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Progenic Hair Regrowth Treatment
The Use of Platelet-Released Growth Factors for Treating Androgenetic Alopecia (AGA) by Activating Hair Follicle Stem Cells

Jack Sung,[1] Jiang, Meili,[2]
Wang, Zunyan[3]

President, Asiamedic Biotechnology; Director, Jiang's Anesthetic Clinic;
President, Taiwan Society of Trichological and Anti-aging Medicine

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Major challenges in AGA

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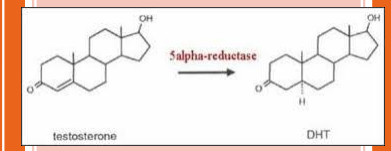
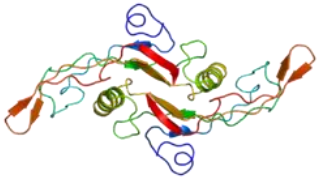


DHT converted by 5-α Reductase suppresses hair follicle growth, miniaturing follicle tissue and life span



TGF-ß1 secreted by DPCs induces catagen, leading to prematured hair loss

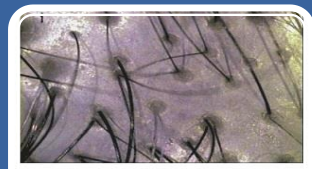


Figure 13: Peripilar signs. Are associated with an inflammatory infiltrate and perifollicular

Hair follicle microinflammation & fibrosis block follicle regeneration to next anagen and diminish hair density

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DHT miniatures hair follicles in AGA affected zone

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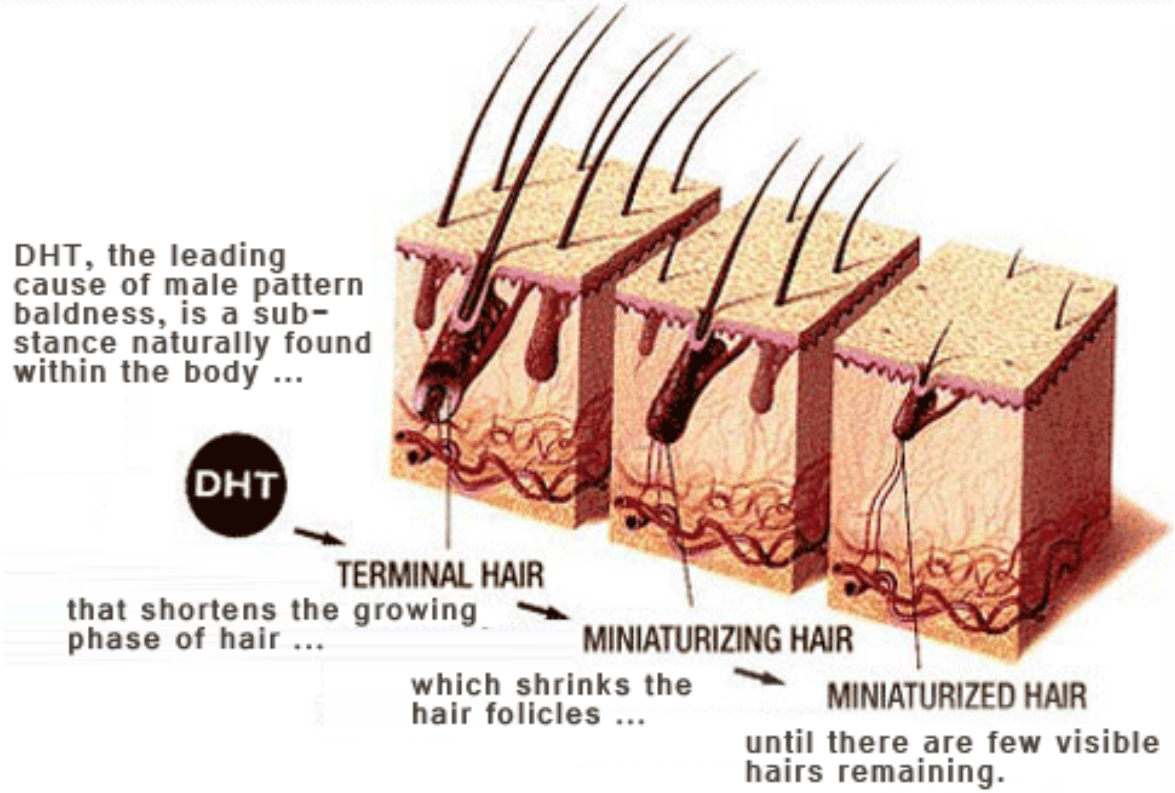
- Androgenetic Alopecia (AGA) is a common disease affecting over 50% male population over 50 years old in the United Stats.



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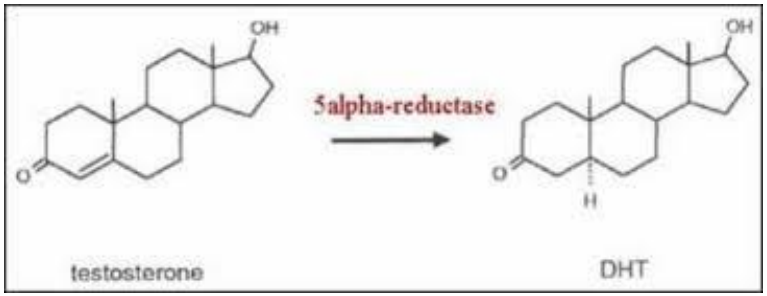

- The main molecular pathway has been accepted that 5-alpha reductase in the fast growing cells outside dermal papilla of hair follicle converting testosterone into dihydrotestosterone (DHT). DHT then binds androgen receptor and the complex of which next binds DNA in cell nucleus, resulting in growth arrest of follicle cell and gradual decrease of protein synthesis. Such molecular pathway prevents vellus hair growing into terminal hair in the next shortened anagen phase

