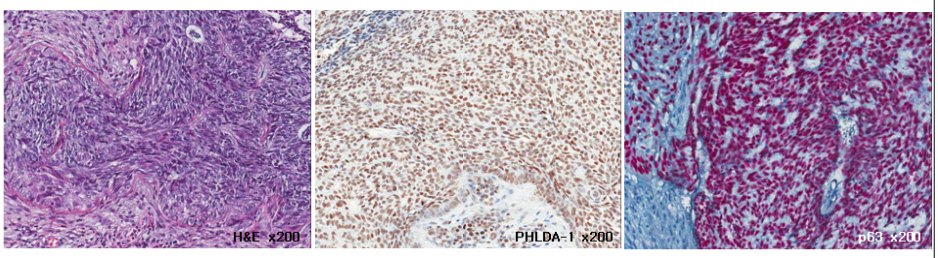


Trichilemmal carcinoma (moderately trichilemmal differentiation)



The H & E and IHC of follicular tumors

Trichilemmal carcinoma (poorly trichilemmal differentiation)



- PHLDA-1 was highly expressed in the ORS and peripheral tumor cells of benign, hyperplastic follicular tumors, while its expression was decreased in the cells of other hair follicle layers or the center of tumors

- In addition, PHLDA-1 was highly expressed in poorly-differentiated trichilemmal carcinoma cells, and decreased in the most well-differentiated trichilemmal carcinoma cells

- The expression of p63 was predominantly observed in the nuclei of peripheral tumor cells and poorly differentiated carcinoma cells

The localization patterns of PHLDA-1 with staining intensity

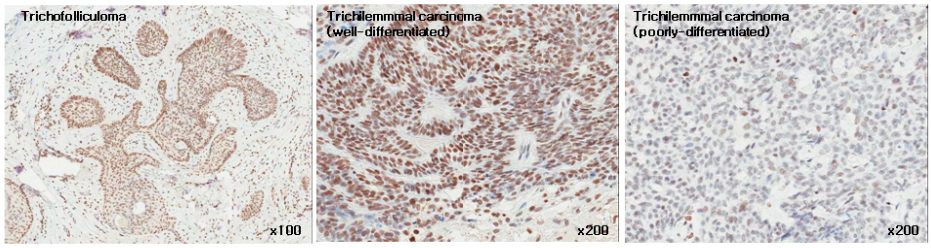
Follicular tumor	Intensity	Localization
Trichofolliculoma	2(1), 3(1)	N&C
Pilar sheath acanthoma	2(1), 3(2)	N&C
Desmoplastic trichoepithelioma	2(1), 3(1)	N&C
Trichilemmal carcinoma (well trichilemmal differentiation)	2(1)	N&C
Trichilemmal carcinoma (moderately trichilemmal differentiation)	3(1)	N&C
Trichilemmal carcinoma (poorly trichilemmal differentiation)	4(2)	N&C
Morpheic basal cell carcinoma	0(2), 1(2)	N&C

The localization patterns of p63 with staining intensity

Follicular tumor	Intensity	Localization
Trichofolliculoma	2(1), 3(1)	N
Pilar sheath acanthoma	2(1), 3(2)	N
Desmoplastic trichoepithelioma	3(2)	N
Trichilemmal carcinoma (well trichilemmal differentiation)	2(1)	N
Trichilemmal carcinoma (moderately trichilemmal differentiation)	3(1)	N
Trichilemmal carcinoma (poorly trichilemmal differentiation)	4(2)	N
Morpheic basal cell carcinoma	3(3), 4(1)	N

The localization patterns of TGF-β1 with staining intensity

Follicular tumors

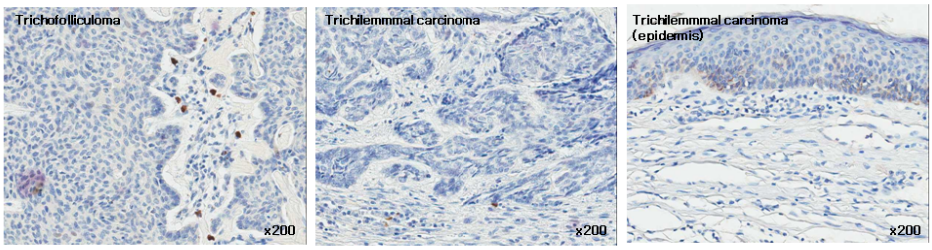


- TGF-β1 was highly expressed in the nuclei of ORS and peripheral tumor cells in benign, hyperplastic follicular tumors, in contrast to its decreased expression in the cells of other hair follicle layers or the center of tumors

- TGF-β1 was also highly expressed in the nuclei of well-differentiated trichilemmal carcinoma cells, although its expression was decreased in the most poorly differentiated trichilemmal carcinoma cells

The localization patterns of TGF-β2 with staining intensity

Follicular tumors



- TGF-β2 was expressed in normal keratinocytes in the lower portion of the epidermis

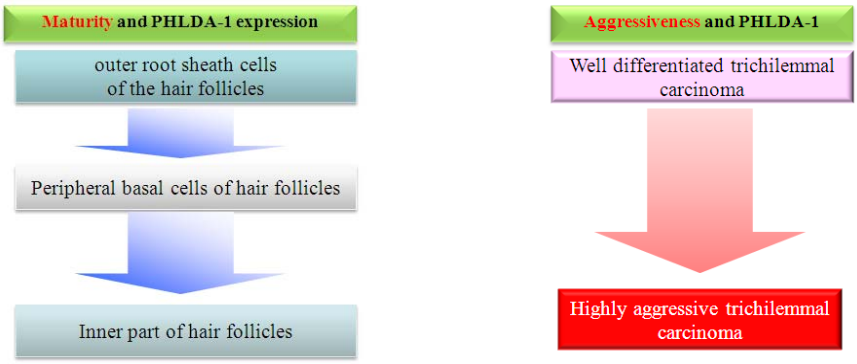
- However, TGF-β2 was not expressed in follicular tumor cells

- TGF-β2 expression was observed only in the stromal cells of the peritumoral regions in follicular tumors

PHLDA-1 — Discussion

- PHLDA-1 expression is highly correlated with the ORS cells and differentiation degree of malignant follicular tumors

- In contrast to other follicular tumor, PHLDA-1 expression was not seen in morpheic basal cell carcinoma
→ Basal cell carcionma might be originated from other follicular stem cells



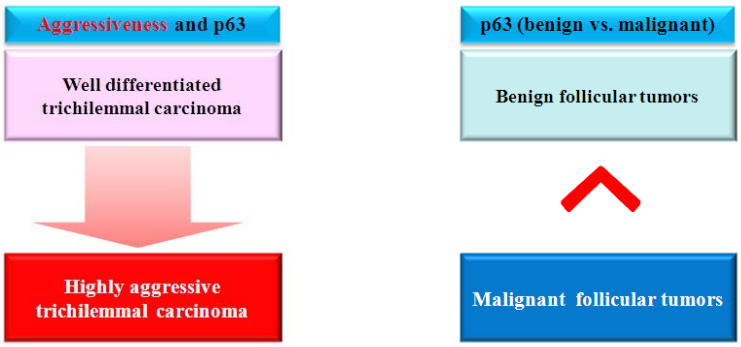
Sellheyer K, Krahl D. PHLDA1 (TDAG51) is a follicular stem cell marker and differentiates between morphoeic basal cell carcinoma and desmoplastic trichoepithelioma. Br J Dermatol 2011;164:141-147.

p63 — Discussion

- The p63 is well known as a marker for epidermal stem cells

- Previous studies showed an important role of p63 in epidermal morphogenesis and tumorigenesis

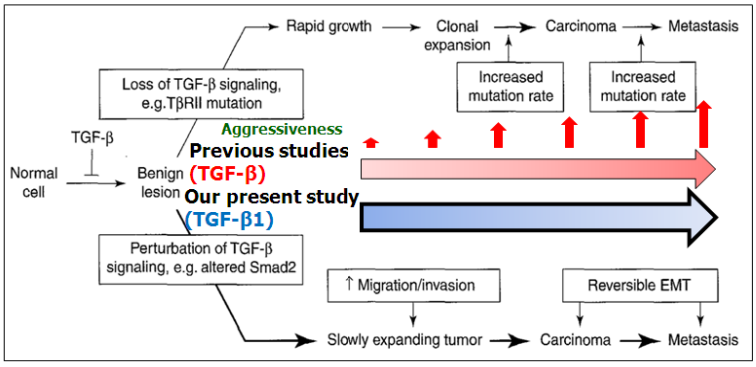
- Our data indicate that p63 expression may play some roles in the differentiation and carcinogenesis (aggressive biological behavior) of follicular tumors



TGF-β1 in the follicular tumor — Discussion

-Previous studies demonstrated that TGF-β expression levels showed a positive correlation with (aggressive biological behavior) in the tumors

-But, our data showed **a negative correlation between TGF-β1 expression and aggressive biological behavior** in follicular tumors, although the follicular organoid differntiation is more conspicuous in benign, hyperplatic follicular tumors than in trichilemmal carcinoma

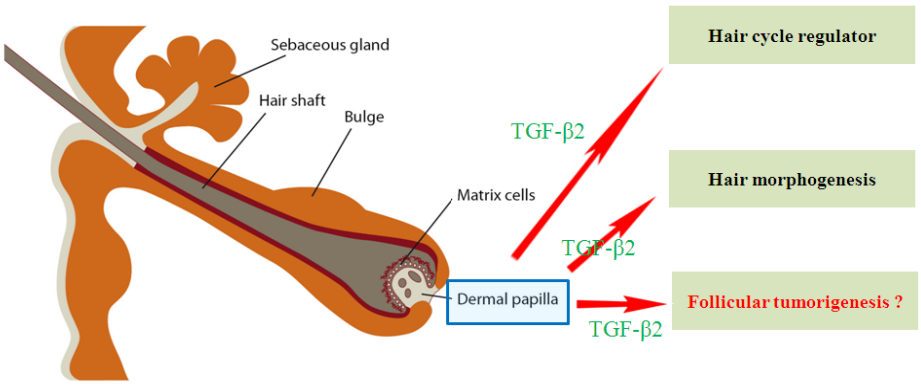


Akhurst RJ, Derynck R. TGF-beta signaling in cancer--a double-edged sword. Trends Cell Biol 2001;11:S44-51

TGF-β2 in the follicular tumor — Discussion

- A recent study suggests that dermal papilla cells (DPCs) express TGF-β2, which plays an important role in hair follicle morphogenesis

- Therefore, these TGF-β2-positive stromal cells were likely DPCs and might have an important role in the tumorigenesis of follicular tumors



Inoue K, Aoi N, Yamauchi Y, Sato T, Suga H, Eto H, et al. TGF-beta is specifically expressed in human dermal papilla cells and modulates hair folliculogenesis. J Cell Mol Med 2009;13:4643-4656.

Conclusions

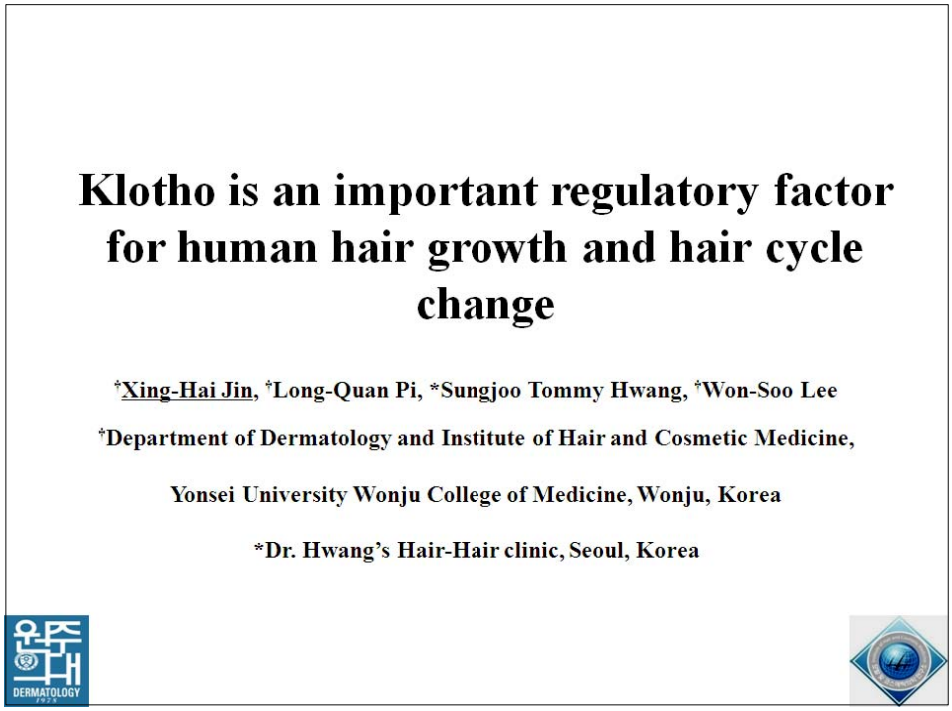
- PHLDA-1 may be a useful maker for hair follicle tumors
- We propose p63 may be useful to determine the differentiation degree and malignancy potential of follicular tumors
- Our data show TGF-β1 may be useful in determining the differentiation degree and malignancy potential of hair follicle tumors

- However, we suggest that further study with large sample size is needed in future to confirm this preliminary study results

Klotho is an important regulatory factor for human hair growth and hair cycle change

Xing-Hai Jin[1], Long-Quan Pi[1], Sungjoo Tommy Hwang[2], Won-Soo Lee[1]

[1]Department of Dermatology and Institute of Hair and Cosmetic Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea
[2]Dr. Hwang's Hair-Hair clinic, Seoul, Korea

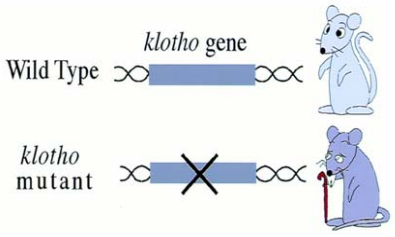


Introduction

- Klotho is a newly identified anti-aging protein that plays an important role in regulating aging.

- In mice model, klotho accelerates aging when disrupted and extends life span when over-expressed.

(Kuro-o M, et al. Nature 390:45, 1997)



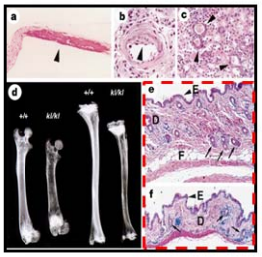
Klotho knockout mice

Klotho knockout mice

Introduction

Klotho$^{-/-}$ mice is the first documented mammalian model for human aging that manifest multiple aging-like phenotypes in a single individual.

- Skin atrophy
- Hair loss
- Short lifespan
- Growth retardation
- Reduced activity
- Hypogonadism
- Premature thymic involution
- Skin atrophy
- Muscle atrophy
- Pulmonary emphysema
- Motor neuron degeneration
- Hypoglycemia
- Hearing loss
- Ectopic calcification
- Vascular calcification

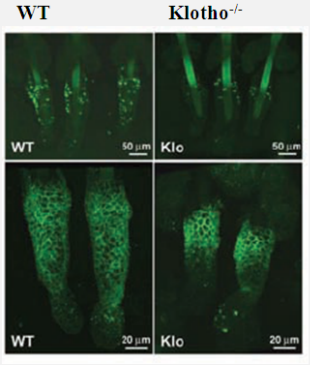


Histological examinations of the skin showed
- A reduction in the number of hair follicles;
- A reduction in dermal and epidermal thickness;
- The subcutaneous fat is barely detectable;
- The skin displayed overall atrophy.

(Kuro-o M, et al. Nature 390:45, 1997)

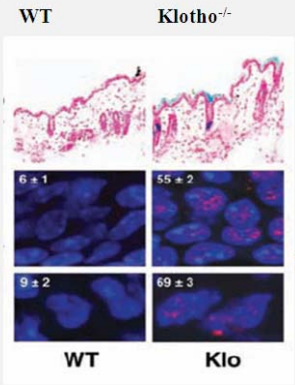
Introduction

Hair bulge stem cells ↓



BrdU : 5-bromo-2′-deoxyuridine

Hair Senescence↑

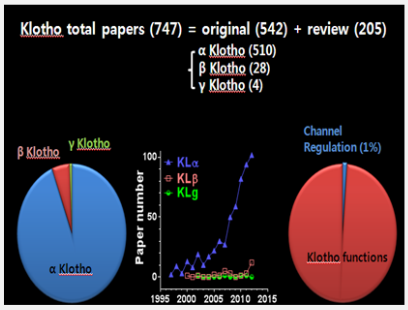


SAβ-gal: senescence associated endogenous β-galactosidase
DDW pathway: DNA damage response pathway molecules

(Hongjun Liu, et al. Science 317:803, 2007)

Introduction

Studies for Klotho



α Klotho function

- Insulin/IGF1 signal
- TGFβ signal
- WNT signal
- Oxidative stress
- Mineral metabolism
- Ca^{2+} channel

Introduction

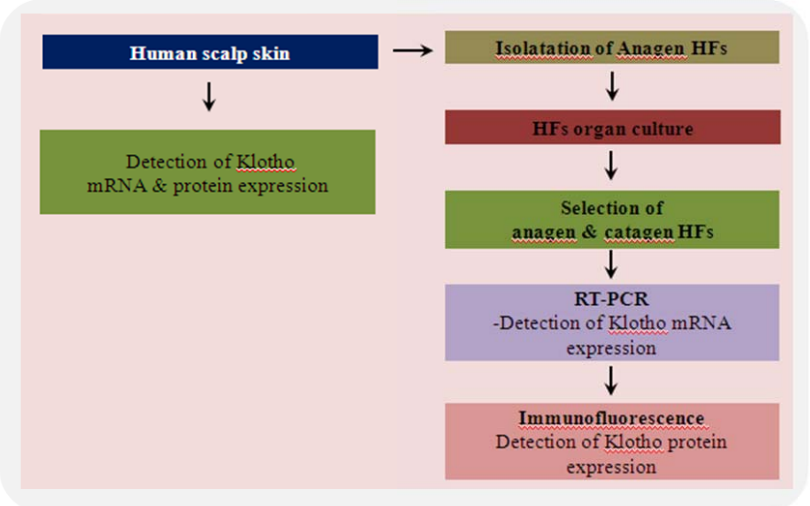
- To date, Klotho expression is detected only in a few human tissues and cell lines.
- However, whether klotho expresses in human hair follicles (HFs) and whether klotho expression correlates with hair growth have not yet been clearly shown.

Objectives

Accordingly, the purpose of the current study was to investigate:

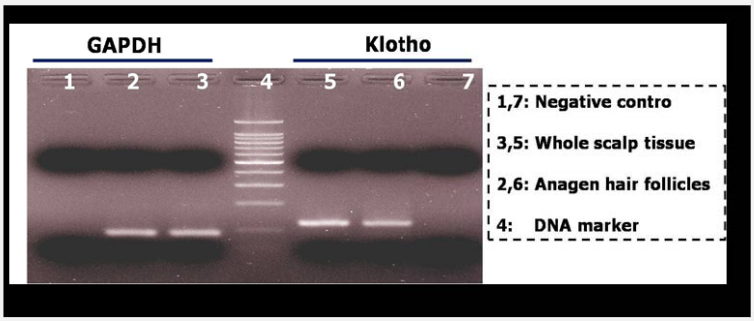
- The expression of klotho in human hair follicles.
- The functional roles of klotho in the human hair growth.