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DHT pathway in AGA

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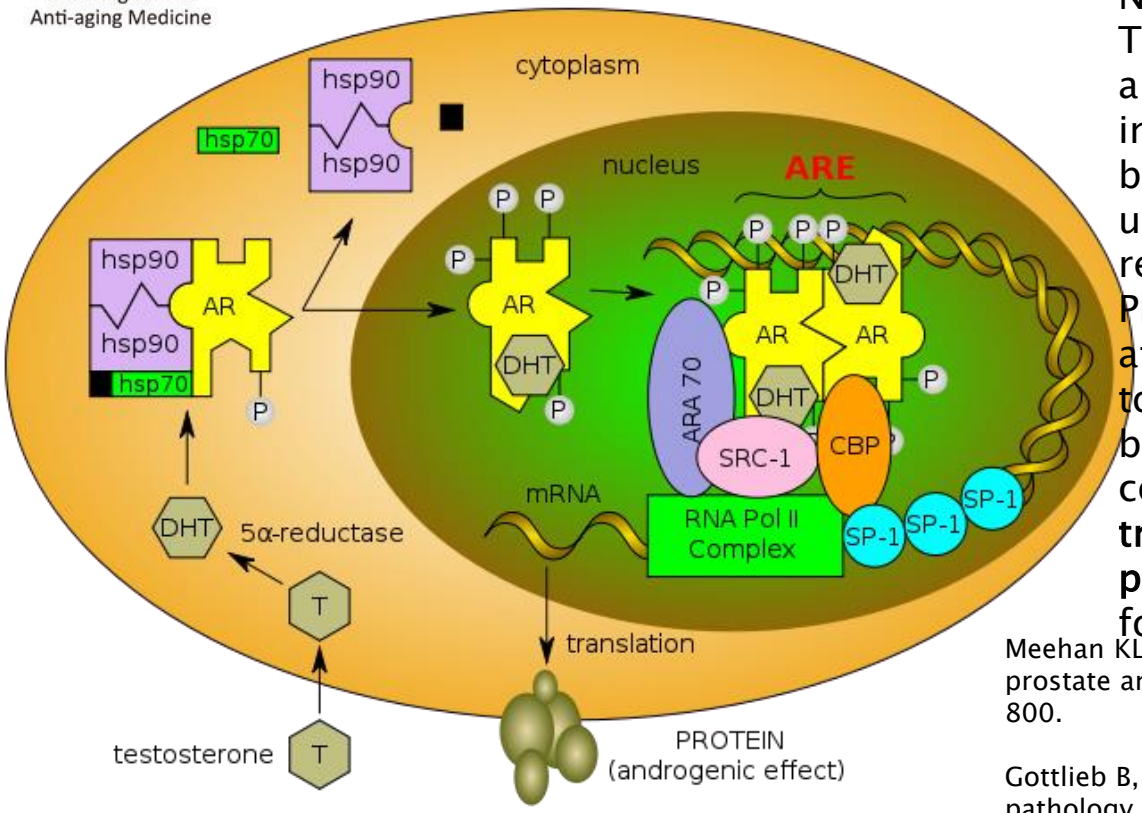

Normal function of the androgen receptor. Testosterone (T) enters the cell and, if 5-alpha-reductase is present, is converted into dihydrotestone (DHT). Upon steroid binding, the androgen receptor (AR) undergoes a conformational change and releases heat shock proteins (hsps). Phosphorylation (P) occurs before and / or after steroid binding. The AR translocates to the nucleus where dimerization, DNA binding, and the recruitment of coactivators occur. **Target genes are transcribed (mRNA) and translated into proteins**. Original work, adapted from the following sources:

Meehan KL, Sadar MD. Androgens and androgen receptor in prostate and ovarian malignancies. Front Biosci. 2003;8780-800.

Gottlieb B, Lombroso R, Beitel LK, Trifiro MA. Molecular pathology of the androgen receptor in male (in)fertility. Reprod biomed online. 2005;10:42:48.

Choong CS, Wilson EM. Trinucleotide repeats in the human androgen receptor: a molecular basis for the disease. J Mol Endocrinol. 1998;21:235 - 257.

Quigley CA, De Bellis A, Marschke KB, El-Awady MK, Wilson EM, French FS. Androgen receptor defects: historical, clinical, and molecular perspectives. Endocr Rev. 1995;16:271 - 321.

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TGF-ß1
Transforming Growth Factor-Beta 1

The major follicle killer

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Identification of Androgen-Inducible TGF-β1 Derived from Dermal Papilla Cells as a Key Mediator in Androgenetic Alopecia

Shigeki Inui, Yoko Fukuzato, Takeshi Nakajima, Kunihiko Yoshikawa and Satoshi Itami
Department of Dermatology, Osaka University School of Medicine, Osaka, Japan

We attempted to establish a coculture model of human dermal papilla cells (DPCs) from androgenetic alopecia (AGA) and keratinocytes (KCs) to study the pathomechanism of AGA. Since expression of mRNA for the androgen receptor (AR) decreased during subcultivation of DPCs *in vitro*, we transiently transfected the AR expression vector into the DPCs and cocultured them with KCs. In this coculture, androgen inhibited the growth of KCs by 50%, indicating that the DPCs produce diffusible growth suppressive factors into the medium in an androgen-dependent manner. Since recently increasing evidence has shown the importance of transforming growth factor-β1 (TGF-β1) in hair growth, we further examined the concentration of TGF-β1 in this coculture medium after androgen treatment by ELISA assays. The results showed that androgen treatment increased the secretion of TGF-β1 into the conditioned medium. Moreover, neutralizing anti-TGF-β1 antibody reversed the inhibition of KC proliferation. Thus, we suggest that androgen-inducible TGF-β1 derived from DPCs mediates hair growth suppression in AGA.
Keywords: androgen receptor/in vitro coculture model. JID Symposium Proceedings 8:69–71, 2003

Androgens stimulate hair growth in some sites such as the beard and pubic areas but inhibit growth on the scalp in genetically disposed individuals (Ebiling, 1986). In human androgenetic alopecia (AGA), postpubertal elevation of testosterone causes irreversible regression of hair follicles, whereas prepubertal castration prevents AGA (Hamilton, 1942). With respect to the mechanism of hair growth regulation by androgen, beard, axillary and frontal scalp dermal papilla cells (DPCs) were recently shown to possess the characteristics of androgen target cells (Itami *et al*, 1990, 1991, 1993, 1995a; Chodry *et al*, 1992; Randall *et al*, 1992). While the androgen receptor (AR) is expressed in beard, axillary, and frontal scalp DPCs, follicular epithelial cells do not have the characteristics of androgen target cells (Chodry *et al*, 1992; Itami *et al*, 1995a; Inui *et al*, 2000). Thus, the primary targets of androgens in the hair follicle are the DPCs, which mediate signals to the follicular epithelial cells. The coculture system using follicular epithelial cells and DPCs enabled us to investigate the effects of androgen on these cells (Itami *et al*, 1995b). Androgen stimulated the proliferation of follicular epithelial cells cocultured with beard DPCs by stimulating the production of insulin-like growth factor-I (IGF-I) from DPCs (Itami *et al*, 1995b). Obana *et al* cocultured follicular epithelial cells and DPCs isolated from the frontal balding scalp of stumptailed macaques, a model animal for human AGA, and demonstrated testosterone-induced inhibition of proliferation of epithelial cells (Obana *et al*, 1997). In this study, we attempted to establish a coculture system using AR-transfected DPCs from human AGA and KCs.

Accepted for publication February 1, 2003
Reprint requests to: Dr Satoshi Itami, Department of Dermatology, Osaka University School of Medicine, 2-2, C-5, Yamada-oka, Suita-shi, Osaka, 565-0871, Japan; E-mail: itami@derma.med.osaka-u.ac.jp
Abbreviations: DPC, dermal papilla cell; KC, keratinocyte; AGA, androgenetic alopecia; AR, androgen receptor; IGF-I, insulin-like growth factor-I; DMEM, Dulbecco's modified Eagle's medium; FCS, fetal calf serum; TGF-β1, transforming growth factor-β1.

MATERIALS AND METHODS

Isolation and culture of human dermal papilla cells and keratinocytes DPCs from hair follicles were isolated and cultured as described previously (Itami *et al*, 1991a,b). In brief, skin specimens were obtained at plastic surgery, and then DPCs were isolated and cultured in Dulbecco's Modified Eagle's Medium (DMEM) (Nissui Phamaceutical, Tokyo, Japan) supplemented with 10% fetal calf serum (FCS) (jrh Biosciences, Lenexa, KS, USA), penicillin (50 units/ml), streptomycin (50 μg/ml) at 37°C, under a humidified atmosphere of 95% O_2 and 5% CO_2. Normal human KCs were isolated from human skin and cultured in MCDB 153 supplemented with insulin (5 μg/ml), hydrocortisone (0.4 μg/ml), ethanolamine (0.1 mM), phosphoethanolamine (0.1 mM), 0.1 mM Ca^{++} and bovine pituitary extract (Clonetics, San Diego, CA, USA) (keratinocyte growth medium: KGM). Semi-quantitative RT-PCR for AR was performed as previously described (Ando *et al*, 1999).

Transfection of the AR expression vector into DPCs DPCs were inoculated at a density of 2×10^5 cells/well into tissue cultured multiplates (6 wells, Corning, New York, USA) and cultured with DMEM supplemented with 10% FCS. At subconfluency the medium was changed to FCS-free DMEM and the cells then transfected with 2 μg of the AR expression vector, pSG5-AR (kindly given by Dr Chawnshang Chang, the University of Rochester), using 6 μL of the transfection reagent Fugene-6 (Roche Diagnostics Corp Indianapolis, IN). After three h, the medium was changed to DMEM supplemented with 10% charcoal-treated FCS. At 24 h after transfection, cells were harvested or combined with the KC culture. The transfection efficiency was about 50%, estimated by green fluorescence.

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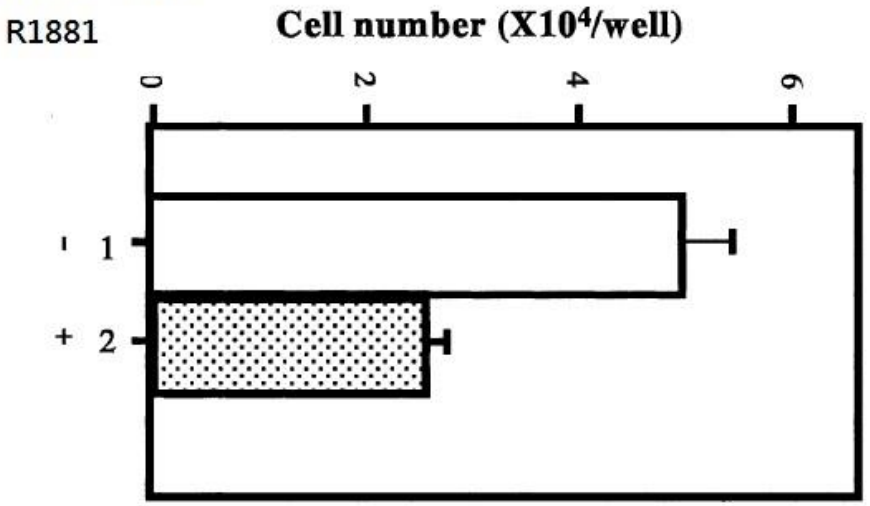
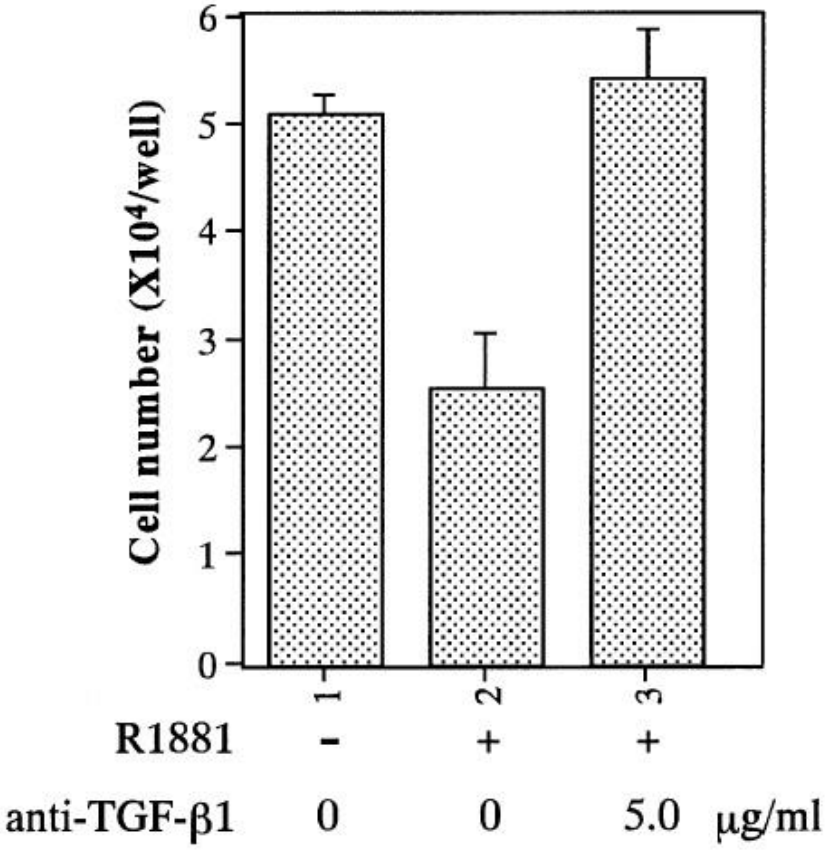


Figure 2. Effect of R1881 on the proliferation of KCs cocultured with DPCs from bald frontal scalp skin of a male human, transiently transfected with pSG5-AR. The cells were cultured in the presence of ethanol as a mock (*lane 1*) or 10^{-9} M R1881 (*lane 2*). The graph shows cell numbers for KCs after coculturing for four days as a mean ± SD of three determinations.



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TGF-ß1 Induces follicle catagen

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Androgen inhibited the growth of KCs by 50%, indicating that the DPCs produce dffusible growth suppressive factors into the medium in an androgen-dependent manner."

"The results showed that androgen treatment increased the secretion of TGF-b1 into the conditioned medium. Moreover, neutralizing anti-TGF-b1 antibody reversed the inhibition of KC proliferation. Thus, we suggest that androgen-inducible TGF-b1 derived from DPCs mediates hair growth suppression in AGA.".