Experimental design



Results

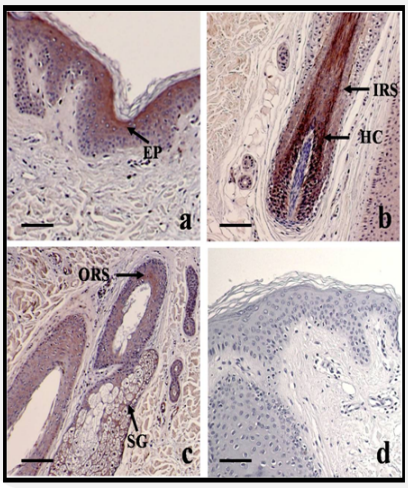
Klotho mRNA expression



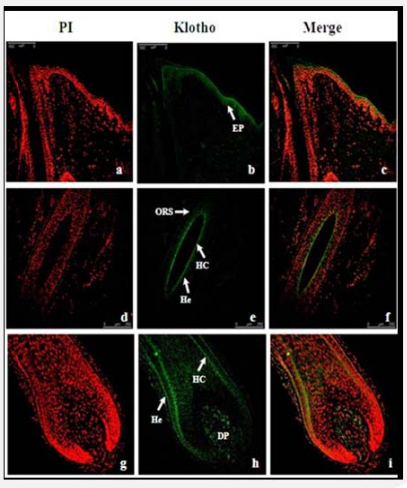
RT-PCR analysis showed that Klotho mRNA is expressed in whole human scalp skin and isolated human anagen hair follicles.

Results

Immunohistochemistry

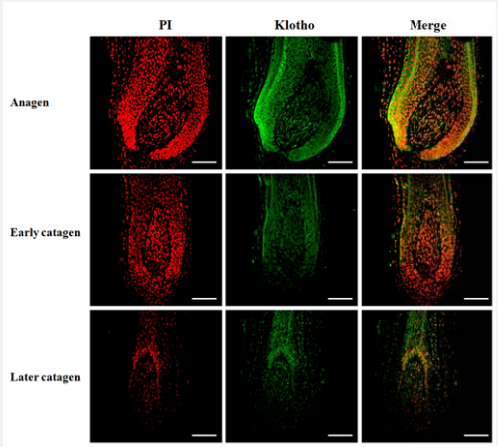


Immunofluorescence



Results

Dynamic changes in klotho expression during the transformation from anagen to catagen



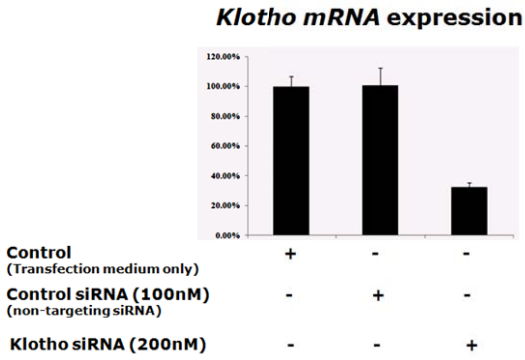
During transformation from anagen to catagen,, klotho expression appear to be down-regulated.

Experimental design

In human hair follicle organ culture

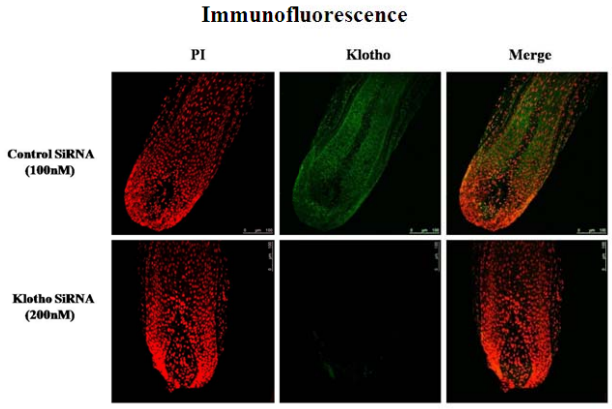
0 days	1 days	4 days	8 days
Transfection of Klotho siRNA	Detection of Klotho mRNA&protein	Detection of Ki67&apoptotic cells	Measurement of hair growth

Results



Transfection of Klotho siRNA in Hair follicles markedly reduced the Klotho *mRNA* expression , compared with controls (no siRNA group, non-targeting siRNA group). * $P < 0.05$.

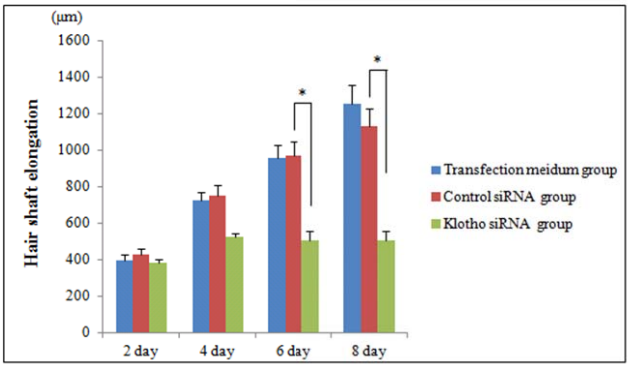
Results



Transfection of Klotho siRNA in Hair follicles markedly reduced the Klotho protein expression , compared with controls (non-targeting siRNA group).

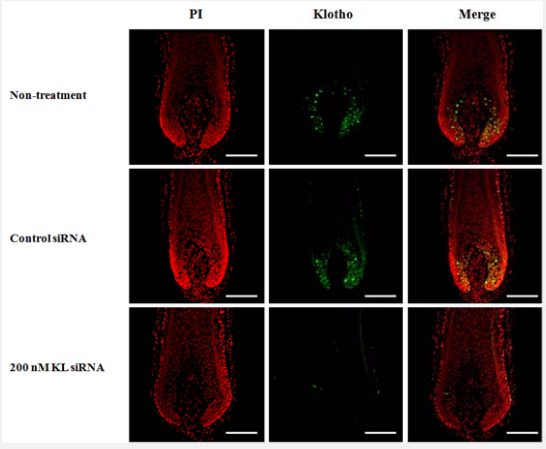
Results

Klotho knockdown inhibits hair shaft elongation



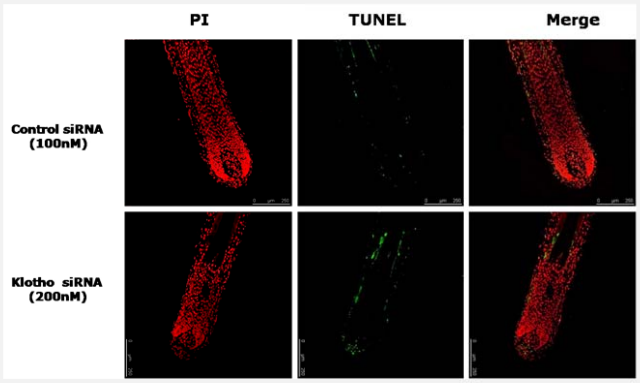
Results

Klotho knockdown reduces keratinocyte proliferation



Results

Klotho knockdown increases TUNEL-positive cells



Discussion

▪Human hair follicles expressed Klotho at the mRNA and protein levels.

▪ Klotho immunoreactivity was mainly detected in the epithelium of anagen hair follicles.

▪ During the transformation from anagen to catagen, Klotho expression appeared to be down-regulated.

▪ In human hair follicle organ culture, Klotho knockdown inhibited hair shaft growth, reduced hair matrix keratinocyte proliferation and increased apoptosis.

▪ These results indicate that Klotho might be an important regulatory factor for human hair growth and hair cycle change.


Thank you for your attention!

Distribution and maturation of integral hair lipid based barrier in human hair follicle according to the hair keratinization

Long-Quan Pi, Won-Soo Lee

Department of Dermatology and Institute of Hair and Cosmetic Medicine,
Yonsei University Wonju College of Medicine, Wonju, Korea

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Yonsei University Wonju College of Medicine, Wonju, Korea

Introduction

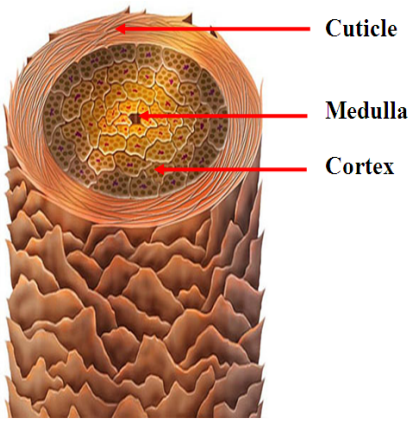
- Concept of Skin Barrier

Brick & Mortar Model

The outmost layer of the epidermis, the stratum corneum, is the predominant barrier layer. The stratum corneum is described as the Brick and Mortar model, with the bricks being annucleated, keratin-rich corneocytes and the mortar the extracellular, lipid-enriched matrix organized into lipid bilayers.

Introduction

- Concept of Hair Barrier



Integral hair lipid is bound to the cuticle cell surface to make an environmentally resistant lipid envelope, as stratum corneum lipid.

Introduction

- Importance of bound lipid

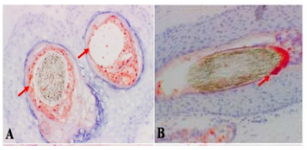
Common features of Stratum Corneum Lipid and Integral Hair Lipid

- **Integral part of cell envelop**
- **Consist of a covalently bound layer to surface protein of cell membrane**
- **Essential function as structural elements of plasma membrane or lipid envelope surrounding the cells**

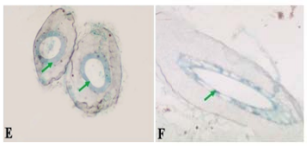
Introduction

- Localization of integral hair lipid

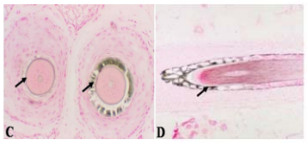
Oil red O stain
(for total lipid)
Red

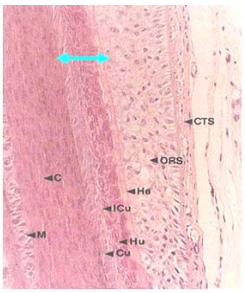


Holczinger's copper rubeanic acid modification
(for free fatty acid)
Dark green



Perchloric acid naphthoquinone reaction(PAN)
(choleterol and cholesteryl ester)
Gray blue



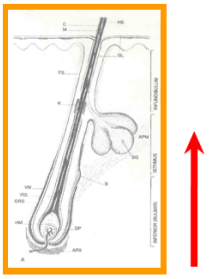


Hair cuticle
Inner root sheath cuticle
- **IRS cuticle**
- **Huxley layer**
- **Henle layer**

Lee et al, 2006

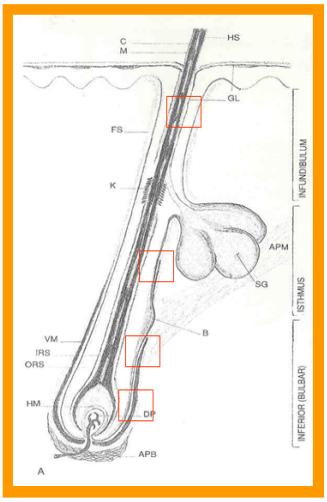
Objectives

In this study, we described the ultra-structural localization and maturation of Integral Hair Lipid in human hair follicle, along the longitudinal hair axis.



Experimental design

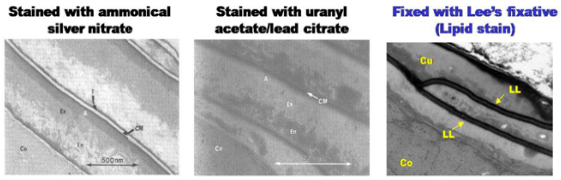
- **Electron microscopy was performed to observe the ultrastructure of the integral hair lipid in human anagen hair follicle .**
- **Hair follicles were cut and observed at**
  - **Hair bulb region**
  - **Hair suprabulbar region**
  - **Isthmus region**
  - **Infundibulum region**



Experimental design

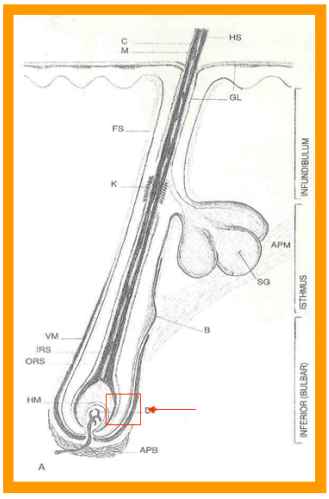
- Lee's fixative

- It is difficult to observe the ultra-structure of integral hair lipid with conventional staining methods using OsO_4 or RuO_4.
- OsO_4 cannot reveal lipid component in tissue.
- On the other hand, RuO_4, which is routinely used as revealing epidermal lipids cause severe hair damage.
- We used the Lee's fixative (0.5% RuO4: 2% OsO4: 0.2 M cacodylate buffer=1:1:1) to minimize hair injury and observe the integral hair lipid in the hair follicle.



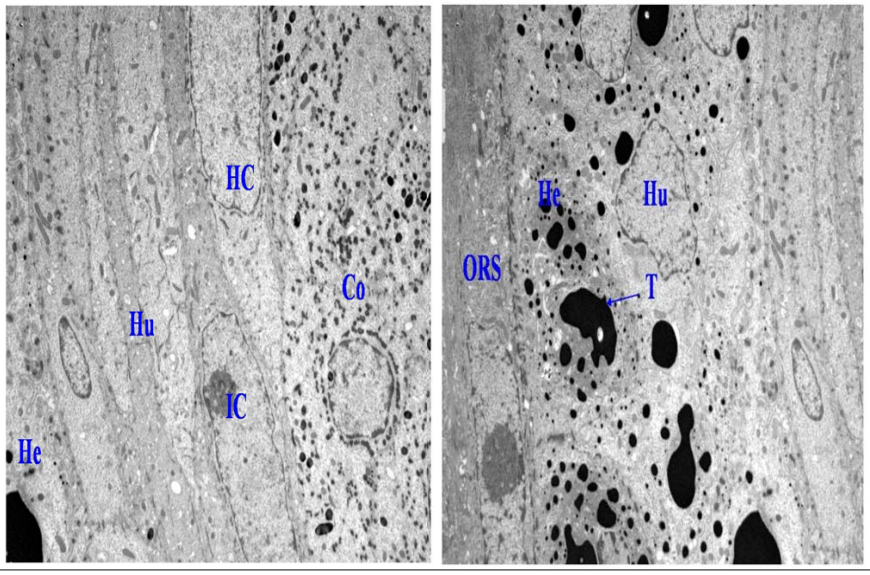
Results

- Hair bulb region



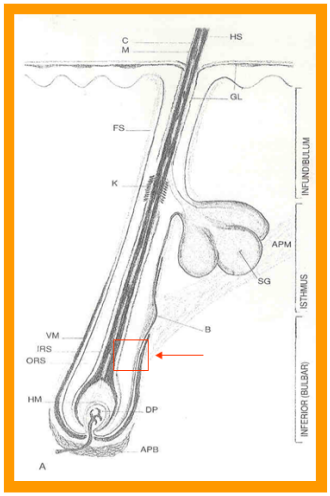
Results

- Hair bulb



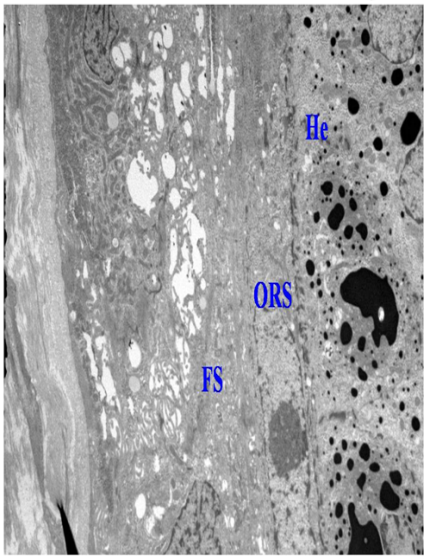
Results

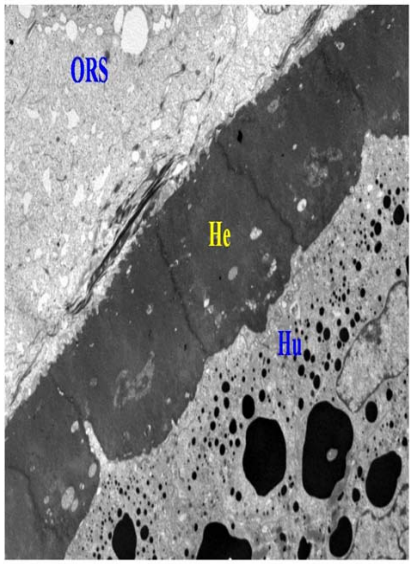
- Hair Suprabulbar Region



Results

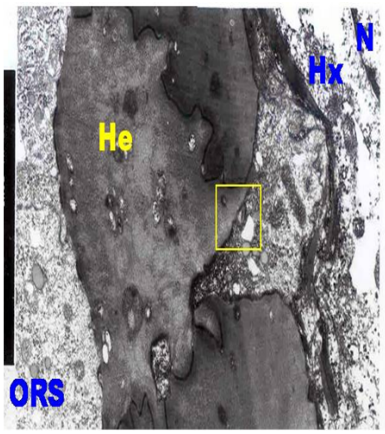
- Hair Suprabulbar Region

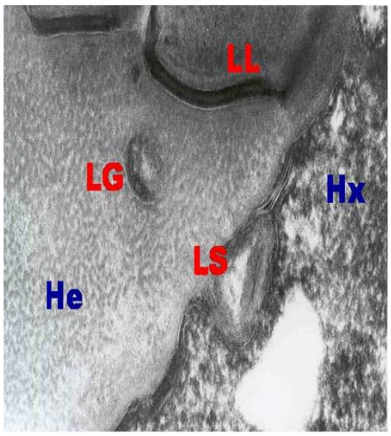




Results

- Hair Suprabulbar Region

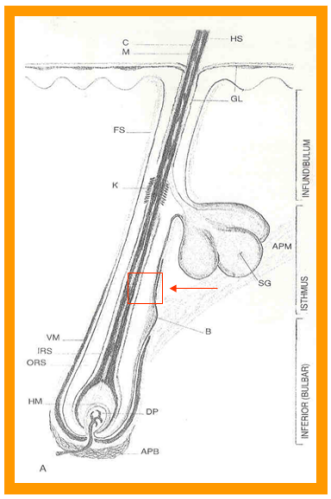




- Lipid layer (LL) and lamellar structure (LS)
- A continuous LL is observed between keratinized cells in the Henle and the Huxley layer , and the LS s observed in its center.

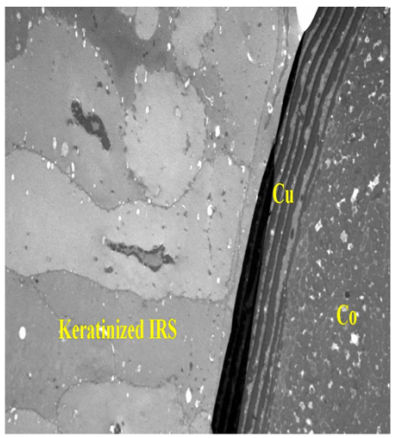
Results

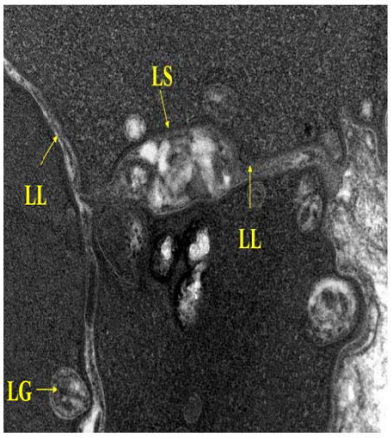
- Isthmus region



Results

- Isthmus region



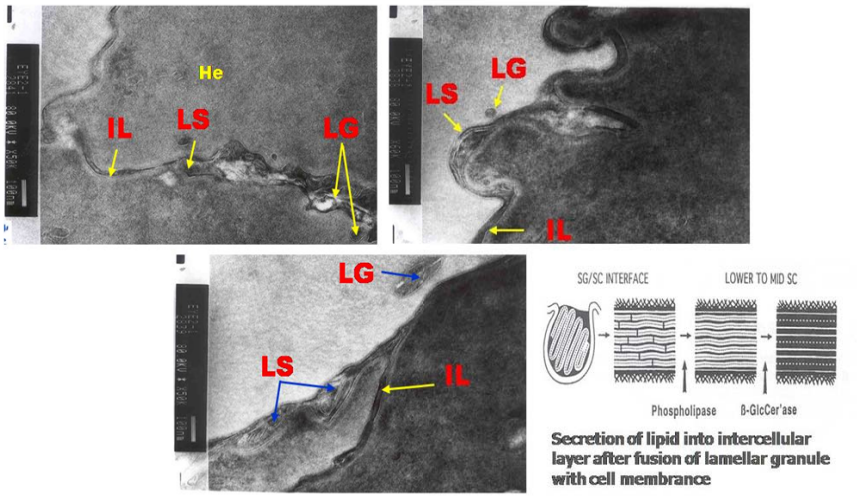


- Fully keratinized inner root sheat (IRS)
- Multiple LS, LL and lamellar granules (LG).

Results

Hair Barrier Formation

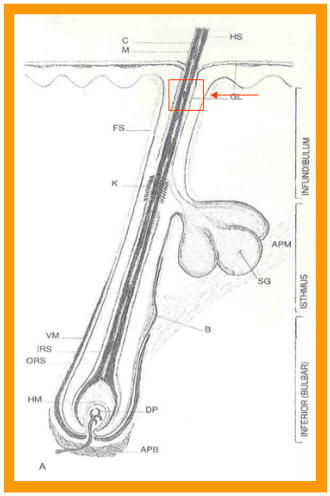
- Incorporation of lamellar granule into intercellular layer -



Secretion of lipid into intercellular layer after fusion of lamellar granule with cell membrance

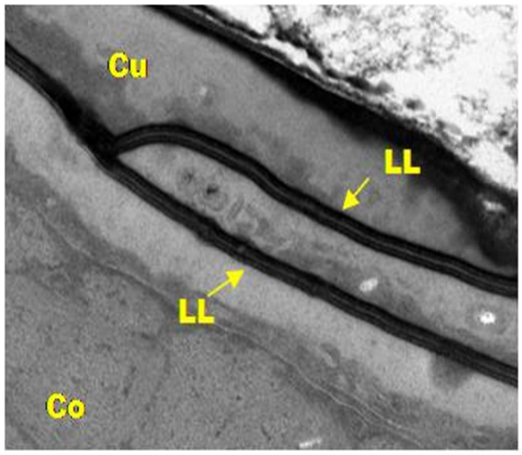
Results

- Infundibulum region



Results

- Infundibulum region



Lamellar granule : not yet discovered in cuticle

Discussion & Conclusion

➢ **In suprabulbar region:**

- Ultrastructure of anagen hair follicle at the level where Henle layer are keratinizing, showed the intercellular lipid layer (IL) and lamellar structure (LS).

- A continuous IL is observed between keratinized cells in the Henle layer and the Huxley layer, and the LS is observed in its center.

➢ **In isthmus region:**

- Ultrastructure of anagen hair follicle at the level where the inner root sheath (IRS) is completely keratinized showed multiple LS and lamellar granules (LG). Multitudes of LS and IL are observed between the keratinized cells in IRS.

Discussion & Conclusion

➢ **In Infundibulum region:**

When IRS cuticle and hair cuticle separate from each other, the LS on one side covers the outer surface of the hair cuticle and that on the other side is positioned on the surface of IRS cuticle.

➢ **In conclusion, the integral hair lipid in the hair follicle may regard as hair barrier to be similar to the epidermal lipid layer functioning as skin barrier**

Therapeutic effect of 308nm excimer laser on alopecia induced C3H/HeJ mice

Jong Hyuk Moon, Chan Yl Bang, Min Ji Kang, Hye Soo Ko, Ji Won Byun, Jeonghyun Shin, Gwang Seong Choi

Department of Dermatology, College of Medicine, Inha University, Incheon, Korea

Back ground: Eximer laser which induces apoptosis of T cell is used to treat various skin disease. There are many case reports about excimer laser therapy for alopecia areata but there has not been a domestic paper which suggests theoretical basis yet. Thus, we have done an analysis in histopathologic findings using TUNEL kit after 308nm excimer laser therapy using an animal model to confirm the apoptotic effect of excimer laser to T cells.

Method: We measured the minimal erythema dose (MED) of the skin of back of about 6.5-week-old, alopecia-induced 5 C3H/HeJ mice and had radiated the 308nm excimer laser on only right side of the alopecic patch twice a week for 12weeks. We took venous blood samples from the mice before and after the 12-week-laser therapy and evaluated serum cytokine using Quantibody array kit. We also performed skin biopsies and the tissue samples were checked for the number of follicles, change of perifollicular inflammatory cells and nerve fibers and activity of mast cells by 3 dermatologist and pathologist using H&E, CD4, CD8, CD56, substance P and mast cell tryptase stain. We also had radiated the 308nm excimer laser with 1 MED on right upper quadrant and 2 MED on the right lower quadrant of the alopecic patch to two mice. One mouse was radiated once a week for 1 week, the other was radiated once a week for 2 weeks. We performed skin biopsies and the tissue samples were checked for the number of follicles, change of perifollicular inflammatory cells and apoptosis of T cells using TUNEL kit.The control group is the left side of alopecic patch which are left without excimer laser therapy.

Result:

1. The growth of hair is clinically observed from 3 mice of 5 mouse.
2. The increase of the number of follicles and the decrease of the number of perifollicular in-

flammatory cells are observed.

3. By immunostaining, perifollicular infiltration of CD4+ and CD8+ T cell is decreased and the change of CD56+ NK cell is not definite. Any change of nerve fibers which responds to substance P is not observed and activation of mast cell, either.

4. After excimer laser therapy, IGF-1, IL-12, IL-13, IL-2 and IL-4 of all the three mice are decreased and IL-17 is increased.

Conclusion: From the results above, we suggests that 308 nm excimer laser therapy induce the decrease of perifollicular infiltration of CD4+T cell and CD8+ T cell by decreasing the level of IL-2 and IL-12 and apoptosis of T cell and this induces the regrowth of hair on the alopecic patch.

Effect of home-use microneedle device on pattern hair loss

Soo Yuhl Chae, Kyung Hea Park, Hyun Ho Son, Hong Dae Jung Yong Hyun Jang, Do Won Kim, Seok-Jong Lee, Weon Ju Lee

Department of Dermatology, Kyungpook National University School of Medicine, Daegu, Korea

2013 Hair Forum

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Kyungpook National University School of Medicine, Daegu, Korea

2013 Hair Forum

I Introduction

- **Pattern hair loss treatment[1]**
  - ✓ FDA approval treatment : finasteride, minoxidil
  - ✓ Minoxidil : Not penetrate the skin rapidly despite the use of penetration enhancers
- **Microneedle therapy**
  - ✓ Traditional uses: Collagen induction to fade scars and to improve wrinkle[2]
  - ✓ Recent advances: Successful treatment of hair loss
- **Key benefit of microneedle therapy in the treatment of hair loss**
  - ✓ Increased transdermal penetration[3]
    - ➔ Helps topical treatments, such as minoxidil, to be more effective as well as more affordable

1. Dhurat et al, Int J Trichology 2013;5:6-11 2. Dhurat *et al*, Int J Trichology, 2013 3. Wu *et al*, Biomedical Microdevices, 2008

2013 Hair Forum

II Objective

To investigate the efficacy and safety of **home-use microneedle device** for the treatment of **pattern hair loss**

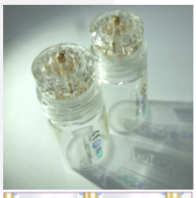
2013 Hair Forum

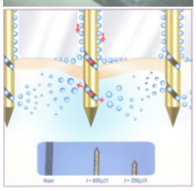
III Design

➢ **3 arms in this study (n=29, 20 to 60 years)**

- **Home-use microneedle only**
  - Needle length: 250μm
  - Gold plated microneedle with screw thread
- **Home-use microneedle and 5% minoxidil**
- **5% minoxidil only**

➢ **Treatment duration: 24 weeks**





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IV Demographics

	Microneedle	Microneedle + Minoxidil 5% sol.	Minoxidil 5% sol.	Total
No. of subjects	11	9	9	29
Age (y)				
Mean	37.1	39.3	42.9	39.6
Min:Max	28:49	32:45	33:59	28:59
Sex (%)				
Male	8 (73)	8 (89)	8 (89)	24 (83)
Female	3 (27)	1 (11)	1 (11)	5 (17)
Baseline hair count				
Mean	34.8	37.6	37.4	36
Min:Max	22:56	19:48	24:48	19:56
Stage of MPHL, No. (%)				
II	2 (25)	0	6 (75)	8 (33)
IIa	2 (25)	0	0	2 (8)
IIIa	1 (13)	5 (63)	0	6 (25)
III vertex	3 (37)	2 (25)	2 (25)	7 (29)
IV	0	0	0	0
V	0	1 (12)	0	1 (4)
Stage of FPHL, No. (%)				
Grade I	1 (33)	1 (100)	1 (100)	3 (60)
Grade II	2 (67)	0	0	2 (40)

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V-1 Methods

- **Home-use microneedle only**
  - ➔ *Tapping about 20 times on designated site*
  - ➔ *Twice a week*
- **Home-use microneedle and 5% minoxidil**
  - ➔ *Tapping about 20 times on designated site*
  - ➔ *Twice a week*
- **5% minoxidil**
  - ➔ *Twice a day*

- **Time-point of efficacy evaluation**

① Visit 1 : month 0 (baseline)
② Visit 2 : month 1
③ Visit 3 : month 3
④ Visit 4 : month 6

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V-2 Methods

- **Assessment**

1. ***Primary efficacy variable: hair counts***
   - ✓Hair counts (1 cm^2) with macrophotographic technique
   - ✓Hair counts (1 cm^2) with folliscope ®

Folliscope®

2. ***Secondary efficacy variable***
   - ✓Investigator's assessment of improvement
   - ✓Subjects' global assessment of improvement

Improvement Scale(score)	-25~-1%	0~24%	25~49%	50~74%	75~100%
	Bad(0)	Poor(1)	Fair(2)	Good(3)	Excellent(4)

- **Safety and tolerability**

: Evaluation of irritation, pruritus and others on the day of visit

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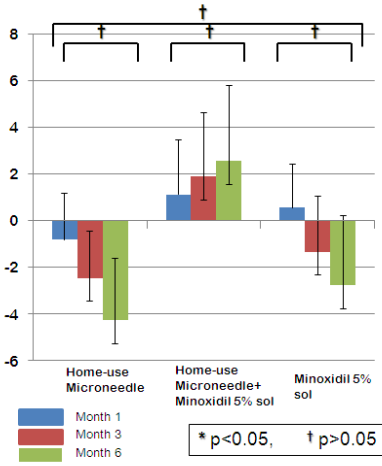
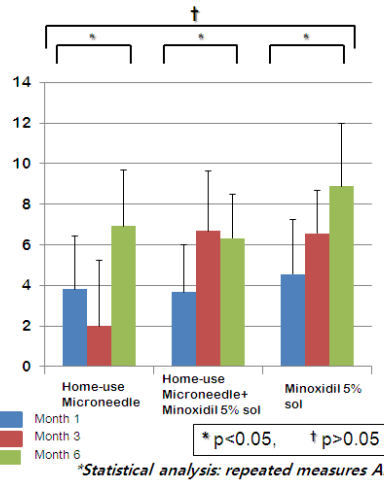
VI-1 Results

- **Change from baseline in hair count**
  - **Macrophotograhic hair count**



  - **Folliscope hair count**



*Statistical analysis: repeated measures ANOVA

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VI-3 Results

- **Safety and tolerability**

	Home-use microneedle	Home-use microneedle + Minoxidil 5% sol	Minoxidil 5% sol
Pain	-	-	-
Pruritus	1*	-	-
Erythema	-	-	-
Infection	-	-	-
Agitation	-	-	-
Scale	-	-	-
Crust	-	-	-
Oozing	-	-	-
Edema	-	-	-
Hypertrichosis	-	-	-

*Pruritus 30 minutes after using the device ➔ *Mild and transient !!*

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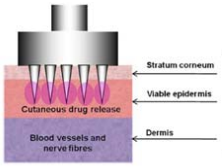
VII-1 Discussion

1. **Electrical stimulation**
2. **Photostimulation**
3. **Microneedle**
   - 가정용 <500 μm
   - 의료용 ≥500 μm



- ✓ **Stratum corneum : rigorous barrier**
- ✓ **Epidermis : 100 μm**
- ✓ **Dermis : blood vessel and nerve fibers**

***Only 30~50% of microneedle in length penetrate into skin[1]**

- ✓ **Due to elastic defomation of skin**

1. Park *et al.* Eur J Pharm Bopharm, 2010

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VII-2 Discussion

Microneedle의 모발성장에서 분자생물학적 반응

✓ **Encourages new hair growth independently[1]**

1.Release of PDGF and EGF through platelet activation and skin wound regeneration process

2.Activation of stem cells in the hair bulge area under wound healing conditions

3.Overexpression of hair growth-related genes such as VEGF, β-catenin, Wnt3a and Wnt10b.

- Wnt 'trigger' protein: produced by skin during wound healing[2,3]
  - ✓Increases the follicle regeneration
  - ✓Acts on the β-catenin pathway
  - ✓Down-regulate TGF-β expression

1. Dhurat *et al.* Int J Trichology, 2013 2. Ito M *et al.* Nature, 2007 3. Cotsarelis G et al, Molecular Medicine, 2001

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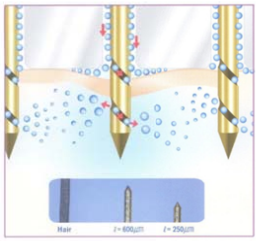
VII-3 Discussion

Drug delivery를 위한 microneedle의 모발 치료 이용



- **Water dissoliving Microneedles[1]: 250, 750μm**
  - ✓ **250μm microneedle : Minoxidil was delivered to 80μm of skin**
  - ✓ **750μm microneedle : Minoxidil was delivered to 200μm of skin**
  - ✓ **Efficacy of microneedles : 750μm > 250μm > only minoxidil or no treatment control**

1. MR Han *et al*,*Polymer(Korea)*, 2013

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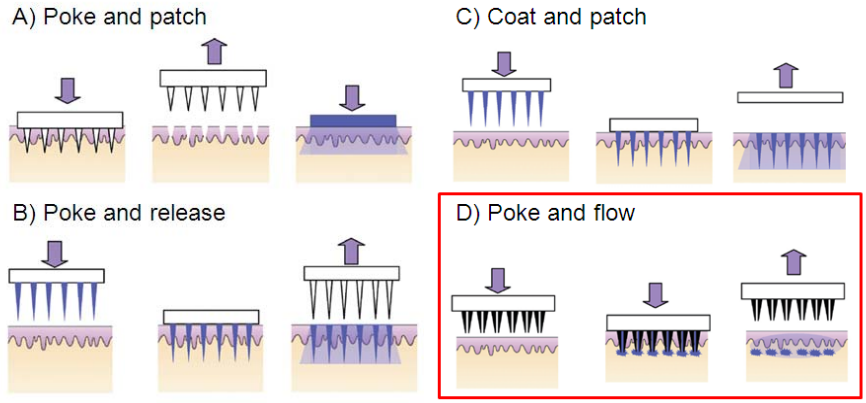
VII-4 Discussion

- **Types of microneedle device[1]**



1. Bariya *et al*, J Pharm Pharmacol, 2012

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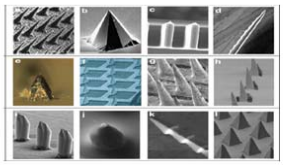
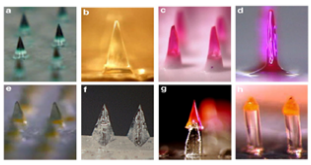
VII-5 **Discussion**

- **Types of microneedle device**[1]

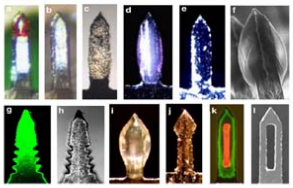
A) Solid microneedles



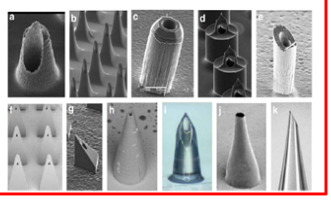
C) Dissolving microneedles



B) Coated microneedles



D) Hollow microneedles



1. Kim *et al*, Adv Drug Deliv Rev, 2012

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VIII **Limitation**

- Small number of patients
- Patient compliance
- No measurement of hair length and thickness

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IX Conclusion

- **Home-use microneedle only is inferior to 5% minoxidil only in hair growth.**
- **Home-use microneedle and 5% minoxidil is not inferior to 5% minoxidil only.**
- **Home-use microneedle is considered as a new therapeutic modality to stimulate hair growth to enhance transepidermal delivery.**

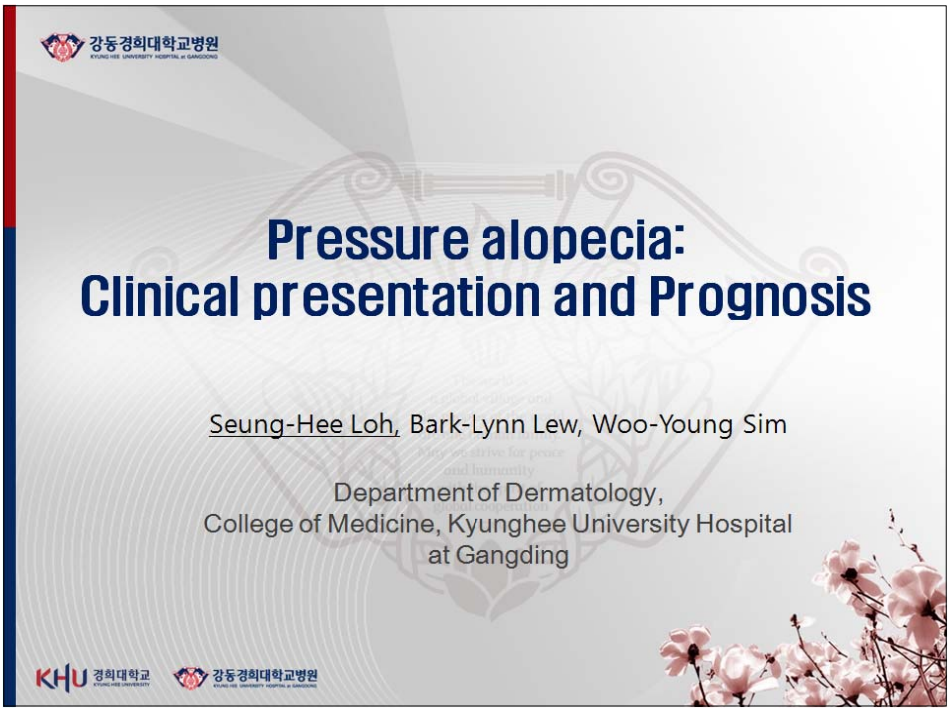
2013 Hair Forum

Thank you for your attention.