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Microinflammation & Fibrosis

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Medical Treatments for Ageing Male and Female Hairloss and Alopecia

Ralph M. Trüeb, M.D.
Center for Dermatology and Hair Diseases
Bahnhofplatz 1A
8304 Wallisellen (Zurich)
Switzerland

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Hair Follicle Microinflammation and Fibrosis

1992 Jaworsky et al refer to an **inflammatory infilrate of activated T cells and macrophages in the upper third of the hair follicle** associated with an enlargement of the follicular dermal sheath composed of collagen bundles

1993 Whiting demonstrates in morphometric studies on patients with male pattern androgenetic alopecia (AGA) a **frequency of 40% significant perifollicular inflammation and fibrosis**, and finds with 55% of patients with follicular inflammation and fibrosis vs. 77% in those without, **lesser regrowth in response to treatment** with minoxidil

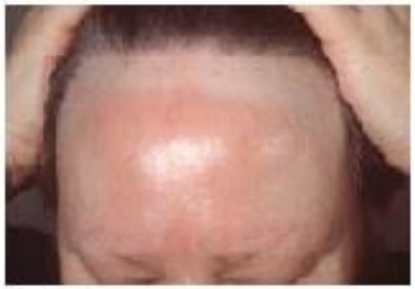
2000 Mahé et al propose in a review on AGA and inflammation the **term „microinflammation"** in contrast to the inflammatory and destructive process in the classical inflammatory scarring alopecias

2004 Deloche et al demonstrate in a study of the scalp in a large cohort of volunteers with AGA using macrophotographs presence of **peripilar signs** (PPS) around the hair ostia, and find a significant relationship between PPS and superficial perifollicular infiltrates in early AGA

2005 Olsen acknowledges existence of clinically significant inflammatory phenomena and fibrosis in androgenetic alopecia and proposes the term **„cicatricial pattern hair loss“**

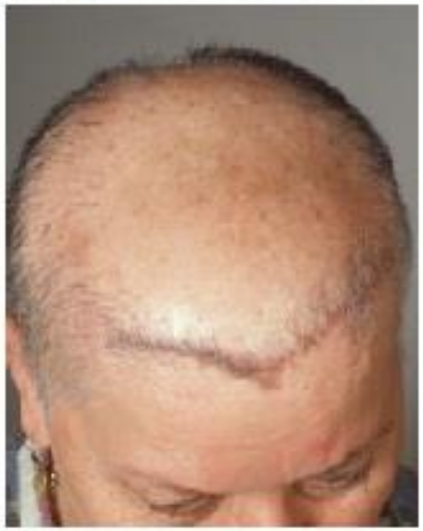
Olsen EA. J Investig Dermatol Symp Proc 2005;10:217-21

Follicular microinflammation and fibrosis:
Whiting D. Diagnostic and predictive value of horizontal sections of scalp biopsy specimens in male pattern androgenetic alopecia.
JAAD 1993;28:755-763

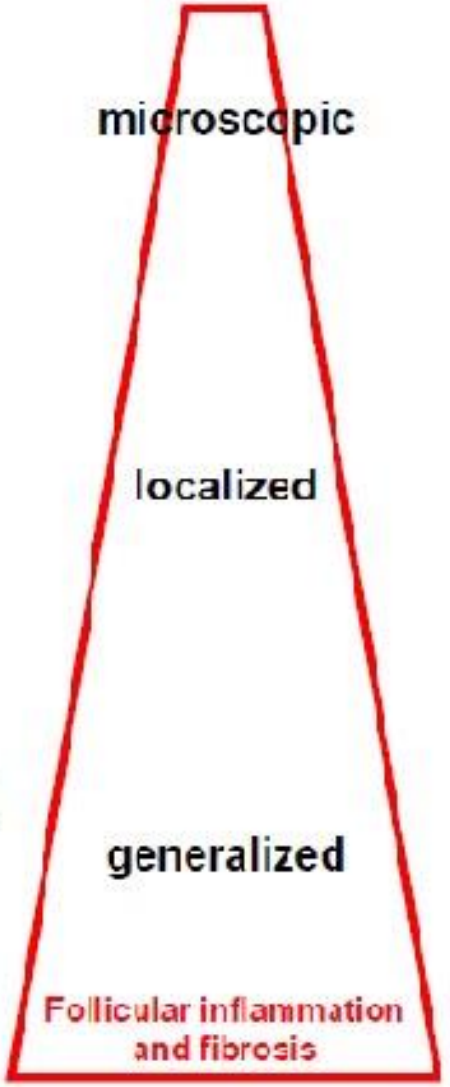


Kossard S. Postmenopausal frontal fibrosing alopecia. Scarring alopecia in a pattern distribution.
Arch Dermatol. 1994;130:770-4

Kossard S, Lee MS, Wilkinson B. Postmenopausal frontal fibrosing alopecia: a frontal variant of lichen planopilaris.
J Am Acad Dermatol 1997;36:59-66



Zinkernagel MS, Trüeb RM. Fibrosing alopecia in a pattern distribution: patterned lichen planopilaris or androgenetic alopecia with a lichenoid tissue reaction pattern?
Arch Dermatol 2000;136:205-11



Pathobiology of Perifollicular Inflammation and Fibrosis

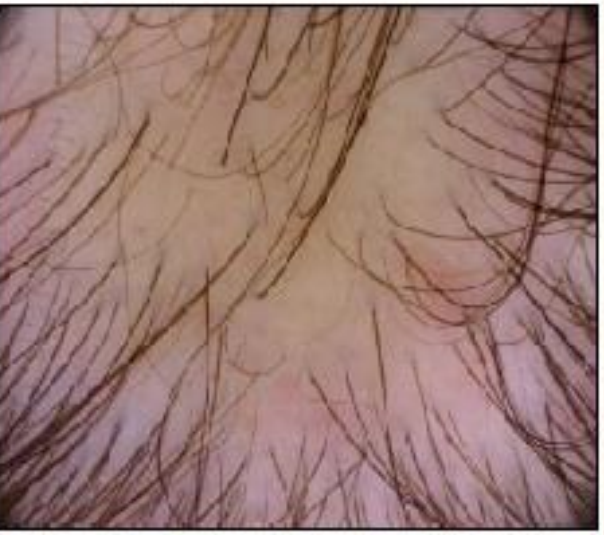
Inflammation is a **multistep process** with the question arising with regard to the **primary event:**

- Localization of the inflammation near the infundibulum
- **Role of microbial colonization?**
- Specifically, bacterial toxins, antigenic stimulus, and porphyrins?
- **Role of environmental stress from irritants and pollutants?**
- **Role of UVR?**
- Follicular keratinocytes themselves can respond to stressors by producing radical oxygen species, nitric oxid, and **releasing IL-1α**
- Transcription of IL-1 reponsive genes: IL-1b, TNFa, IL-8, MCP-1,-3
- **Antigen presentation to T lymphocyte and induction of T-cell proliferation**
- **Sustained inflammation** results in **connective tissue remodeling (fibrosis)**, where collagenases (MMP's) play a role,
- ultimately preventing the follicle to reform a terminal hair follicle in the course of the hair cycle