Pressure alopecia: Clinical presentation and prognosis

Seung-Hee Loh, Bark-Lynn Lew, Woo-Young Sim

Department of Dermatology, College of Medicine,
Kyunghee University Hospital at Gangding



Introduction

- Acute or chronic exogenic trauma to the scalp hair may lead to transient or permanent hair loss, by different mechanisms.

- **Pressure alopecia (PA)**
  - Described as a group of scarring and non-scarring alopecia that occurs following prolonged immobile state of the scalp.
  - Hair loss is due to ischemic changes to the scalp, caused by the pressure to a certain area of the scalp.

Introduction

- Usually occurs in the occiput and often presents as a discrete skin colored hairless patch.
- Rare condition but a preventable complication that is mostly observed after a certain time of surgical procedures under general anesthesia or a prolonged period of lying in an Intensive Care Unit.

- **Objective**
  - To describe the clinical manifestations, course and histological characteristics of pressure alopecia
  - To assess the prognostic factor for permanent scarring alopecia

Patients and Method

- **Patients**
  - All consecutive patients referred for pressure alopecia to the dermatology department of the Kyunghee University Hospital at Gangdong during a 8-year period
- **Diagnosis of pressure alopecia**
  - Based on the sudden onset of localized hair loss after immobilization of the head during surgery and following prolonged stays on beds

Patients and Method

- Retrospective character of the study, not possible to determine the exact date of onset of hair loss in all patients
  - Therefore, arbitrarily chose to consider the date corresponding to the first day of visiting our department
- At the initial visit, a 5-mm scalp biopsy specimen taken from the site of hair loss
- Hair regrowth confirmed by direct clinical examination and medical photographs

Result

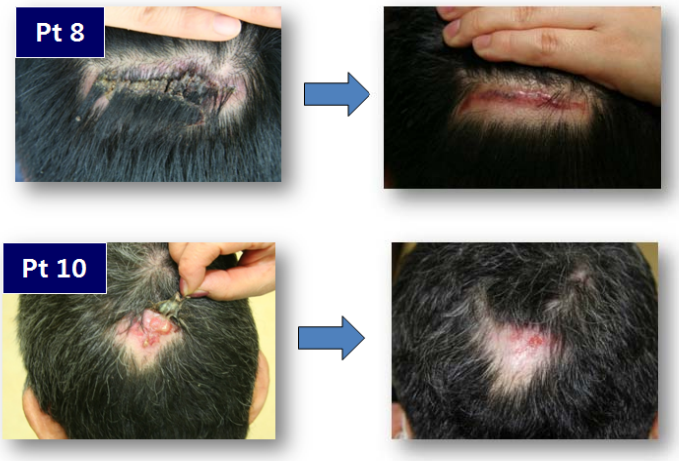
Pt	Sex /age	Op (hr)	Bed rest (wk)	Site involved	Clinical findings	Regrowth (wk)	Recovery (wk)	Final Course
1	F / 43	+ (3)	-	occipital	round, 2 X 3 cm	2	6	Complete recovery
2	F / 71	+ (4)	1	occipital	diffuse, 10 X 10 cm	4	10	Complete recovery
3	M / 36	+ (3)	1	Rt. temporo occipital, vertex	round, 14 X 10, 12 X 12 cm	5	10	Complete recovery
4	F / 48	+ (7)	2	occipital	multiple, round, 2~5 cm	3 (partial)		Permanent alopecia
5	F / 39	+ (5)	3	occipital	round, 5 X 5 cm	5	8	Complete recovery
6	F / 24	-	3	occipital	round, 6 X 4 cm	4	14	Complete recovery
7	M / 48	-	5	occipital	diffuse, 8 X 8 cm	2	4	Complete recovery
8	M / 36	+ (12)	-	occipital	linear, 8 X 2 cm	4 (partial)		Permanent alopecia
9	M / 51	-	8	occipital	linear, 23 X 3 cm	4	8	Complete recovery
10	M / 51	+ (10)	2	occipital	round, 8 X 6 cm	2 (partial)		Permanent alopecia
11	M / 23	-	2	Occipital	round, 4 X 4 cm	3	4	Complete recovery
12	F / 50	+ (5)	2	Lt. temporal	diffuse, 12 X 10 cm	4	8	Complete recovery
13	F / 44	-	2	occipital	round, 5 X 7 cm	3	10	Complete recovery
14	F / 64	+ (6)	2	Lt. parieto-occipital	round, 15 X 15 cm	3	9	Complete recovery
15	F / 62	+ (7)	3	occipital	round, 12 X 13 cm	3	9	Complete recovery
16	M / 25	-	4	occipital	round, 2 X 3 cm	6	10	Complete recovery
17	M / 43	+ (3)	3	occipital	square, 15 X 15 cm	4 (partial)		Permanent alopecia
18	M / 54	-	3	occipital	round, 2 X 3 cm	3	7	Complete recovery
19	F / 50	+ (5)	1	occipital	round, 5 X 8 cm	5	10	Complete recovery
20	M / 53	+ (3)	1	occipital	round, 10 X 10 cm	1	4	Complete recovery
21	F / 44	+ (10)	2	occipital	square, 15 X 7 cm	5 (partial)		Permanent alopecia
22	F / 78	-	4	occipital	round, 3 X 5 cm	2	4	Complete recovery
23	M / 58	-	3	occipital	round, 3 X 3 cm	3	10	Complete recovery
24	M / 52	7	-	occipital	Linear, 6 X 2 cm	4	9	Complete recovery
25	F / 48	4	-	Rt. temporal	square, 3 X 3 cm	5	10	Complete recovery
26	M / 50	2	2	occipital	square, 4 X 2 cm	5	10	Complete recovery

Clinical Findings

- At first visit

Clinical Findings

- Clinical photos of patients with progression to permanent alopecia

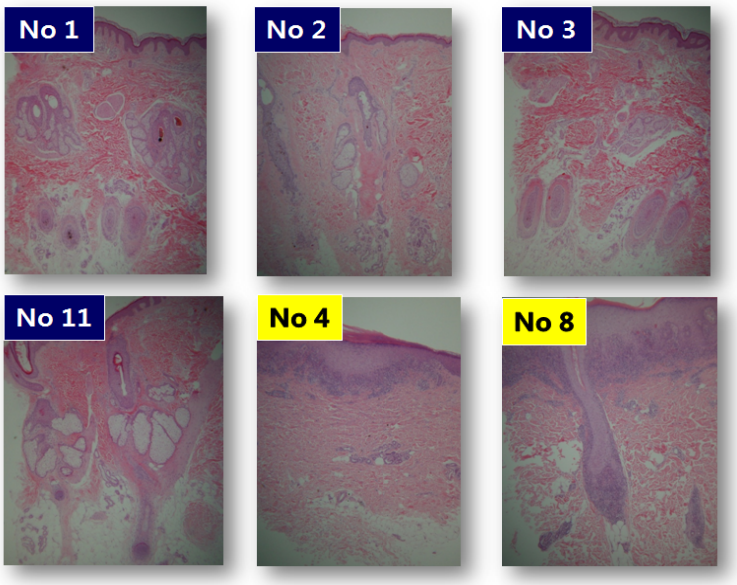


Course of pressure

	Mean duration (Weeks)		
	From op (pressure) to alopecia	From alopecia to hair regrowth	From alopecia to recovery
Operation (n=17)	3.24	3.76	8.58 *
Without Operation (n=9)	4.33	3.33	7.89

*(excluding 5 permanent alopecia in operation group)

Histopathological Findings



Discussion

Group	N	Age (yr)	Op.	Op. time (Hr)	Onset time of alopecia (wk)	Duration of HRG (wk)
Recovery (+)	21	48.71	53%	4.71	3.71	3.64
Recovery (-)	5	44.40	100%	8.00*	3.75	3.67 (partial)

Discussion

- **Pathophysiology of pressure alopecia**
  - Duration with pressure : most important factor
  - Tissue hypoxia → inflammatory reaction with fibrosis → alopecia
- **Histopathologic differences**
  - With complete recovery
    - Few or minimal perifollicular inflammation
    - Increased catagen hair
    - Prominent perifollicular fibrosis
  - With permanent alopecia
    - Prominent inflammation at DEJ and around HF
    - Dermal fibrosis and marked decrease of HF

Conclusion

- All cases of pressure alopecia can not be recovered spontaneously, some cases could progress to cicatricial alopecia.
- Duration with pressure(especially operation time) was the most important prognostic factor.

Reference

1. Lee D, Kang MS, Lee SS, et al. Korean J Dermatol 2005;43:1155-1163
2. Dominguez E, Eslinger MR, McCord SV. Anesth Analg. 1999;89:1062-1063
3. Wiles JC, Hansen RC. J Am Acad Dermatol. 198512:195-198

2013

대한모발학회

제12차 Hair Forum

제 2 부 :

7th World Congress for Hair Research Review

The Korean Hair Research Society

5월 5일 오전 프로그램 리뷰

중앙대학교 의과대학 피부과학교실

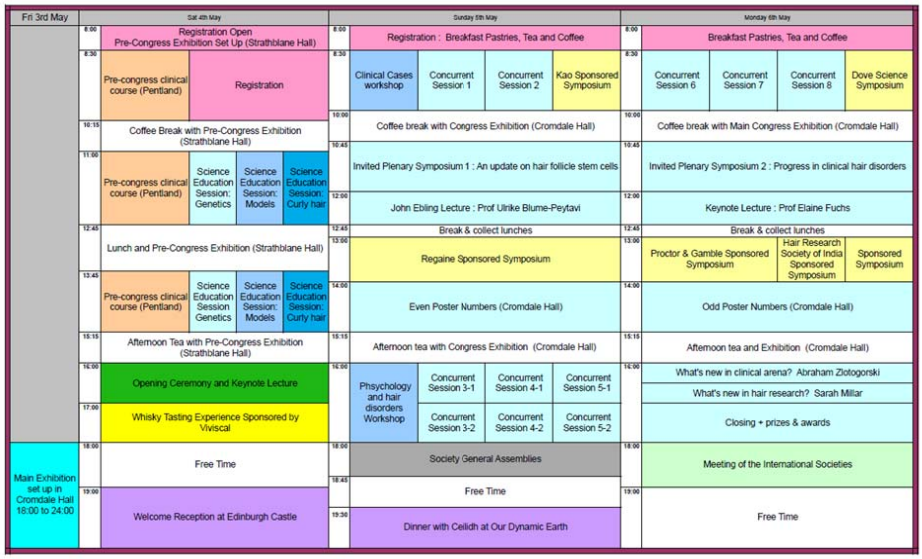
손 인 평

12th Hair Forum

7th World Congress for Hair Research
May 4-6, 2013 Edinburgh, Scotland

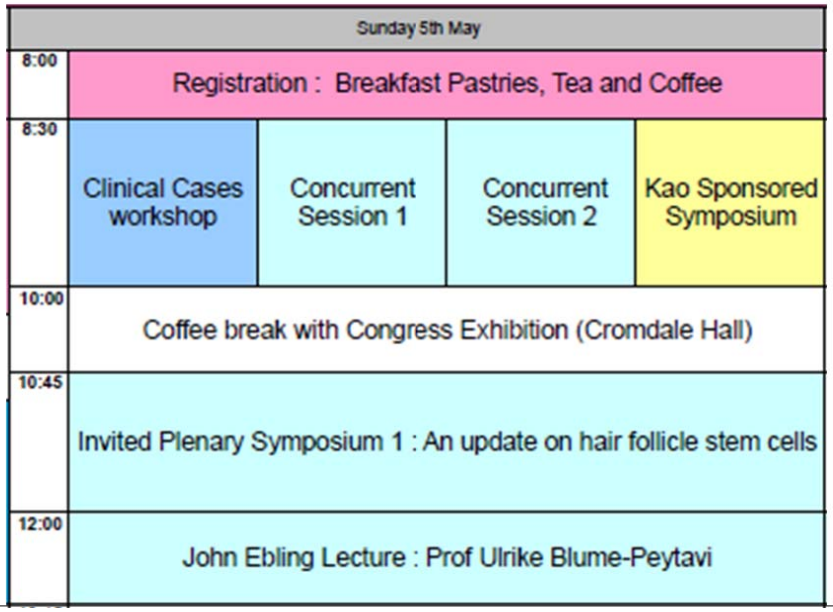
In Pyeong Son
Chung-Ang University Hospital

WCHR 2013 Programme



Fri 3rd May	Sat 4th May	Sunday 5th May	Monday 6th May
	8:00 Registration Open Pre-Congress Exhibition Set Up (Strathblane Hall)	8:00 Registration : Breakfast Pastries, Tea and Coffee	8:00 Breakfast Pastries, Tea and Coffee
	8:30 Pre-congress clinical course (Pentland) / Registration	8:30 Clinical Cases workshop / Concurrent Session 1 / Concurrent Session 2 / Kao Sponsored Symposium	8:30 Concurrent Session 6 / Concurrent Session 7 / Concurrent Session 8 / Dove Science Symposium
	10:15 Coffee Break with Pre-Congress Exhibition (Strathblane Hall)	10:00 Coffee break with Congress Exhibition (Cromdale Hall)	10:00 Coffee break with Main Congress Exhibition (Cromdale Hall)
	11:00 Pre-congress clinical course (Pentland) / Science Education Session: Genetics / Science Education Session: Models / Science Education Session: Curly hair	10:45 Invited Plenary Symposium 1 : An update on hair follicle stem cells	10:45 Invited Plenary Symposium 2 : Progress in clinical hair disorders
		12:00 John Ebling Lecture : Prof Ulrike Blume-Peytavi	12:00 Keynote Lecture : Prof Elaine Fuchs
	12:45 Lunch and Pre-Congress Exhibition (Strathblane Hall)	12:45 Break & collect lunches	12:45 Break & collect lunches
		13:00 Regaine Sponsored Symposium	13:00 Proctor & Gamble Sponsored Symposium / Hair Research Society of India Sponsored Symposium / Sponsored Symposium
	13:45 Pre-congress clinical course (Pentland) / Science Education Session Genetics / Science Education Session: Models / Science Education Session: Curly hair	14:00 Even Poster Numbers (Cromdale Hall)	14:00 Odd Poster Numbers (Cromdale Hall)
	15:15 Afternoon Tea with Pre-Congress Exhibition (Strathblane Hall)	15:15 Afternoon tea with Congress Exhibition (Cromdale Hall)	15:15 Afternoon tea and Exhibition (Cromdale Hall)
	16:00 Opening Ceremony and Keynote Lecture	16:00 Phsychology and hair disorders Workshop / Concurrent Session 3-1 / Concurrent Session 4-1 / Concurrent Session 5-1	16:00 What's new in clinical arena? Abraham Zlotogorski What's new in hair research? Sarah Millar
	17:00 Whisky Tasting Experience Sponsored by Viviscal	Concurrent Session 3-2 / Concurrent Session 4-2 / Concurrent Session 5-2	Closing + prizes & awards
Main Exhibition set up in Cromdale Hall 18:00 to 24:00	18:00 Free Time	18:00 Society General Assemblies	18:00 Meeting of the International Societies
	19:00 Welcome Reception at Edinburgh Castle	18:45 Free Time 19:30 Dinner with Ceilidh at Our Dynamic Earth	19:00 Free Time

Sunday 5 May 2013



Sunday 5th May				
8:00	Registration : Breakfast Pastries, Tea and Coffee			
8:30	Clinical Cases workshop	Concurrent Session 1	Concurrent Session 2	Kao Sponsored Symposium
10:00	Coffee break with Congress Exhibition (Cromdale Hall)			
10:45	Invited Plenary Symposium 1 : An update on hair follicle stem cells			
12:00	John Ebling Lecture : Prof Ulrike Blume-Peytavi			

Concurrent Session 4: Clinical Cases

0830 **Concurrent Session 4: Clinical Cases** — Tinto

Chairs: Patrick Yesudian, Antonella Tosti, Elise Olsen

P078 **Analysis of quantitative changes in hair growth during treatment with chemotherapy or tamoxifen in breast cancer patients: a cohort study**
N Garcia Bartels, K Hillmann, J Lindner, R Nuwayhid, A Stroux, J Lademann, U Blume-Peytavi
Klinik für Dermatologie, Venerologie und Allergologie, Charité-Universitätsmedizin Berlin, Berlin, Germany

P079 **Adalimumab to treat recalcitrant dissecting cellulitis of the scalp**
Y Mansouri, MR Kaur
Dermatology, Heart of England NHS Trust, Solihull Hospital, Solihull, United Kingdom

P080 **Clinical characteristics and prevalence of chemotherapy-induced alopecia in childhood**
M Choi[1], SY Park[1], DL Jin[1], MS Kim[2], KH Cho[1], HJ Kang[2], OS Kwon[1,3]
[1]Department of Dermatology, Seoul National University College of Medicine, Seoul, Korea, Republic of, [2]Division of Hematology/Oncology, Department of Pediatrics, Seoul National University College of Medicine, Seoul, Korea, Republic of, [3]Institute of Human-Environment Interface Biology, Seoul National University College of Medicine, Seoul, Korea, Republic of

P088 **Appearance of mycosis fungoides (MF) localized on the scalp with clinical signs of alopecia areata**
A Miesel[1], M Fleischer[1], C Rose[1], TW Fischer[1], D Zillikens[1]
[1]Department of Dermatology, Allergology and Venerology, University Hospital of Luebeck, Luebeck, Germany

P082 **A pilot clinical study of hair grafting in chronic leg ulcers**
F Jimenez[1], C Garde[2], E Poblet[3], B Jimeno[3], J Ortiz[3], M Martinez[4], A Gutierrez-Rivera[5], V Perez-Lopez[5], U Ebxanz[5], C Navedo[5], JL Higuera[6], N Egües[7], E Escario[4], A Izeta[5]
[1]Clinica Dr. Jimenez-Acosta, Las Palmas, Gran Canaria, Spain, [2]Outpatient Care Unit, Hospital Donostia, San Sebastian, Spain, [3]Anatomia Patológica, Universidad de Murcia, Murcia, Spain, [4]Dermatology, Hospital General Universitario de Albacete, Albacete, Spain, [5]Department of Bioengineering, Instituto Biodonostia, San Sebastian, Spain, [6]Department of Vascular Surgery, Hospital Donostia, San Sebastian, Spain, [7]Research Unit, Instituto Biodonostia, San Sebastian, Spain

P085 **Sebaceous gland atrophy: a potential pitfall in the histopathologic evaluation of non-scarring alopecia associated with psoriasiform dermatitis of the scalp**
NL Clayton, DA Fenton, CM Stefanato
St John's Institute of Dermatology, St Thomas' Hospital, London, United Kingdom

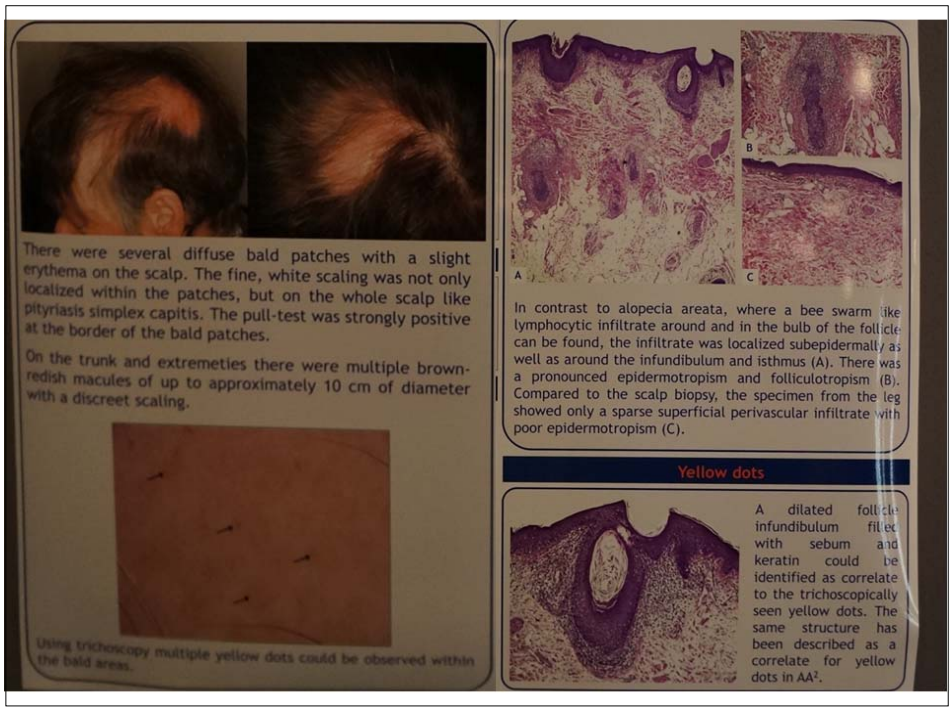
P087 **Invisible bleeding from clean-shave haircuts**
NP Khumalo[1,2], K Mkentane[3,4], C Muthukarapan[5], D Hardy[6], S Korsman[5], P Berman[7], T Mthebe[8], LM Davids[4], J Rousseau[5]
[1]Division of Dermatology, University of Cape Town, Cape Town, South Africa, [2]Division of Dermatology, Groote Schuur Hospital, Cape Town, South Africa, [3]Dermatology, University of Cape Town, Cape Town, South Africa, [4]Human Biology, University of Cape Town, Cape Town, South Africa, [5]Genetics, University of Cape Town, Cape Town, South Africa, [6]Divisions of Medical Virology, University of Cape Town, Cape Town, South Africa, [7]Chemical Pathology, University of Cape Town, Cape Town, South Africa, [8]Department of Clinical Laboratory Sciences, Groote Schuur Hospital, Cape Town, South Africa

P088

Appearance of mycosis fungoides (MF) localized on the scalp with clinical signs of alopecia areata

A Miesel, M Fleischer, C Rose, TW Fischer and D Zillikens *Department of Dermatology, Allergology and Venerology, University Hospital of Luebeck, Luebeck, Germany*

A 67-year-old woman presented in our weekly hair disease clinic with massive, patchy hair loss and strongly positive pull test. She had a history of 30 years of parapsoriasis on the trunk and extremities. On the scalp, several slightly reddish, up to 8-cm-large, scaly patches of nearly complete, diffuse hair loss without signs of scarring were visible. One of the differential diagnoses was an initial alopecia areata (AA), but the slight erythema and the whitish dandruff did not support this diagnosis. On the extremities and the trunk there were multiple oval, livid-red macules. A biopsy from the scalp showed histologically a folliculotropic mycosis fungoides (F-MF) with a peri- and intrafollicular infiltrate of mostly CD4-positive, atypical T-lymphocytes. Prior biopsies of the trunk showed the histological picture of a parapsoriasis. Not only histologically there are parallels between F-MF and AA, but also clinically, an AA-like appearance of hair loss in patients with MF has been described. In patients with AA we could recently demonstrate that an oral prednisolone pulse therapy descending from 50 to 10 mg per day over 8 weeks showed good results with hair regrowth in 81% of the cases. In the case presented here, we therefore applied this treatment scheme and observed a stop of hair loss with negativation of pull test after 8 weeks of therapy. Dense hair regrowth occurred another 8 weeks later. In conclusion, F-MF should be considered and a biopsy should be taken if the diagnosis of AA is clinically doubtful. Therapeutic options are glucocorticoids or bexarotene, both topical and oral.



There were several diffuse bald patches with a slight erythema on the scalp. The fine, white scaling was not only localized within the patches, but on the whole scalp like pityriasis simplex capitis. The pull-test was strongly positive at the border of the bald patches.

On the trunk and extremeties there were multiple brown-redish macules of up to approximately 10 cm of diameter with a discreet scaling.

Using trichoscopy multiple yellow dots could be observed within the bald areas.

In contrast to alopecia areata, where a bee swarm like lymphocytic infiltrate around and in the bulb of the follicle can be found, the infiltrate was localized subepidermally as well as around the infundibulum and isthmus (A). There was a pronounced epidermotropism and folliculotropism (B). Compared to the scalp biopsy, the specimen from the leg showed only a sparse superficial perivascular infiltrate with poor epidermotropism (C).

Yellow dots

A dilated follicular infundibulum filled with sebum and keratin could be identified as correlate to the trichoscopically seen yellow dots. The same structure has been described as a correlate for yellow dots in AA[2].

P082

A pilot clinical study of hair grafting in chronic leg ulcers

F Jimenez[1], C Garde[2], E Poblet[3], B Jimeno[2], J Ortiz[2], M Martínez[4], A Gutierrez-Rivera[5], V Perez-Lopez[5], U Etxaniz[5], C Naveda[2], JL Higuera[6], N Egües[7], E Escario[4] and A Izeta[5] *[1]Clínica Dr. Jimenez-Acosta, Las Palmas, Gran Canaria, Spain; [2]Outpatient Care Unit, Hospital Donostia, San Sebastian, Spain; [3]Anatomía Patológica, Universidad de Murcia, Murcia, Spain; [4]Department of Dermatology, Hospital General Universitario de Albacete, Albacete, Spain; [5]Department of Bioengineering, Instituto Biodonostia, San Sebastian, Spain; [6]Department of Vascular Surgery, Hospital Donostia, San Sebastian, Spain and [7]Research Unit, Instituto Biodonostia, San Sebastian, Spain*

Epidermal sheets spread centrifugally post injury from the hair follicle infundibulum to reepithelialize the wound bed. Healing progresses faster in skin areas rich in terminal hair follicles. These observations are consistent with the role of the hair follicle as a major reservoir for progenitor cells. To evaluate the feasibility and potential healing capacity of autologous scalp follicular grafts transplanted into the wound bed of chronic leg ulcers, 10 patients with ulcers of an average size of 36.8 cm^2 and a 10.5-year duration were included in this pilot study. Within each ulcer we randomly assigned a 2 cm × 2 cm "experimental" square to receive 20 hair grafts and a nongrafted "control" square of equal size. The procedure seemed to be safe. At the 18th-week end point, we observed a 27.1% ulcer area reduction in the experimental square as compared with 6.5% in the control square ($P = 0.007$). Histological analyses showed enhanced epithelialization, neovascularization, and dermal reorganization. We conclude that terminal hair follicle grafting into wound beds is feasible in an outpatient setting and represents a promising therapeutic alternative for nonhealing chronic leg ulcers. We conclude that terminal hair follicle grafting into wound beds is feasible in an outpatient setting and represents a promising therapeutic alternative for nonhealing chronic leg ulcers.

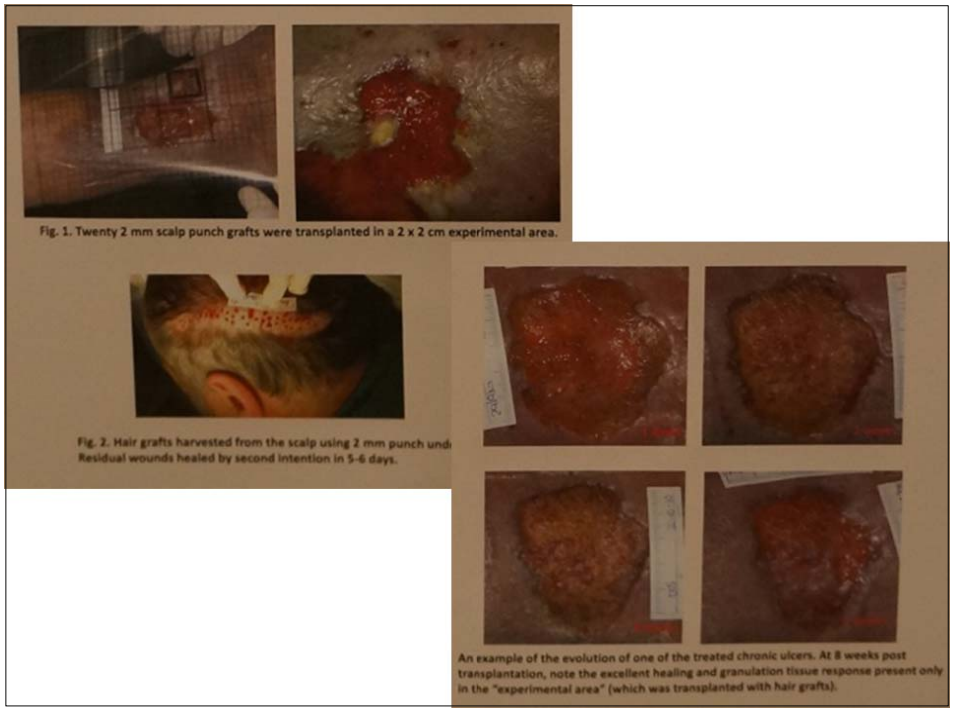


Fig. 1. Twenty 2 mm scalp punch grafts were transplanted in a 2 x 2 cm experimental area.
Fig. 2. Hair grafts harvested from the scalp using 2 mm punch und
Residual wounds healed by second intention in 5-6 days.
An example of the evolution of one of the treated chronic ulcers. At 8 weeks post transplantation, note the excellent healing and granulation tissue response present only in the "experimental area" (which was transplanted with hair grafts).

Plenary Symposium 1:
An Update on Hair Follicle Stem Cells

1030 **Plenary Symposium 1:** — Pentland Auditorium
An Update on Hair Follicle Stem Cells
Chairs: Satoshi Itami, Rod Sinclair

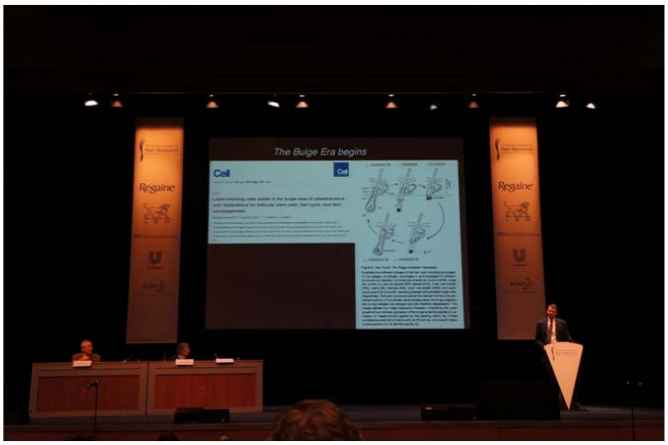
PS1.1 Hair follicle stem cells in alopecia
George Cotsarelis, USA

PS1.4 Cellular and signaling mechanisms that regulate hair follicle stem cells by live imaging
Valentina Greco, USA

PS1.2 Mechanisms of hair follicle aging and stem cell regulation
Emi Nishimura, Japan

PS1.3 Biological and translational potential of hair follicle mesenchymal cells
Colin Jahoda, UK

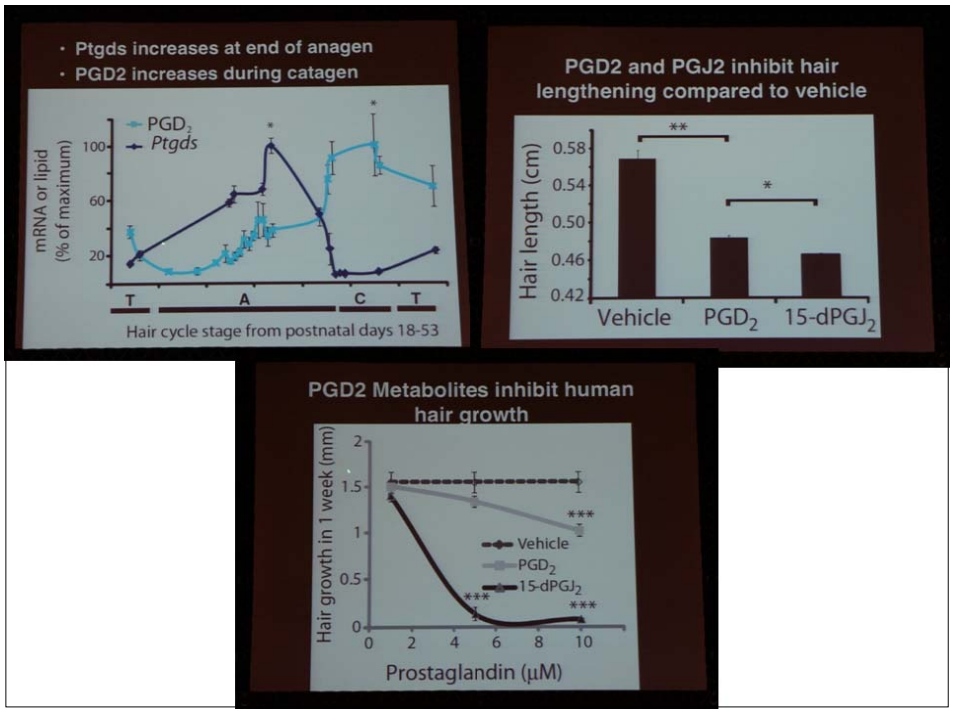
PS1.1 Hair follicle stem cells in alopecia



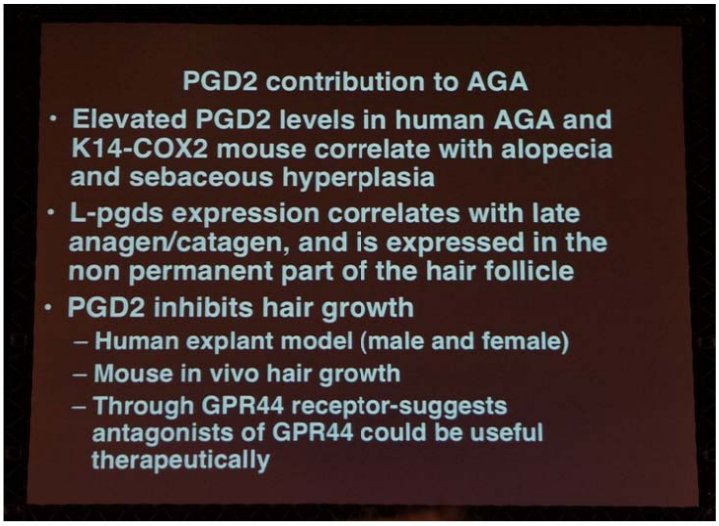
George Cotsarelis, USA

PS1.1 Hair follicle stem cells in alopecia

- Prostaglandin D2 synthase (PTGDS)
  - Elevated at the mRNA and protein levels in bald scalp compared to haired scalp of men with AGA
- Prostaglandin D2 (PGD2)
  - Product of PTGDS enzyme activity
  - Similarly elevated in bald scalp
  - Inhibits hair growth in explanted human hair follicles and when applied topically to mice
- Hair growth inhibition requires the PGD2 receptor (GPR44)
- Transgenic mouse, K14-Ptgs2
  - Elevated levels of PGD2 in the skin
  - Develops alopecia, follicular miniaturization, and sebaceous gland hyperplasia
    - Hallmarks of human AGA
- PGD2
  - Inhibitor of hair growth in AGA
- PGD2–GPR44 pathway
  - Potential target for treatment



PS1.1 Hair follicle stem cells in alopecia



PS1.4 Cellular and signaling mechanisms that regulate hair follicle stem cells by live imaging

Valentina Greco, USA

PS1.2 Mechanisms of hair follicle aging and stem cell regulation

Emi Nishimura, Japan

PS1.2 Mechanisms of hair follicle aging and stem cell regulation

- Expression of various aging phenotypes is characterized by
  1. Functional tissue decline and organismal changes
  2. Decreased regenerating capabilities
- Hair loss and hair graying
  - Typical aging phenotypes in mammals
  - Underlying mechanisms of aging are still largely elusive in most tissues
- Some signaling pathways that determine organismal lifespan and molecules responsible for progeroid syndromes
  - Identified in some organisms in recent decades
- Underlying cellular mechanisms of aging-associated tissue decline and diseases
  - Still largely unknown

PS1.2 Mechanisms of hair follicle aging and stem cell regulation

- Mechanisms of aging-associated hair graying and hair loss by focusing on adult stem cells
  - Chronological analysis of melanocyte stem cells (McSCs) and hair follicle stem cells (HFSCs)
    → Mouse hair follicles age through defective renewal of McSCs and HFSCs
- McSCs
  - Differentiate into pigment-producing melanocytes in the niche without renewing themselves under excessive genomic stress or with aging
- HFSCs with a sustained DNA damage response
  - Also showed characteristic fate changes that are clearly distinguished from cellular senescence

PS1.3 Biological and translational potential of hair follicle mesenchymal cells

Colin Jahoda, UK

1200 **Keynote Lecture** — Pentland Auditorium
Chair: Valerie Randall

K1 **Skin Stem Cells: In Silence and in Action**
Elaine Fuchs, USA

Elaine Fuchs, USA

K1 Skin Stem Cells: In Silence and in Action

- How stem cells balance self-renewal and differentiation
  - Fundamental importance to understanding of normal tissue maintenance and wound repair
- In the mouse..
  - Hair cycles are synchronous, making them an especially attractive model to explore
    - How quiescent stem cells become mobilized to actively regenerate tissue
    - How they self-renew to maintain a pool of stem cells
    - How they return to quiescence following tissue production

1. How the hair cycle works
2. Why the resting phase gets longer as we age
3. How hair follicle and melanocyte stem cells coordinate their behavior
4. How this can be uncoupled in disease states
5. New insights into the process of stem cell activation

5월 5일 오후 프로그램 리뷰

전북대학교 의과대학 피부과학교실

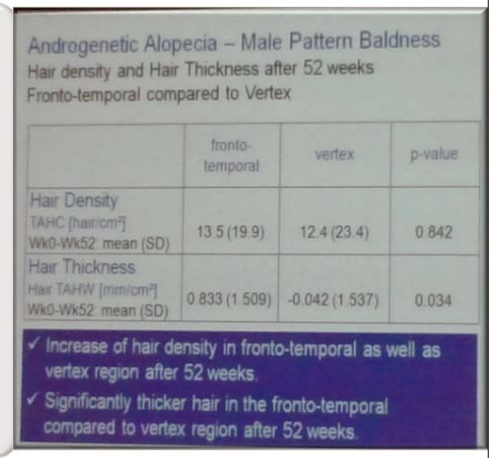
송 기 훈

A Look into the future of AGA management and product innovation with Minoxidil

2013. 05. 05 Sunday 13:00 ~ 14:00
Pentland Auditorium

AGA and 5% minoxidil topical foam (MTF)

- 5% MTF twice daily for AGA
  - Proved to be effective and well tolerated in men with male pattern hair loss in the vertex area
  - Also known to be effective in the frontotemporal region



Androgenetic Alopecia – Male Pattern Baldness
Hair density and Hair Thickness after 52 weeks
Fronto-temporal compared to Vertex

	fronto-temporal	vertex	p-value
Hair Density TAHC [hair/cm²] Wk0-Wk52: mean (SD)	13.5 (19.9)	12.4 (23.4)	0.842
Hair Thickness Hair TAHW [mm/cm²] Wk0-Wk52: mean (SD)	0.833 (1.509)	-0.042 (1.537)	0.034

✓ Increase of hair density in fronto-temporal as well as vertex region after 52 weeks.
✓ Significantly thicker hair in the fronto-temporal compared to vertex region after 52 weeks.