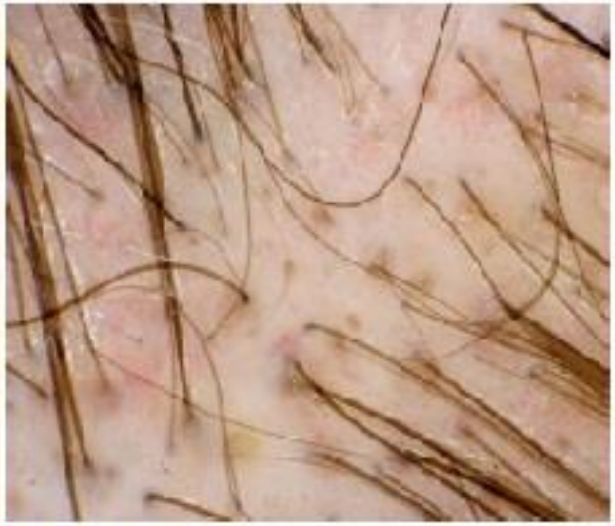
Mahé et al. Int J Dermatol 2000;39:576-584

Inflammatory Phenomena and Fibrosis

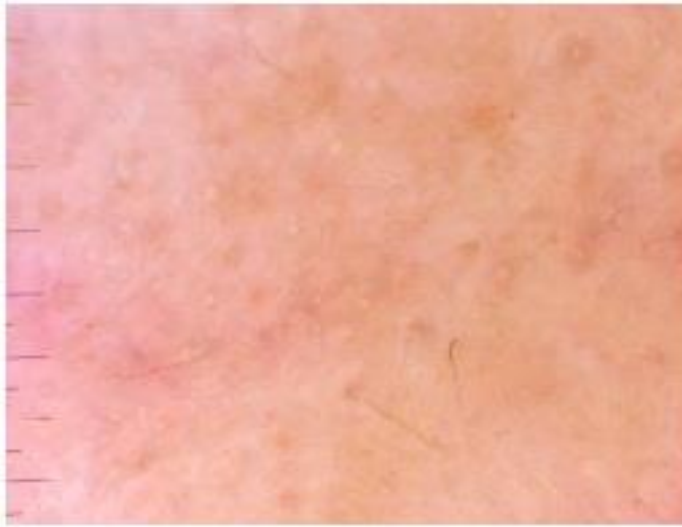
Androgenetic alopecia with inflammatory phenomena and fibrosis



Androgenetic alopecia (diversity of hair shaft diameters)

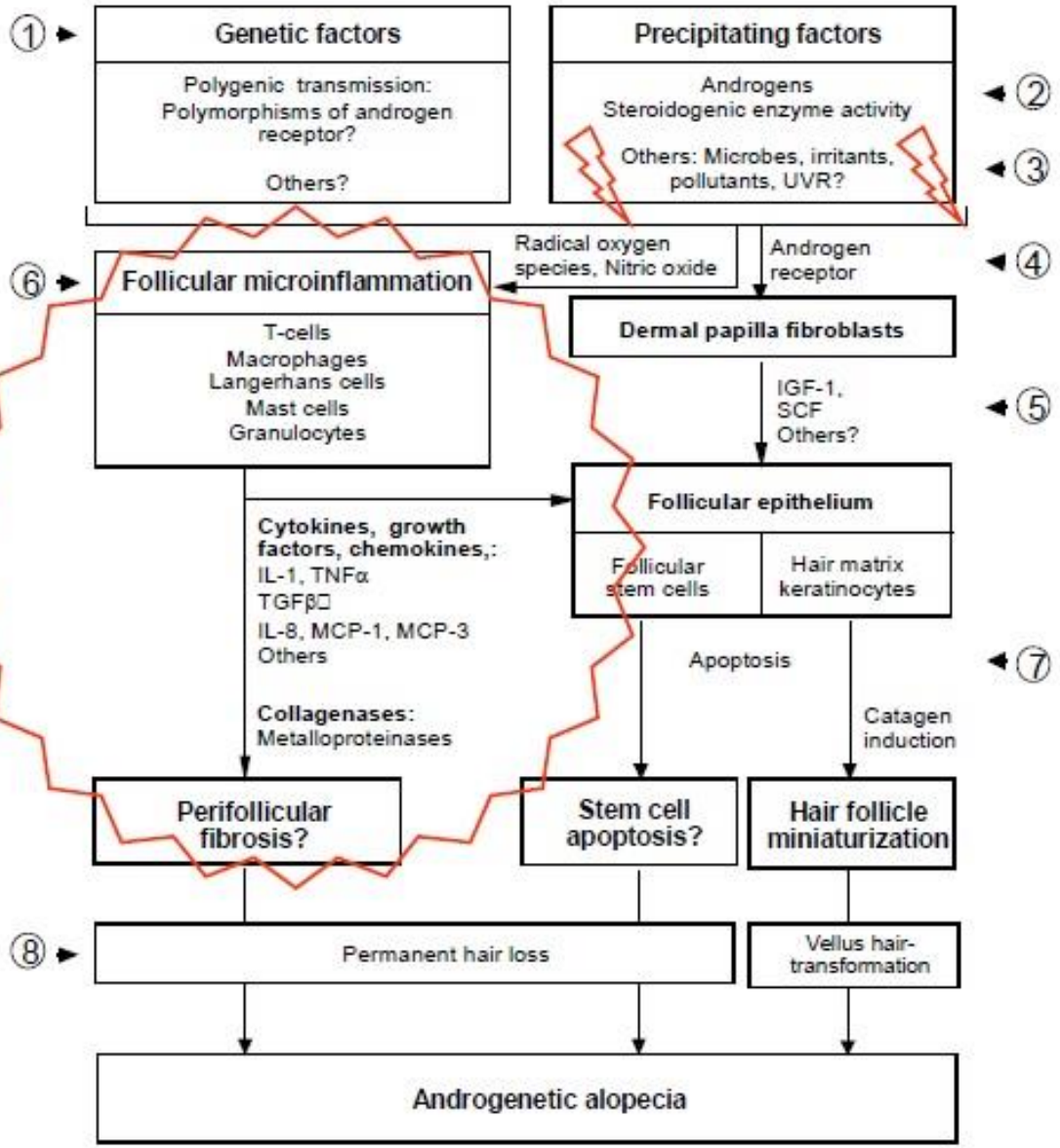


Androgenetic alopecia with peripilar signs (early)



Fibrosing alopecia in a pattern distribution (late)

Revised Concept of Pathobiology and Treatment of Androgenetic Alopecia



Therapeutic strategies:

1. Gene therapy?
2. Modifiers of androgen metabolism: finasteride, dutasteride
3. Antimicrobial treatments?
4. Antiandrogens: CPA, spironolactone
5. Hair growth promoters: minoxidil
6. Antiinflammatory agents?
7. Apoptosis modulating agents?
8. Hair transplantation/implantation of dermal papilla cells or cells of follicle dermal-sheath

From: Trüeb RM. Molecular mechanisms of androgenetic alopecia. Exp Gerontol. 2002;37:981-90.