SA and 5% MTF

- Senescent alopecia (SA)
  - Hair thinning that occurs in 60's and 70's and older
  - Great decrease in scalp levels of 5a-reductase type 1 & 2 after age 60
  - Not DHT related
    - Millions of men taking finasteride 5mg for benign prostatic hypertrophy are not regrowing their scalp hair.
    - Supportive evidence that SA is not DHT-mediated
  - Finasteride is not recommended after age 60.
    - 5% MTF could be an alternative.

Miscellaneous

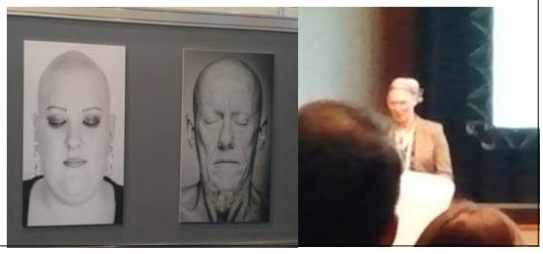
- Finasteride 1mg
  - Not hazardous to women
  - Male fetus in uterus is at risk from exposure to finasteride
    - Female fetus : (-)
  - Semen does not pose a risk to a pregnant female.

Psychology and Hair Disorders Workshop

2013. 05. 05 Sunday 16:00 ~ 17:40
Tinto room

Psychology and hair disorders

- Psychosomatic aspects of alopecia areata (AA)
  - Stress may play a role in AA
    - However, this depends on the individuals involved.
    - "Stress responders" versus "non-stress responders"



Psychology and hair disorders

- Psychosomatic aspects of telogen effluvium (TE)
  - Psychological stress has been commonly cited as a trigger of TE.
    - Yet, not even a case report or study that supports these statements has been published.

Psychology and hair disorders

- Somatopsychic aspects of hair loss
  - Persons with hair loss seem to have a higher prevalence of psychiatric comorbidities.
  - Somatopsychic effect correlated better with the emotional and psychological state related to alopecia rather than objective clinical severity of alopecia.
- Psychogenic pseudomeffluvium
  - Patients are frightened of the possibility of going bald without any objective findings of hair loss.
  - The most common underlying psychiatric disorders
    - Depressive disorder and body dysmorphic disorder

Psychology and hair disorders

- Management of patients with hair problems
  - Explain the "good news" and "not so good news"
    - Take the time to explain
      - The diagnosis and what to expect
      - What current treatments can and cannot do
      - Clarify misconceptions
  - Make short term expectations and term aspects for therapy goals.
  - Look for mental health comorbidities.
    - Depression, social phobia, body dysmorphic disorder
    - Offer special psychotherapy if necessary and help to find someone.
      - Active involvement for correction of psychological comorbidities is necessary.

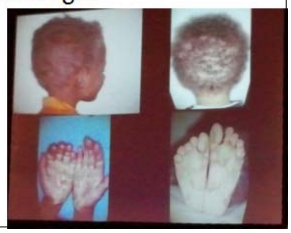
Concluding Plenary
: What's new in clinical hair research?

Abraham Zlotogorski, Israel

2013. 05. 06 Monday 16:00 ~ 17:00
Pentland Auditorium

What's new in clinical hair research?

- Trichologists, what are they for?
  - 14-year-old boy being resuscitated from cardiac arrest and underwent implantation of cardioverter defibrillator
    - He had woolly hair and his soles showed areas of hyperkeratosis.
  - Naxos disease
    - Woolly hair is congenital.
    - Keratoderma starts around age 1.
    - But the heart manifestations start only at teenage.
- Early diagnosis may save life
  - Importance of trichologists!!



What's new in clinical hair research?

- Platelet-rich plasma (PRP) may serve as a safe and effective treatment option in AA.
  - Far better than triamcinolone IL injection

Trink A et al. Br J Dermatol 2013 Apr 22

- British association of dermatologists' guidelines for the management of AA (2012)
  - Leaving AA untreated is a legitimate-option for many patients.
  - Spontaneous remission occurs in up to 80% of patients with limited patchy hair loss of short duration (<1 year).
    - Such patients may be managed by reassurance alone.

Messenger AG et al. Br J Dermatol 2012;166(5):916-26

- Prognosis in longstanding extensive alopecia is poor.
  - Wig may be a better option than indulging in treatment that are unlikely to be effective in this group.

Messenger AG et al. Br J Dermatol 2012;166(5):916-26

What's new in clinical hair research?

- Pulse corticosteroid therapy for AA
  - Not effective for alopecia totalis and alopecia universalis

Acikgoz G et al. Dermatolog Treat 2013 Jan 22
Staumorit-Salle D et al. Dermatol 2012;225:81-7

- AGA and risk of prostate cancer
  - Vertex pattern AGA was associated with a significant increased risk of prostate cancer.
    - Any pattern AGA did not show a significant increase.
  - Unexpected new important role for hair as a herald of cancer
  - Importance of meticulous examining and documentation of hair phenotypes in routine physical examinations

Amoretti A et al. J Am Acad Dermatol 2013 Feb 7

Thank you for your kind attention!

5월 6일 프로그램 리뷰

서울대학교 의과대학 피부과학교실

최 미 라

Plenary Symposium 2

Progress in Clinical Hair Disorders

Genetics and immunology of alopecia areata

- **Identification of several susceptibility loci in AA**
  - Genome wide association study (GWAS)
    - Uncover new genetic pathways

    → Lead to unanticipated therapeutic approaches guided by the underlying genetics
    - NKG2D axis
      - Activating receptor found on NK cells and CD8 T cells (both αβ and γδ)

Angela Christiano, USA

Genetics and immunology of alopecia areata

- C3H/HeJ mouse model
  - Systemic anti IL-15Rβ
  - Topical JAK3 inhibitor (Tofacitinib)

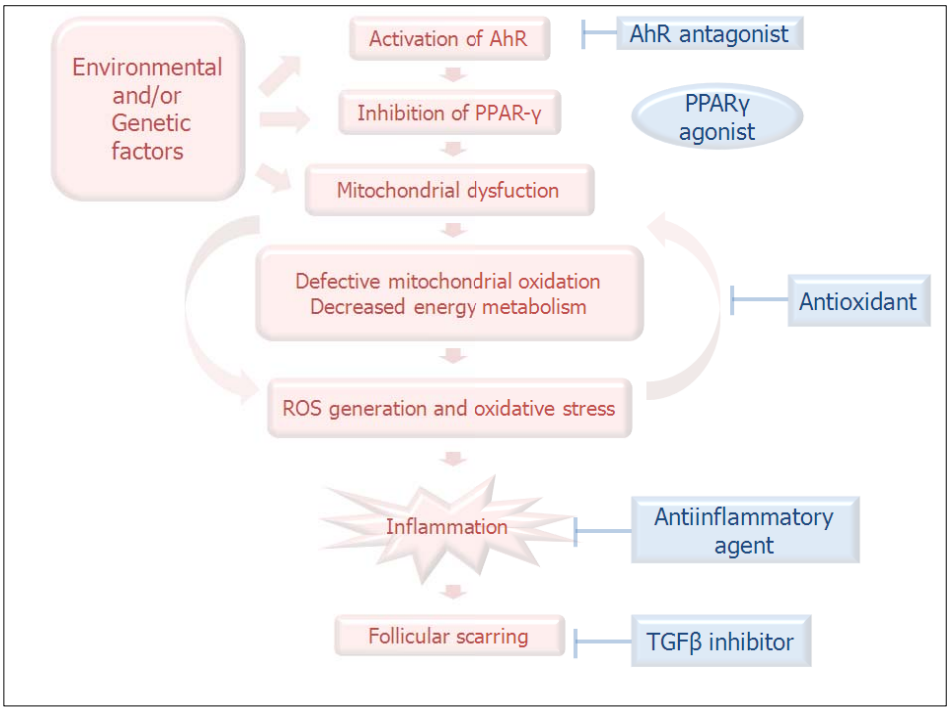
GWAS can reveal new therapeutic targets for complex diseases

Xenobiotic receptors in cicatricial alopecia:
linking environment to disease pathogenesis

- **AhR (Aryl hydrocarbon receptor)**
  - Transcription factor activated by xenobiotic ligands
  - Induce enzymes which metabolize environmental toxins
    - Dioxins, polycyclic aromatic hydrocarbons
  - Expression of AhR-target genes in human primary cicatricial alopecia ↑
  - AhR transgenic mouse
    - Excellent experimental model for scarring alopecia

Novel link between environmental factors and the etiology of primary cicatricial alopecia

Pratima Karnik, USA



The latest updates of the management of pattern hair loss

- **5α-reductase inhibitor**
  - Effect on spermatogenesis
    - Positive benefit-to-risk ratio for the use of finasteride daily for MPHL
    - But, overall impact of negative findings on fertility in extremely small proportion of patients is unknown

  → Should be considered when evaluating men for unexplained oligospermia, and clinical judgement should be exercised when these drugs are given to men who desire fertility

Won Soo Lee, Republic of Korea

The latest updates of the management of pattern hair loss

- **Is finasteride effective in FPHL?**
  - 10 of 12 clinical studies or case reports
    - Improvement (+)
  - 2 controlled clinical studies
    - No benefit
  - Unclear whether the success was due to a higher doses of FNS
  - Although objective evidence is limited, FNS may be considered for treatment for FPHL

The latest updates of the management of pattern hair loss

- **Ketoconazole shampoo**
  - Antiinflammatory properties
  - Local disruption of the DHT pathway
  - Inhibition cytochrome P450 enzyme
- **Topical bimatoprost/latonoprost**
  - PGF2α analogue
- **Topical PP-303 solution**
  - 5% minoxidil + 0.01% tretinoin

The surgical management of cicatricial alopecia

Post cessation of medication

- To wait for 12–24 months of stability post cessation of medication management
- No medication "cover" during the surgical process

During medication

- Surgery during medication management if the patient has completed a successful "stable" period of 12 months on medication

- Greater risk of re-activation in patients with frontal fibrosing alopecia (FFA) compared to other cicatricial alopecias

Russell Knudsen, Australia

포스터 짝수번 리뷰

가톨릭대학교 의과대학 피부과학교실

정 관 호

WCHR 2013
세계모발학회 참관기

Poster session

THE CATHOLIC UNIVERSITY OF KOREA
ST. PAUL'S HOSPITAL

Kwan Ho, Jeong

Poster No.	Category
46	ANDROGENETIC ALOPECIA
108	FACTORS INFLUENCING HAIR GROWTH
114	
118	
130	
136	GENETIC HAIR DISORDERS AND HAIR FIBER SCIENCE
150	HAIR FOLLICLE DEVELOPMENT, CONTROL OF THE HAIR CYCLE AND PIGMENTATION
152	
156	
158	
162	
172	
184	STEM CELLS AND EPIGENETICS
192	
194	THE SCIENCE OF HAIR CARE
200	
230	TISSUE ENGINEERING/REGENERATION
232	

P046

P046

Platelet-rich plasma promoting hair growth in human hair follicle dermal papilla cells associated VEGF and VEGFR-2

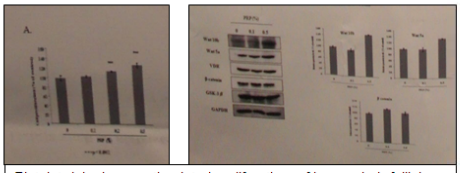
Beom Joon Kim[1,2*], So Young Kim[1,2], Tae Rin Kwon[1,2], Young Hee Lee[2], Yi Sub Song[1,2], Kapsok Lee[2], Yang Won Lee[3], Chang Hun Huh[4], Chang Kwun Hong[2]

[1]Department of Convergence Medicine and Pharmaceutical Biosciences, Graduate School, Chung-Ang University, Seoul, Korea
[2]Department of Dermatology, Chung-Ang University College of Medicine, Seoul 156-756, Korea
[3]Department of Dermatology, Konkuk University, College of Medicine, Seoul, Korea, [4]Department of Dermatology, Seoul National University Bundang hospital, Seongnam, Gyeonggi, Korea

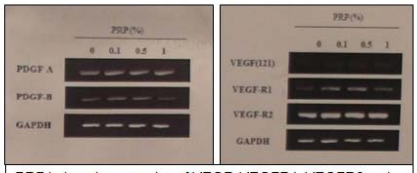
Platelet-rich plasma(PRP) – accelerate wound repair

- PRP contains various growth factors
  a. PDGF
  b. VEGF
  c. FGF
  d. TGF

To determined effect of PRP to enhance hair growth on human dermal papilla cells



Platelet-rich plasma stimulated proliferation of human hair follicles DP cells in a dose-dependent manner and up-regulated expression of Wnt10b, 5a and β-catenin on DPCs.



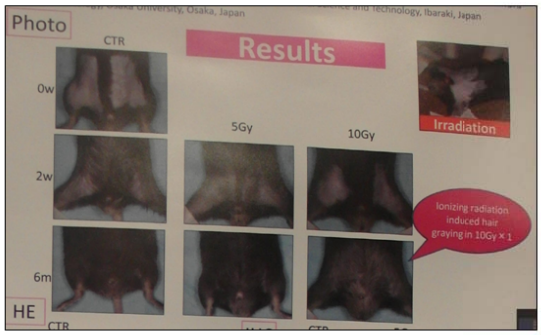
PRP induced expression of VEGF, VEGFR1, VEGFR2 and PDGF on DPCs.

In conclusion, possible therapeutic materials of autologous PRP to promote hair growth

P108

Tissue damage after ionizing radiation in skin and hair follicles: short- and long term effects after a single high dose and multiple low doses in mice

K Kinoshita1, H Kato1, H Ishimine2, K Doi1, N Aoi1, K Inoue1, K Shiraishi3, K Nakagawa3, A Kurisaki2, S Itami4 and K Yoshimura1 1Department of Plastic Surgery, University of Tokyo, Tokyo, Japan; 2Research Center for Stem Cell Engineering, National Institute for Advanced Industrial Science and Technology, Ibaraki, Japan; 3Department of Radiology, University of Tokyo, Tokyo, Japan and 4Department of Regenerative Dermatology, Osaka University, Osaka, Japan



Evaluation

Macroscopic (photo)

HE stain
- -The number of epidermal layers
- -The thickness of epidermis, dermis, subcutaneous fat tissue
- -The diameter of hair follicles
- -The number of hair follicles

IHC
- -isolectin (The number of capillaries in dermis and subcutaneous fat tissue)
- - CD34 (as a marker of stem cells in bulge region) (Morris et al. ,2004)
- - Ki67 (as a marker of proliferating cells)

Results		
1 to 4weeks	**Hair follicle and capillaries (↓)**	**Ki67 (↑)**
3 to 6months	Epidermal damage **10Gy x 1 (↑) than 5Gy x 2**	Deep tissue damage **5Gy x 2 (↑)**

Conclusion

These data provide clinical insights for minimizing short- and long-term radiation injury and revitalizing the radiated ischemic and fibrous tissue.

P114

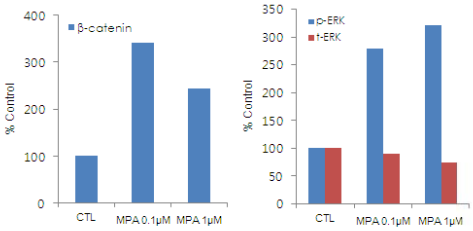
THE CATHOLIC UNIVERSITY OF KOREA
CATHOLIC MEDICAL CENTER

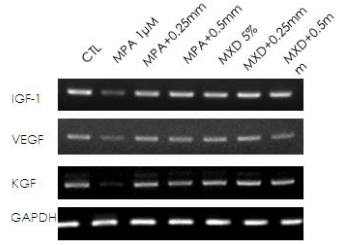
Mycophenolic acid has concentration-controlled effects on the hair growth

Kwanho Jeong, Ye Jin Lee, Jung Eun Kim, Beom Joon Kim[1], Young Min Park, Hoon Kang
Department of Dermatology, College of Medicine, The Catholic University of Korea, Seoul, Korea
[1]Department of Dermatology, College of Medicine, Chung-Ang University, Seoul, Korea

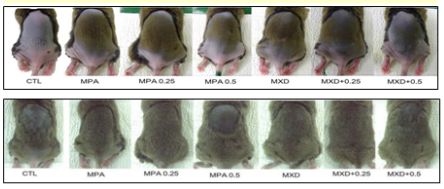
To investigate whether mycophenolic acid (MPA) has hair growing effect directly without the influence of *de novo* purine biosynthesis

MPA on dermal papilla cells





MPA with disk type microneedle(DTS) stimulation



Conclusions

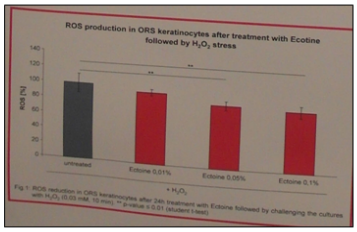
- The expression of Erk and β-catenin signaling significantly increased MPA-group than control-group
- DTS plus MPA and/or MXD group than agents only applied group: IGF-1, VEGF, KGF (↑)
- Microneedle roller plus MPA on the mouse skin demonstrated similar effect compared to 5% minoxidil
- These results suggest that be particularly important to develop new therapeutic option for hair loss

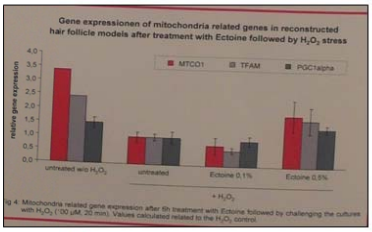
P118

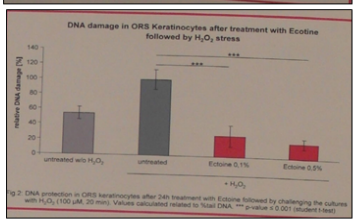
Effects of Ectoine on follicular aging processes

Melanie Giesen, Guido Fuhrmann, Melanie Briese, Sabine Rasche, Tanja Görlach, Dirk Petersohn, Thomas Förster
Henkel AG & Co KGaA, Duesseldorf, Germany

To investigate the effect of Ectoine on hair follicle cells subjected to oxidative stress.