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Hair Follicle Stem Cells

The Prosmises to hair loss tomorrow

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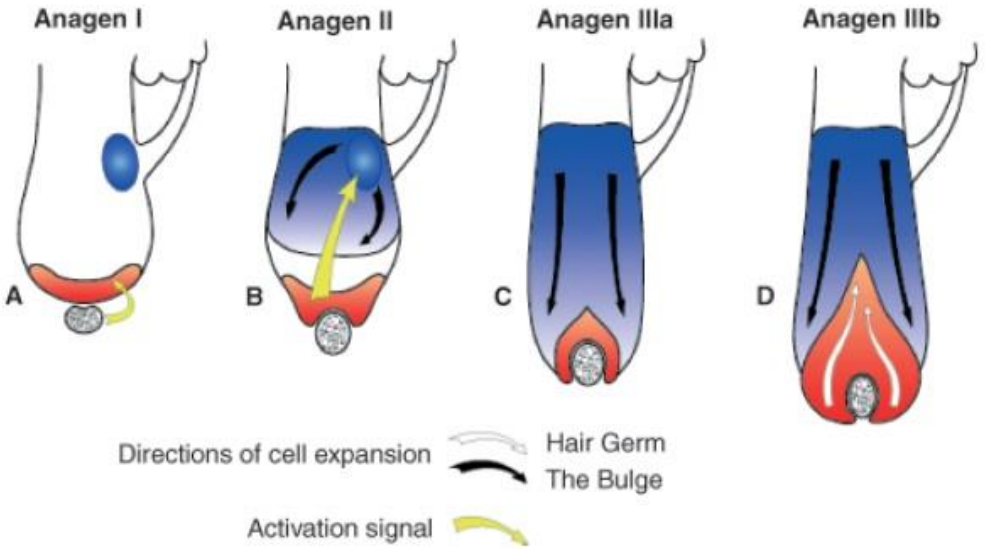

Figure 7. Proposed cellular kinetics in the early anagen hf. (*A*) the activation of hair germ cells by a fp-derived signal (*yellow arrow*). (*B*) in anagen ii, the activity of the hair germ (yellow arrow) induces proliferation of the bulge cells (*black arrows*). (*C*) in anagen iiia, the downward growth of bulge-derived cells (*black arrows*) results in the formation of the ors. (*D*) in anagen iiib, the upward proliferation of hair germ cells (*white arrows*) results in formation of the ascending compartment of the anagen hf (hair shaft and irs).

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Hair Follicle Stem Cells

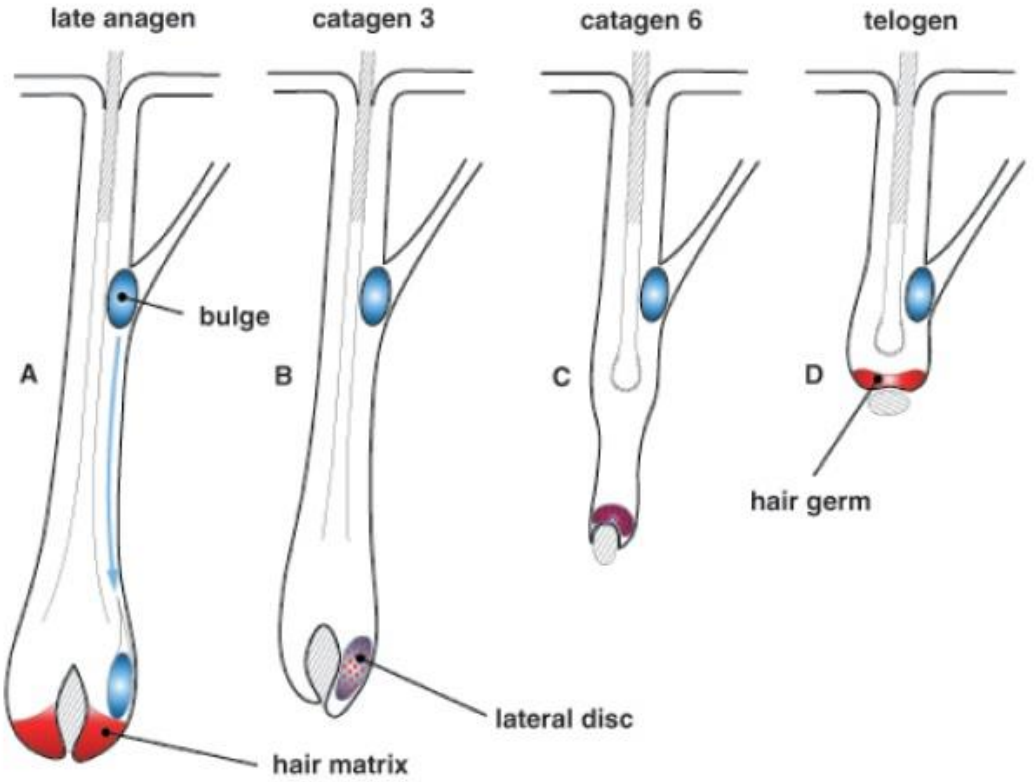

Figure 8. Proposed scheme of the lateral disc transformation into the hair germ. (*A*) During anagen, bulge-derived cells with clonogenic potential migrate downward (*blue arrow*) and form the lateral disc that resides inactively on the periphery of the hair bulb. Hair matrix cells (*red*) are actively proliferating. (*B*) In early catagen, owing to the diminution of the hair matrix, the lateral disc cells come into direct contact with FP. (*C*) In late catagen, lateral disc cells travel upward along with the FP and gradually transform into the hair germ (*change of blue color into red*). (*D*) In the telogen, hair germ and bulge cells reside as two separate and functionally discrete structures. Owing to FP-dependent "priming" during previous catagen, hair germ cells acquire selective sensitivity to FP-derived signaling and the commitment to produce ascending layers of HF of new generation. [1]These experiments were performed 14 months after completion of labeling and the behavior of "younger" LRC (e.g., 8–10 weeks after labeling) has not been reported.

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PDGF isoforms induce and maintain anagen phase of murine hair follicles

Y. Tomita, M. Akiyama and H. Shimizu

Department of Dermatology,
Hokkaido University Graduate School of Medicine,
Sapporo, Japan

J. Dermatological Science 2006

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PDGF isoforms induce and maintain anagen phase of murine hair follicles

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Methods

- Recombinant human PDGF-AA and PDGF-BB were dissolved in sterile and toxin-free phosphate-buffered saline containing 0.1% bovine serum albumin (0.1% BSA-PBS). 1μg PDGF-AA or PDGF-BB dissolved in 100μl of 0.1% BSA-PBS and 0.1%BSA-PBS for controls were intradermally injected into the dorsal skin of 47-day-old male C3H mice (second telogen) once daily for 5 consecutive days (total 5μg of PDGF isoforms) (PDGF-AA, n=5;5 PDGF-BB, n=5; control, n=5). All mice were sacrificed 10 days after the injections
- anti-PDGF-AA antibody or anti-PDGF-BB antibody was injected just after each injection of PDGF-AA or PDGF-BB (anti-PDGF-AA antibody following PDGF-AA, n=5; anti-PDGF-BB antibody following PDGF-BB, n=5).