Results

Ectoine reveals a high potential to protect

1. cellular functions against oxidative stress
2. the resulting DNA damage
3. Impaired keratin synthesis

Ectoine exhibited a restoration of essential cellular parameters under oxidative stress and a reduction of DNA damage up to 80%.

These data suggest that Ectoine shows a high potential to antagonize follicular aging processes.

P130

Human scalp hair follicles possess the enzymes to synthesise prostaglandins & prostamides from phospholipids & contain $PGF_{2\alpha}$ *in vivo*

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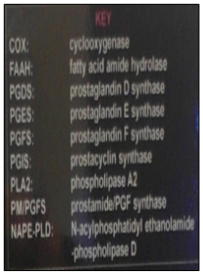
INTRODUCTION

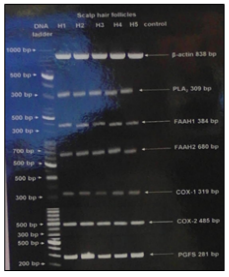
- Some glaucoma treatments stimulate eyelash growth as a side-effect. These include prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) (e.g. latanoprost) & prostamide $F_{2\alpha}$ (bimatoprost) analogues.

AIMS

$PGF_{2\alpha}$ and/or prostamide $F_{2\alpha}$ may play unrecognised roles in follicular cell signalling, since human hair follicles are stimulated by bimatoprost & contain both PG & prostamide $F_{2\alpha}$ receptors. Therefore, we investigated:

- whether human scalp follicles contain the necessary enzymes to synthesise prostaglandins & prostamides *de novo* from phospholipids.
- whether normal scalp follicles contain $PGF_{2\alpha}$.





Results

1. RT-PCR and qPCR analysis showed expression of all the enzymes necessary to synthesise PGs de novo in scalp hair follicles
2. IHC confirmed protein expression of enzymes in the bulb
3. Identified all the enzymes necessary for de novo synthesis of prostamides: NAPE-PLD, COX2 and PM/PGFS

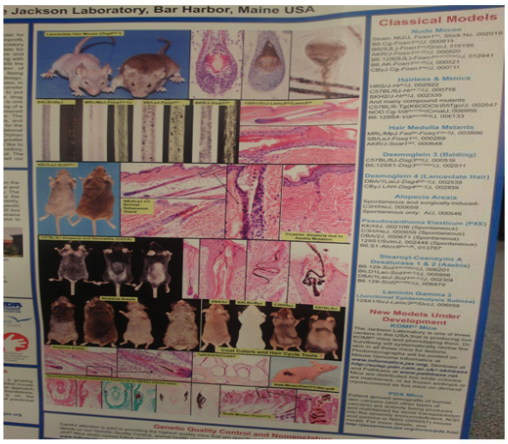
Conclusions

- Scalp hair follicles possess the necessary enzymes to carry out the local synthesis of both prostaglandins and prostamides from phospholipids, also contain PGF
- This suggests that these paracrine mediators may have natural roles in hair follicles; further analysis of these should increase our understanding of hair follicle biology and may lead to further treatments for hair disorders.

P136

An international repository for mouse models of human hair diseases

John P. Sundberg, Stephen F. Rockwood, C. Herbert Pratt, and Cat M. Lutz
The Jackson Laboratory, Bar Harbor, Maine USA



http://jaxmice.jax.org/research/rare-diseases.html

The Jackson Laboratory Rare and Orphan Disease Center was recently launched to focus on partnering with scientists, foundations, and other experts around the world to enable the development, standardization, optimization, and rapid distribution of preclinical mouse models for basic research and drug discovery.

Active research on rare diseases by Jackson Laboratory scientists

- Alopecia areata (John Sundberg)
- Alstrom or Alström syndrome (Jürgen Naggert, Patsy Nishina)
- Amyotrophic Lateral Sclerosis, ALS or Lou Gehrig's disease (Greg Cox, Cat Lutz, Kevin Seburn)
- Ataxia telangiectasia (Rick Maser)
- Charcot-Marie-Tooth (Rob Burgess, Kevin Seburn)
- Cicatricial alopecia (John Sundberg)
- Congenital muscular dystrophy (Greg Cox)
- Congenital myasthenic syndromes (Rob Burgess)
- Costello syndrome (Dave Bergstrom)
- Craniofacial and skeletal defects (Leah Rae Donahue, Steve Murray)
- Cystic fibrosis (Steve Murray)
- Duchenne muscular dystrophy (Greg Cox, Cat Lutz)
- Dyskeratosis congenital (Rick Maser)
- Epidermolysis bullosa (Derry Roopenian, John Sundberg)

P150

Mammalian target of rapamycin complex 1 (mTORC1) may modulate the timing of anagen entry in mouse hair follicles

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mTOR complex 1 (mTORC1) has functional significance in hair growth cycle regulation

mTORC1 activation in HF was hair phase-specific	• mTORC1 kinase activity was high during anagen and late morphogenesis and low during telogen. • The results imply mTORC1 role in anagen, possibly in proliferation.
Site-specific activation of mTOR in HFs	•phosphorylated-mTOR localisation was site-specific in a growth-phase dependent manner. •p-mTOR was expressed during the complete hair cycle in different HF components. •The results imply mTOR role in hair growth initiation at the onset of anagen.
mTORC1 inhibition delayed spontaneous anagen initiation	• Rapamycin and vehicle treated HFs showed normal morphology, but different phases. • Rapamycin inhibited mTORC1 activation in anagen HFs

Conclusion: mTOR modulate the signal required for the spontaneous onset of anagen.

P152

A meeting of two chronobiological systems: *Period1* and *BMAL1* modulate the human hair cycle

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1Salford Royal Foundation Trust, Salford Royal Hospital, Salford, UK; 2Inflammation and Repair, University of Manchester, Manchester, UK; 3Hungarian Academy of Sciences, University of Debrecen, Debrecen, Hungary; 4Farjo Medical Centre, Manchester, UK; 5Centre for Cutaneous Research, Queen Mary's University of London, London, UK; 6Italian Institute of Technology, Genova, Italy and 7Department of Dermatology, University of Luebeck, Luebeck, Germany

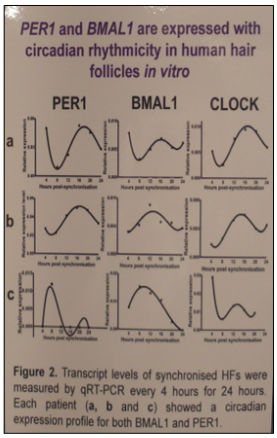
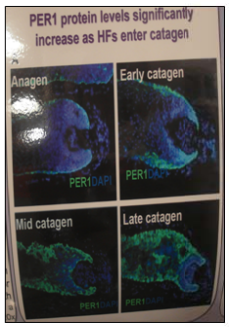


Figure 2. Transcript levels of synchronised HFs were measured by qRT-PCR every 4 hours for 24 hours. Each patient (**a**, **b** and **c**) showed a circadian expression profile for both BMAL1 and PER1.



Results

- The absence of central clock influences isolated, organ-cultured human HFs show circadian changes in the gene and protein expression of core clock genes (CLOCK, BMAL1, Period1) and clock-controlled genes (c-Myc, NR1D1, CDKN1A), and that **Period1 expression is also hair cycle-dependent.**
- **Knockdown of BMAL1 or Period1** in human anagen HFs significantly **prolonged anagen and stimulated hair matrix keratinocyte proliferation.**

Conclusion

- Human HFs show circadian and hair cycle-dependent changes in clock gene/protein expression in the absence of the central clock.
- **PER1, BMAL1 and CLOCK do regulate hair follicle cycling and they produce anagen-terminating signals.**
- The human HF exhibits peripheral clock activity which regulates the human hair cycle under clinically relevant *in vitro* conditions.

P156

Stem cell factor/c-kit signalling in the hair bulb is essential to maintain hair pigmentation in adult human hair follicle *in vivo* and in organ culture

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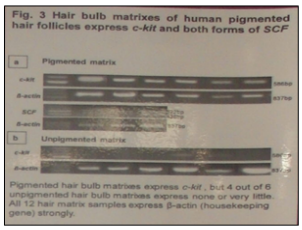
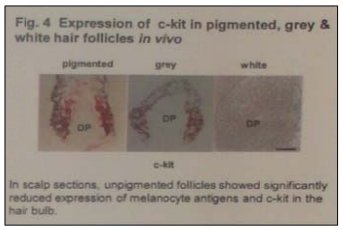
As stem cell factor (SCF)/c-kit signaling is implicated in hair melanocyte development and androgen stimulated changes in hair pigmentation, molecular biological and organ culture methods were used to investigate whether this is also involved in normal human hair graying.





Discussion

- Loss of hair melanocytes and/or melanin facilitates increased cell division/ differentiation.
- **SCF/c-kit signaling is necessary within anagen hair bulbs to maintain bulb melanocytes & hair pigmentation in normal adult scalp follicles in organ culture and *in vivo*.**

P158

IL-1β-mediated protection from chemotherapy-induced alopecia in the wound healing milieu

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Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami FL 33136

To determine the effect of the wound healing milieu itself on the hair follicle remains.

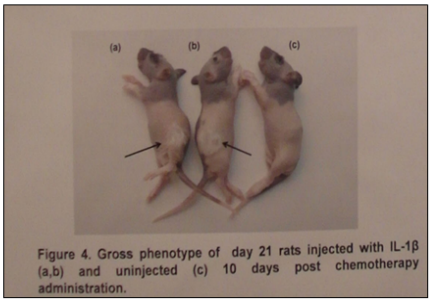

Figure 4. Gross phenotype of day 21 rats injected with IL-1β (a,b) and uninjected (c) 10 days post chemotherapy administration.

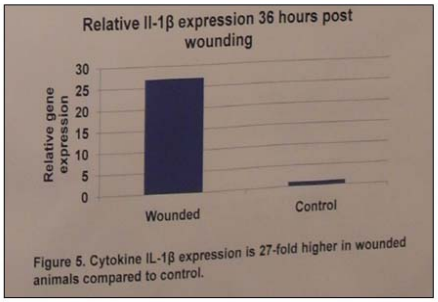

Figure 5. Cytokine IL-1β expression is 27-fold higher in wounded animals compared to control.

Conclusions

- The wound healing milieu confers protection against chemotherapy induced alopecia.
- IL-1β is the specific mediating cytokine within the wound that protects against CIA.
- **IL-1β is up-regulated** compared to other cytokines in the **acute wound healing process**.
- Determining the exact mechanism that is regulating this process will allow for the development of new therapies to manage this dreaded side effect in cancer patients.

P162

A comparison of methods of anagen synchronization in the chemotherapy induced alopecia adult rat model

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Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami FL 33136

To compare the histological profiles of adult rat skin treated with one of four methods of depilation: shaving, clipping, waxing, or plucking to determine whether they induce similar HF changes

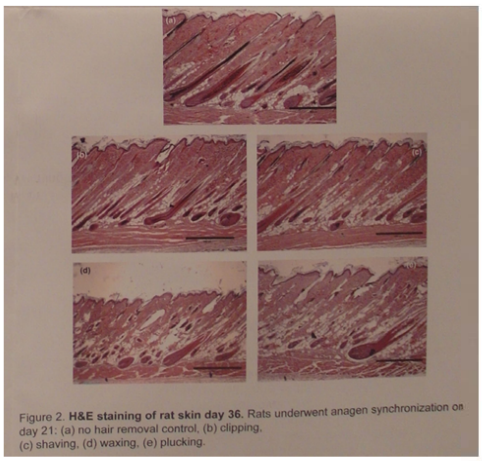

Figure 2. **H&E staining of rat skin day 36.** Rats underwent anagen synchronization on day 21: (a) no hair removal control, (b) clipping, (c) shaving, (d) waxing, (e) plucking.

Conclusions

Shaving and clipping, as methods of anagen synchronization, result in undistubed, atraumatic hair follicles.

Waxing and plucing results in severe hair follicle distortion and can induce small wounds in the process.

We suggest avoiding waxing and plucking to synchronize hair follicles prior to chemotherapy adminstration, as they may affect experimental outcomes.

P172

Low level light enhances hair follicle epithelial-mesenchymal interaction and anagen entry

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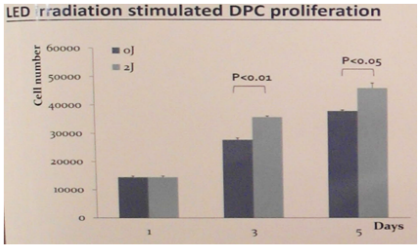
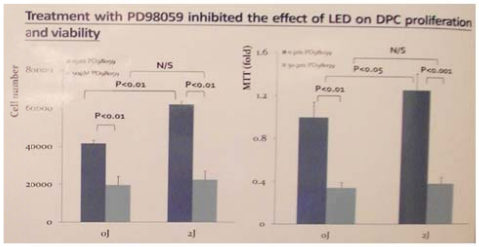
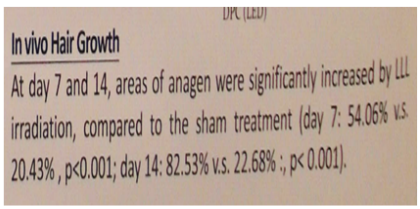
[1] Institute of Biomedical Engineering, National Taiwan University, Taipei, Taiwan
[2]Department of Dermatology, National Taiwan University Hospital and College of Medicine, Taipei, Taiwan

Abstract

The low-level light(LLL) irradiation has gained popularity in the treatment of various types of alopecia in recent years, but the underlying mechanism is unknown. In this research, we aim to investigate the mechanisms.







Conclusion

- In the in vivo condition, **low-level light-shortened telogen** in the irradiated mice.
- promoted cell growth in each cell compartment
- enhanced the epithelial–mesenchymal interaction.

Low level light, leading to earlier anagen entry and reduced alopecia

P184

Roles of MED1 in quiescence of hair follicle stem cells and maintenance of normal hair cycling

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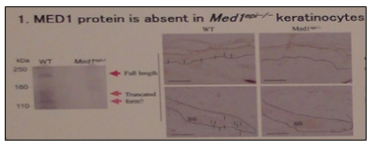
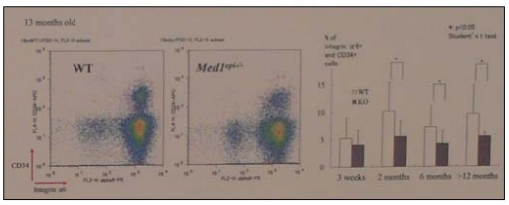
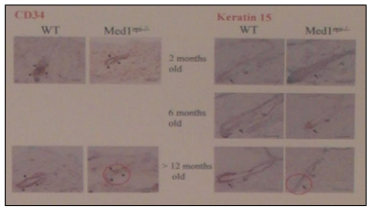
1Osaka University, Suita, Japan and 2Northwestern University, Chicago, Illinois, USA

MED1 (Mediator complex subunit 1) is expressed by human epidermal keratinocytes and functions as a co-activator of several transcription factors, including nuclear receptors.

To elucidate the role of MED1 in keratinocytes, we established keratinocyte-specific Med1-null (Med1$^{epi-/-}$) mice using the K5Cre-LoxP system.







Results

1. CD34 and K15 cells are reduced in the Med1$^{epi-/-}$
2. CD34 positive bulge stem cells of Med1$^{epi-/-}$ mice reduce by aging
3. Expression of SOX9 is reduced in Med1$^{epi-/-}$ derived keratinocytes
4. The skin of phenotype of Med1$^{epi-/-}$ partially supports that Med1 fuctions as a coactivator of VDR in keratinocytes.

P192

Acceleration of skin wound healing in keratinocyte-specific mediator complex subunit 1 null mice

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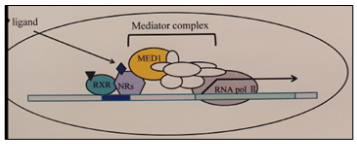
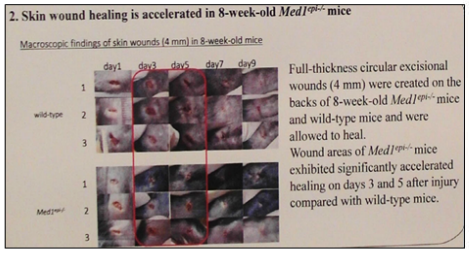
1 Department of Regenerative Dermatology, Graduate School of Medicine, Osaka University
2 Department of Pathology, Feinberg School of Medicine, Northwestern University, USA



MED1 (Mediator complex subunit 1) is a co-activator of several nuclear receptors and functions in multiple transcription signaling pathways

To investigate the function of MED1 in skin wound healing, fullthickness wounds were generated on the backs of Med1$^{epi-/-}$ mice and the healing process



Wound healing

Acceleration	Deceleration
Follistatin ↓ Activin signal ↑ JNK ↑ Keratinocyte proliferation ↑	Hair follicle stem cell ↓ Keratinocyte proliferation ↓

Aging

Conclusion

1. The loss of follistatin expression in keratinocytes enhances the biological activity of endogenous activin
2. Activated JNK singling pathway in the epidermis, resulting in rapid wound healing in Med1$^{epi-/-}$ mice
3. Skin wounding healing in 6-month-old Med1$^{epi-/-}$ mice is significantly delayed with decreased numbers of Ki67

P194

Optimization of intercellular communication inside the human hair follicle

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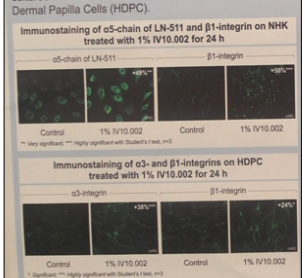
ASI Vincience, Global Skin Research Center, Ashland Specialty Ingredients, Sophia Antipolis, France

In the present study, we were interested in studying the interactions implicating laminin-511 (LN-511), its integrin receptor, and β-catenin. Indeed, the LN-511 pathway was previously associated with hair follicle maintenance in the active phase of the hair cycle (anagen).

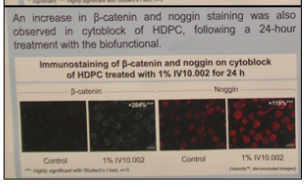
A

The first part of the study consisted in characterizing the expression of LN-511 as well as α3- and β1-integrins in cultured Normal Human Keratinocytes (NHK) and Human Dermal Papilla Cells (HDPC).



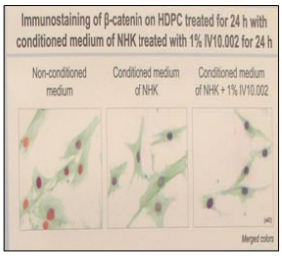
B

An increase in β-catenin and noggin staining was also observed in cytoblock of HDPC, following a 24-hour treatment with the biofunctional.



C

Then, in order to study communication between NHK and HDPC, we applied conditioned medium of NHK treated with the selected compound on HDPC. We observed an increase in β-catenin nuclear staining in HDPC treated with NHK-conditioned medium, suggesting an effect on intercellular communication.



D

Moreover, in hair follicle maintained in culture for a longer time, the compound helped preserve LN-511 expression and HF structure (Hematoxylin-Eosin, H&E) including a better cell organization and melanocyte maintenance at the level of the hair bulb.