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PDGF isoforms induce and maintain anagen phase of murine hair follicles

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Results

- The area in close proximity to the injection sites in 3 out of 5 mice became darkened in color, indicating that HFs were in the anagen hair cycle phase (Figs.1a, 1d), whereas the injection sites using just the vehicle solution alone (0.1% BSA-PBS) all five mice retained their normal white color, suggesting that they remained in telogen phase.
- Expression of Shh, Wnt5a and Lef-1 was upregulated in the skin samples in which anagen had been induced by PDGF local injections

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PDGF isoforms induce and maintain anagen phase of murine hair follicles

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Conclusions

- "These results indicate that both PDGF-AA and -BB are involved in the induction and maintenance of the anagen phase in the mouse hair cycle. Local application of PDGF-AA and -BB might therefore prove to be an effective treatment option for alopecia associated with early catagen induction and elongated telogen phase."

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Adipocyte Lineage Cells Contribute to the Skin Stem Cell Niche to Drive Hair Cycling

Eric Festa, Jackie Fretz, Ryan Berry, Barbara Schmidt, Matthew Rodeheffer, Mark Horowitz, and Valerie Horsley,
Departments of Molecular, Cell, and Developmental Biology
Yale Stem Cell Center

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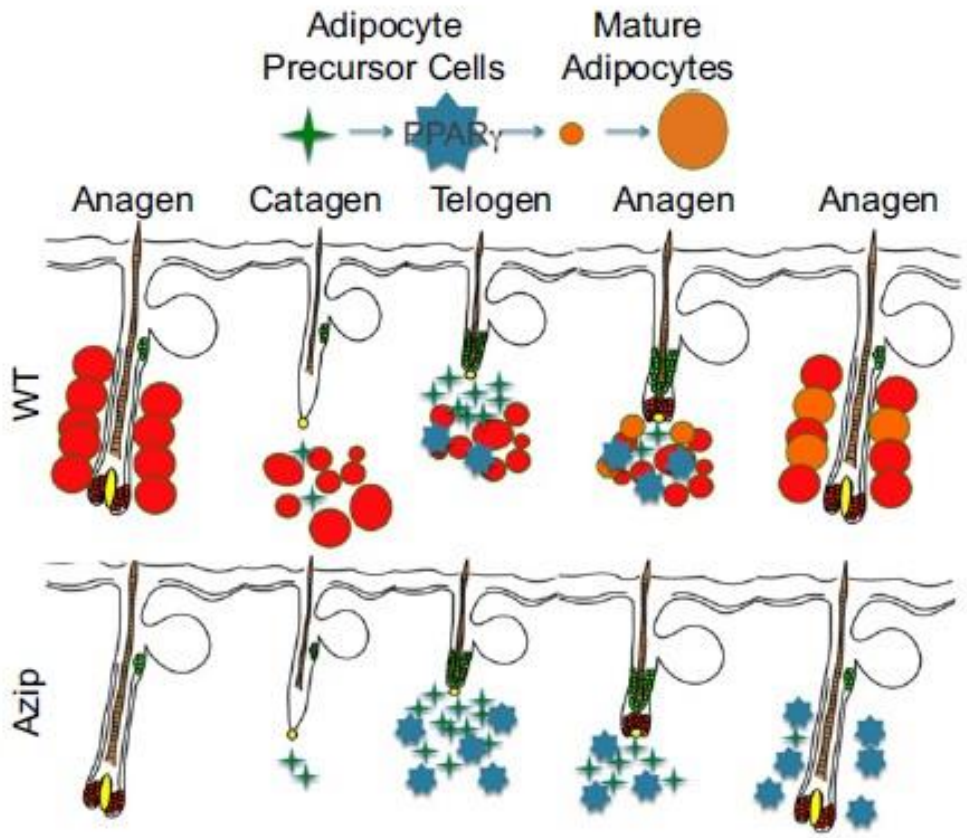
Adipocyte Lineage Cells Contribute to the Skin Stem Cell Niche to Drive Hair Cycling



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Adipocyte Lineage Cells Contribute to the Skin Stem Cell Niche to Drive Hair Cycling

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- We injected PDGFA-coated beads intradermally into Ebf1 null mice at P21. Three days after bead implantation, a majority of follicles adjacent to PDGFA-coated beads displayed morphologies characteristic of anagen follicles. This growth induction increased with elevated concentrations of PDGFA with 100ng/ml activating 86% of adjacent follicles, demonstrating a dose dependency of activation of Ebf1 null hair follicles.

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Adipocyte Lineage Cells Contribute to the Skin Stem Cell Niche to Drive Hair Cycling

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- Expression of PDGFA in adipocyte precursor cells was elevated almost 100 fold over the expression in SVF cells. Mice lacking PDGFA display phenotypic similarities with Ebf1 null mice, including a delay of follicle stem cell activation that blocks anagen induction (Karlsson et al., 1999; Tomita et al., 2006).

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Adipocyte Lineage Cells Contribute to the Skin Stem Cell Niche to Drive Hair Cycling

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- Adipocyte lineage cells are not the only cell type in the skin that expresses PDGF ligands, multiple cells in the follicular epithelium, the matrix and the hair germ, have been shown to express PDGF (Karlsson et al.,1999). Additional signals expressed by intradermal adipocytes may also be involved in signaling to the DP or epithelium (Park et al., 2010).

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Coordinated Activation of Wnt in Epithelial and Melanocyte Stem Cells Initiates Pigmented Hair Regeneration

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SUMMARY

Melanocyte stem cells (McSCs) intimately interact with epithelial stem cells (EpSCs) in the hair follicle bulge and secondary hair germ (sHG). Together, they undergo activation and differentiation to regenerate pigmented hair. However, the mechanisms behind this coordinated stem cell behavior have not been elucidated. Here, we identified Wnt signaling as a key pathway that couples the behavior of the two stem cells. EpSCs and McSCs coordinately activate Wnt signaling at the onset of hair follicle regeneration within the sHG. Using genetic mouse models that specifically target either EpSCs or McSCs, we show that Wnt activation in McSCs drives their differentiation into pigment-producing melanocytes, while EpSC Wnt signaling not only dictates hair follicle formation but also regulates McSC proliferation during hair regeneration. Our data define a role for Wnt signaling in the regulation of McSCs and also illustrate a mechanism for regeneration of complex organs through collaboration between heterotypic stem cell populations.