Conclusion

Maintaining intercellular communication inside the hair follicle, by targeting LN-511, could be considered as a potential way to preserve optimal hair growth environment

P200

P200 Localization of mucins in human skin and hair follicles

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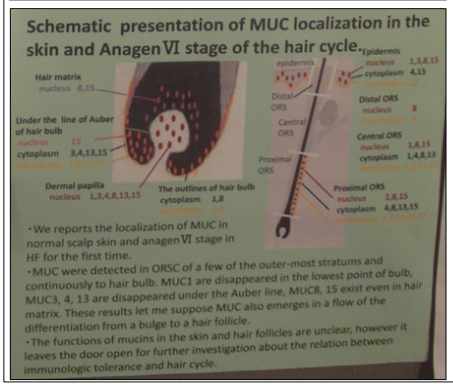
Background: Mucins are high-molecular-weight

Fig.4 Immunohistology for MUC in the skin and HF

To investigate the localization of mucins in human skin and hair follicles

Table. 1 A classification of mucins gene: MUC

mucin		mucins gene
the membrane-bound mucins		MUC1, MUC3A, MUC3B, MUC4, MUC12, MUC13, MUC15, MUC16, MUC17, MUC20, MUC21
the secreted of mucins	polymer	MUC2, MUC5AC, MUC5B, MUC6, MUC19
	monomer	MUC7, MUC8
unclassifiable		MUC22



Results

- In the anagen VI stage at HFs, mucins were strongly deposited in the dermal papilla, but were not observed in the telogen phase.
- Several kinds of MUC were observed in the nuclear of keratinocytes at epidermis.
- MUC1,3,4,8,13 and 15 were observed in the DP and hair bulb in the anagen VI stage.
- MUC3 was present in the DP in the anagen II stage which bulb matrix cells envelop the DP.

P230

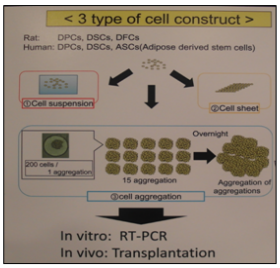
P230 Optimized preparation of dermal papilla cell (DPC) construct for hair regeneration therap

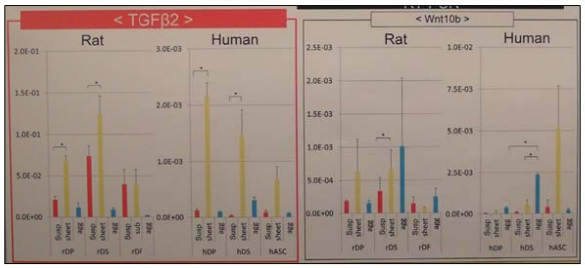
Harunosuke Kato[1], Kahori Kinoshita[1], Noriyuki Aoi[1], Keita Inoue[1], Kotaro Yoshimura[1]
[1] Department of Plastic Surgery, University of Tokyo, Tokyo, Japan

Hemi-vascularized sandwich (HVS) method ?

- DPC culture and DPC transplantation method

To optimize preparation of transplantation construct of cultured DPCs





Conclusion

- The construct form substantially changed DPC function such as hair inductivity.
- TGFβ2 expression appeared to be a reliable index predicting hair inducing capacity of DPCs.
- A sheet was the most efficient form with functioning DPCs, but a combination with undifferentiated aggregates may work better for hair regeneration with cycling.

P232

Maintenance of hair-inducing capacity of cultured dermal cells by addition of cell culture medium

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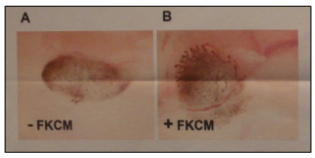
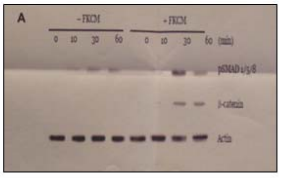
[2]Department of Applied Bioscience, CHA University, Seoul, Korea

To maintain or enhance trichogenicity of cultured dermal cells by addition of cell conditioned medium



Implanted cells		1st	2nd	3rd	4th	5th
together with fresh isolated newborn epidermal cells						
Cultured rat vibrissa DP cells	- FKCM	0	0	0	0	0
	+ FKCM	0	50	80	0	65
Freshly isolated rat dermal cells (positive control)		40	170	250	65	220



Results

- Increment of hair follicle induction in follicular keratinocyte-conditioned media(FKCM)-treated dermal cells.
- Activation of BMP and β-catenin signaling pathway by FKCM (+).

Conclusion

Hair-inductive capacity (trichogenicity) of cultured dermal cells can be maintained and enhanced by supplementation of cell conditioned medium.

포스터 홀수번 리뷰

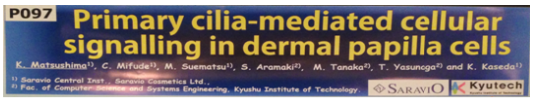
원주대학교 의과대학 모발 및 코스메틱의학연구소

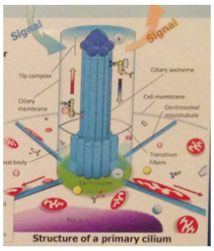
김 성 해

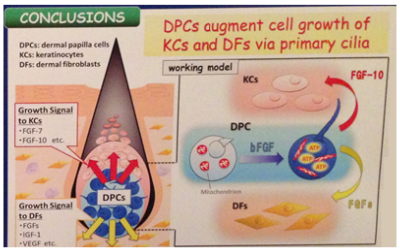
❖ WCHR 2013 poster listings

Category	
Alopecia areata	
Androgenetic alopecia	
Cicatrical alopecia	
Clinical cases	
Genetic hair disorders and hair fibre science	
Hair follicle development, control of the hair cycle and pigmentation	
Hair restoration	
Psychology and hair disorders	
Trichoscopy	
Factors influencing hair growth	**3 편**
Stem cells and epigenetics	**2 편**
The science of hair care	**3 편**
Tissue engineering/regeneration	**2 편**
Total: 234 (홀수 번호 포스터)	

➢ FACTORS INFLUENCING HAIR GROWTH



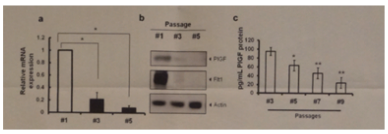


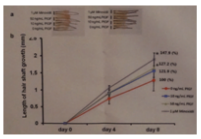


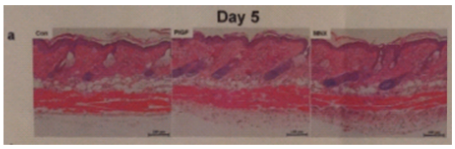
- Primary cilium is a signaling center in mammalian cells, DPC cilium is involved in producing cell growth signals.
-To establish an assay system to investigate roles of primary cilia of DPCs.
-bFGF is an endogenous ciliary elongation factor.
-DPCs augment cell growth of KCs and DFs via primary cilia.

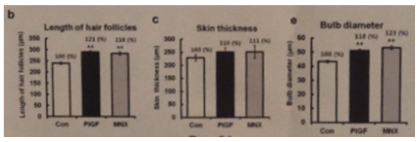
➢ FACTORS INFLUENCING HAIR GROWTH

P101





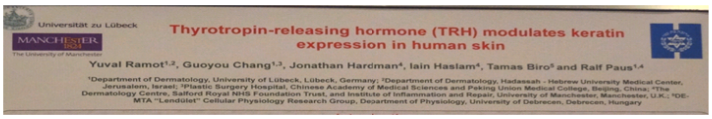


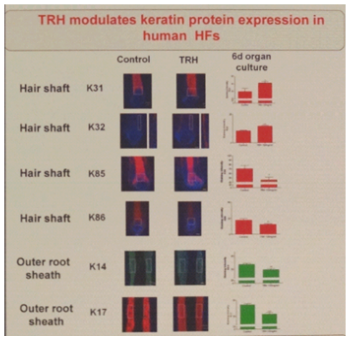


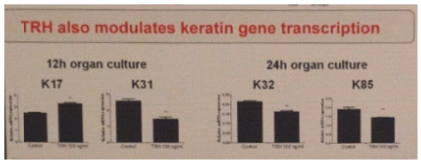
In summary, PIGF
-markedly stimulated hair growth in both in vitro and in vivo models.
-plays a certain role in hair growth promotion.
-may serve as an additional therapeutic target for the treatment of alopecia.

➢ FACTORS INFLUENCING HAIR GROWTH

P133





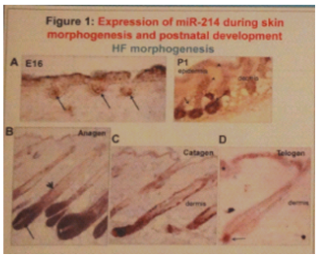


After treatment of TRH or vehicle, and the expression of selected keratins was assessed:
-Hair keratins K31 and K32↑, K85 and K86↓
-Epithelial keratins K14 and K17↓
In the interfollicular epidermis, TRH stimulated expression of K6, K14, and K17.

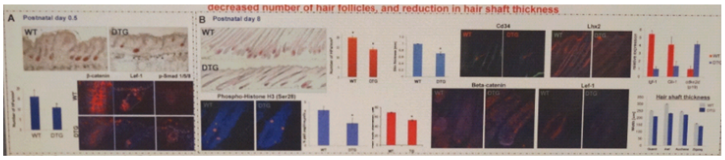
These findings introduce the neuropeptide hormone TRH as a novel modulator of selected human hair keratins in situ.

➢ STEM CELLS AND EPIGENETICS

P183

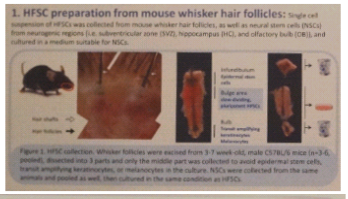


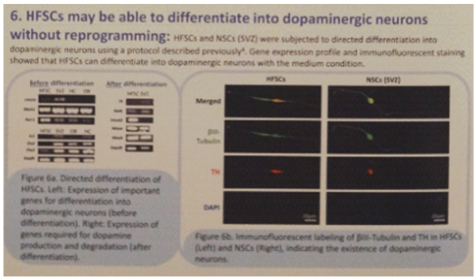
-Expression of MicroRNA-214 during skin morphogenesis and postnatal development.
-Mir-213 decreases beta-catenin expression in keratinocytes and mouse.
-Over-expression of miR-214 results in the retardation of hair follicle development, decreased number of hair follicles, and reduction in hair shaft tickness.
-Over-expression of miR-214 leads to the retardation of anagen development.
-Mir-214 serves as a novel player involved in the regulation of skin and hair follicle development and cycling, at least, in part by modulating the activity of the Wnt/beta-catenin signaling pathway.

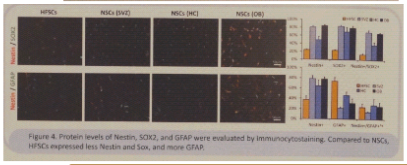


➢ STEM CELLS AND EPIGENETICS

P189







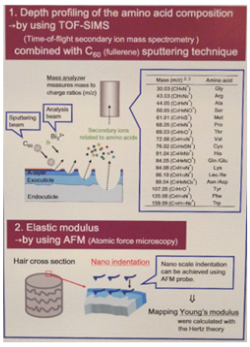
-HFSC preparation from mouse wihisker hair follicles.
- HFSCs express NSC marker proteins.
-HFSCs may be able to differentiate into dopaminergic neurons without reprogramming and release dopamine.
-Taken together, HFSCs have the potential to differentiate into dopaminergic neurons.

➢ THE SCIENCE OF HAIR CARE

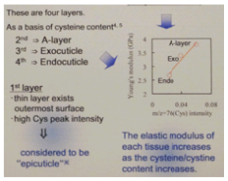
P195

Structural analysis of a hair cuticle using TOF-SIMS and AFM

Kazutaka Ishikawa[1], Masayuki Okamoto[1], Noriyuki Tanji[1] and Satoka Aoyagi[2]
(1)Analytical Science Research Laboratories,Kao Corporation, 1334 Minato, Wakayama-shi, Wakayama 640-8580, Japan
(2)Faculty of Life and Environmental Science, Shimane University, 1060 Nishikawatsu-cho, Matsue-shi, Shimane 690-8504, Japan



Hair cuticle were directly analyzed by two different methods.
First, time-of-flight secondary ion mass spectrometry (**TOFSIMS**).
Second, atomic force microscopy (**AFM**).



Significant information about the nature of the hair cuticle can be obtained by TOF-SIMS and AFM. These methods are powerful to characterize nanostructure of hair fibers.

1) cysteine/cystine↑ ⟶ elastic modulus↑
2) the epicuticle has a characteristic amino acid composition on the outermost hair surface.

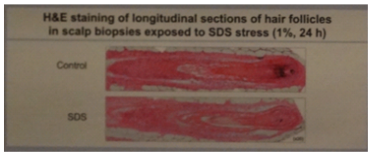
➢ THE SCIENCE OF HAIR CARE

P197

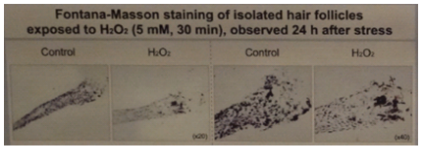
How Does Lifestyle Stress Affect the Hair Follicle? Development of *Ex Vivo* and *In Vitro* Approaches

C Gondran, S Ratz, C Meyrignac, A Perrin, G Menon*, JM Botto and N Dorrloge
Ashland Specialty Ingredients, Vincience, Global Skin Research Center; Sophia Antipolis, France
*Ashland Specialty Ingredients, Wayne, NJ, USA

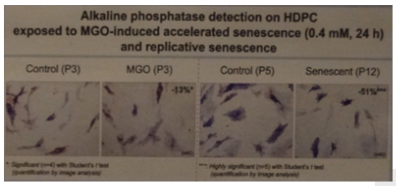
1) Full-thickness scalp biopsies: damaging effects in the hair bulb, resulting from the topical application of a detergent solution.



2) Isolated hair follicles: H_2O_2 stress - a reduction of melanin content was observed in the hair bulb.



3) Human dermal papilla cells (HDPC): applying methylglyoxal (MGO) - altered cell morphology, beta-galactosidase staining↑, alkaline phosphatase activity↓.



➢ THE SCIENCE OF HAIR CARE

P197

Effects of Basic Amino Acids on Hair

Cheryl Taylor, Paul Carpenter, Sachin Chandra

Unilever Unilever

Hair fibre penetration by Arginine and Lysine

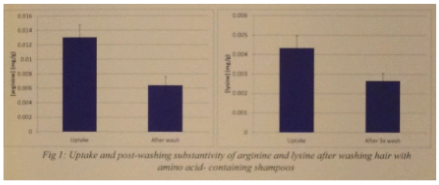


Fig 1: Uptake and post-washing substantivity of arginine and lysine after washing hair with amino acid- containing shampoos

Non-treatment **0.2% w/w arginine**

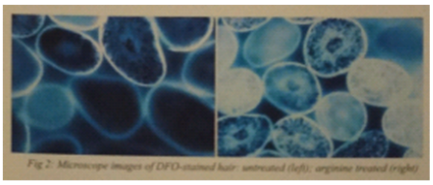


Fig 2: Microscope images of DFD-stained hair: untreated (left); arginine treated (right)

Denaturation temperature

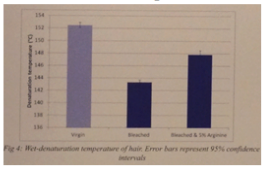
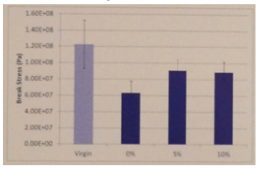
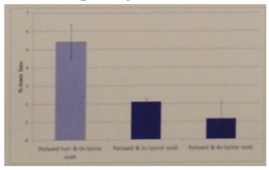


Fig 4: Wet-denaturation temperature of hair. Error bars represent 95% confidence intervals

Tensile analysis



Combing analysis



Arginine and lysine both demonstrate hair care benefits.
-arginine and lysine↑ ⟶ denaturation temperature↑
-arginine and lysine↓ ⟶ fibre breakage↑

➢ TISSUE ENGINEERING/REGENERATION

P221

Calcium microcapsule: a possible scaffold for building Artificial Dermal Papillae

Changmin Lin, PhD; Keng Huang; Yu Li; Yan Liu ; Yanping Yuan; Peichan Huang
Shantou University Medical Collage, Shantou, Guangdong, China

Methods

Morphology and viability of embedded cells	• HE stain; TEM; MTT
Structural stability	• whisking and injection
Biocompa-tibility	• Transplantation into the peritoneal cavity of mice
Penetrability	• Size, molecular weights • Biomaterial and biologic membranes
Functional study	• Transplantation into rat ears

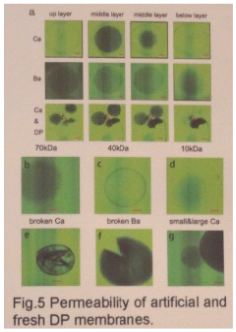


Fig.5 Permeability of artificial and fresh DP membranes.

	CA	BA
Morphology	☆☆☆☆	☆☆☆☆
Cell ability	☆☆☆☆	☆☆
Structural stability	★★	★★★★★
Biocompa-tibility	★★★★★	★★
Penetrability	☆☆☆☆☆	☆☆☆
Functional study (short term)	☆☆☆☆☆	☆☆☆☆☆
Functional study (long term)	☆☆☆☆☆	☆

1) The reasonable diameter of reconstructed DPs was 400 um.
2) Ca microcapsule scaffolds were better than Ba scaffolds in terms of biocompatibility, permeability, and cell viability.
3) Ba may be beneficial in other fields such as short-term induced study or some special sites.

➢ TISSUE ENGINEERING/REGENERATION

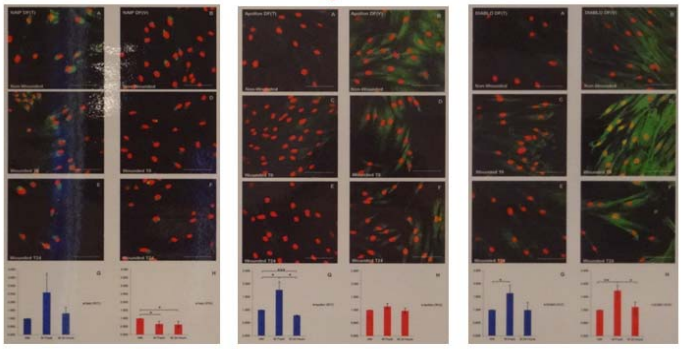
P233

DIFFERENCES IN THE UPREGULATION OF INHIBITOR OF APOPTOSIS PROTEINS (IAPS) IN HUMAN DERMAL FIBROBLASTS DERIVED FROM HAIR-BEARING AND NON HAIR-BEARING SKIN IN A SCRATCH WOUND ASSAY

AM GRAHAM[2], MJ THORNTON[1]
MEDICAL BIOSCIENCE[2], UNIVERSITY OF BRADFORD, UK

NAIP Apollon DIABLO

- Skin containing terminal hair follicles DF(T)
- Skin containing vellus follicles DF(V)



An immediate up-regulation of the expression of IAPs in DF(T) suggests that they have better mechanisms in place for cell survival following wounding.

The Korean Hair Research Society

2013
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제12차 Hair Forum

인 쇄 2013년 8월 12일
발 행 2013년 8월 17일

발행처 **대 한 모 발 학 회**

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