INTRODUCTION

Successful regeneration of a functional organ relies on the organized and timely orchestration of molecular events among distinct stem/progenitor cell populations. The mammalian hair follicle (HF), containing several stem cell populations, serves as an advantageous model for the dissection of such collaboration among distinct cell types. The HF undergoes cyclical periods of growth (anagen) and rest (telogen), driven by the proliferation and differentiation of epithelial stem cells (EpSCs) residing in the bulge area as well as the secondary hair germ (sHG) of the HF (Cotsarelis et al., 1990, Greco et al., 2009, Zhang et al., 2009). The HF bulge and sHG areas maintain not only EpSCs that express Keratin 15 (K15) (Liu et al., 2003), but also hold melanocyte stem cells (McSCs) that are responsible for hair pigmentation (Nishimura et al., 2002). McSCs are undifferentiated and unpigmented melanocytes that reside in the bulge-sHG area. Developmentally, melanocytes originate from the neural crest (Rawles, 1947) and migrate through the dermis and epidermis to eventually reside in the HF. In adult mouse skin, melanocytes are located exclusively in HFs, while in human skin, melanocytes are maintained in the interfollicular epidermis as well.

During anagen, differentiated McSC progeny that are located in the hair bulb produce and transfer pigment to adjacent epithelial cells that differentiate into hair (Nishimura et al., 2002). Upon entry into telogen, differentiated melanocytes are no longer present as they undergo apoptosis in sync with degeneration of the lower part of the HF (Sharov et al., 2005). When EpSCs regenerate the lower follicle at the initiation of a new anagen phase, undifferentiated McSCs coordinately repopulate the hair bulb with differentiated pigment-producing progeny. These two distinct stem cell populations of developmentally distinct origins act in concert to regenerate pigmented hair with each hair cycle. However, the mechanisms behind this coordinated stem cell behavior have not been elucidated.

In this study, we ask how two adult stem cells of different lineages become activated to proliferate and differentiate in a synchronized manner at the onset of HF regeneration. Addressing this question is not only critical to understanding the molecular mechanisms regulating McSCs, but may also provide important insight into how a complex organ can form by cooperation between distinct stem/progenitor cells in adult mammals. Numerous studies have focused on the reciprocal interactions between tissue-producing EpSCs and inductive dermal cells during the induction of HF regeneration (Greco et al., 2009; Rendl

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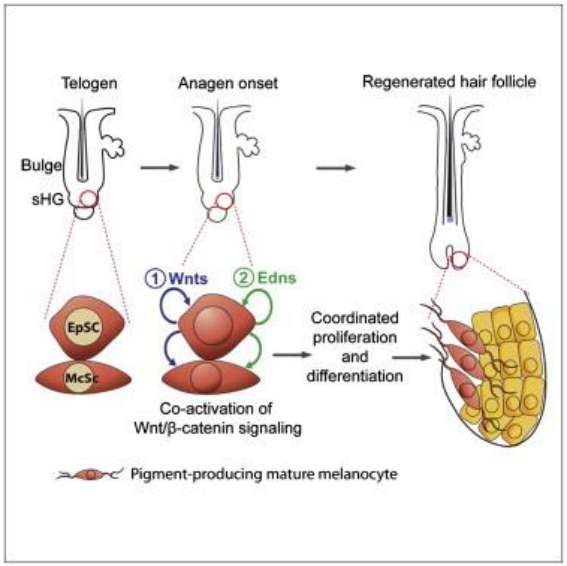

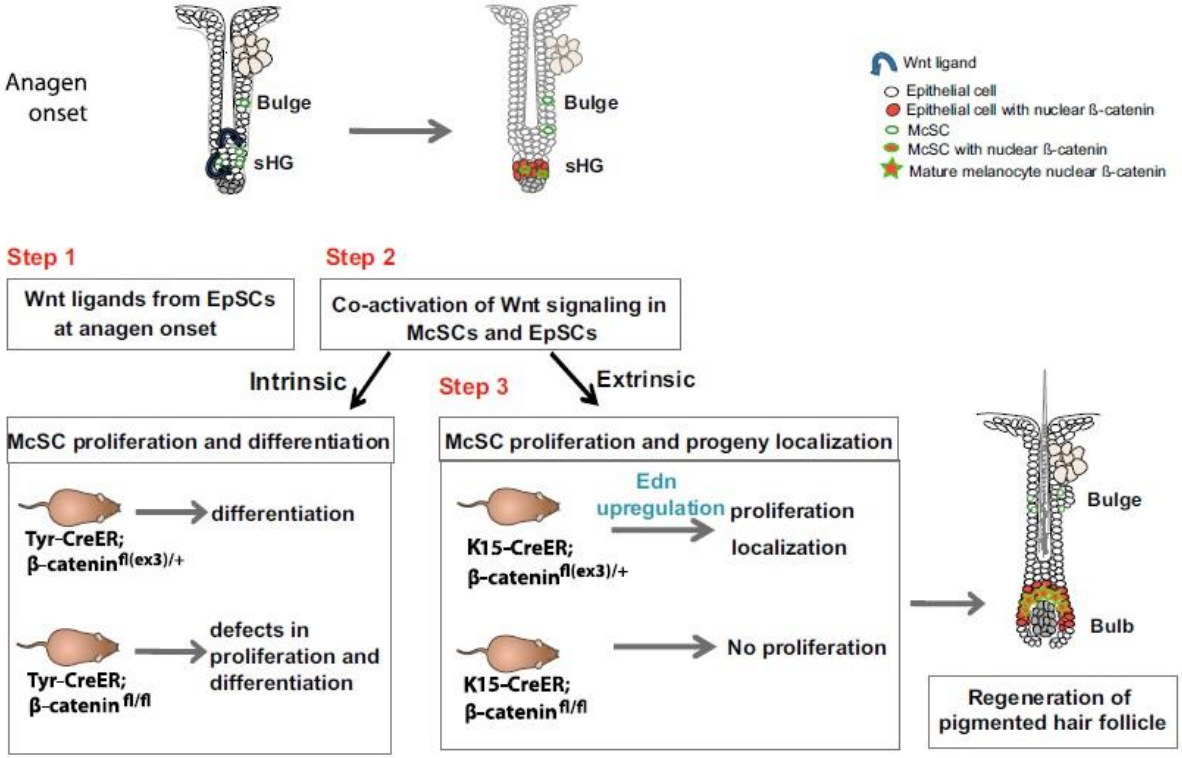

Figure 7. Proposed Model: Stem Cell Coactivation in a Shared HF Niche

At anagen onset, EpSCs, adjacent to McSCs, secrete Wnt ligands for HF regeneration (step 1). Concomitantly, McSCs and EpSCs coactivate Wnt signaling (step 2). Wnt activation within melanocytes results in their differentiation, while Wnt activation in EpSCs results in secretion of Edns which are received by McSCs expressing EdnrB (step 3). Continued Wnt activation in EpSC progeny in the growing edge of the follicle attracts and guides McSC progeny to the Wnt-activated bulb, site of hair differentiation and pigment incorporation into growing hair.

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Progenic Hair Treatment

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Activation

- Hair follicle stem cells should be activated to gain new hairs

Blockage

- 5-α Redutase and TGF-ß1 pathways should be blockaged

Control

- Hair follicle microinflammation & fibrosis should be addressed

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Platelet Derived Growth Factor from PRP

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Material
- PRP (Platelet-Rich-Plasma) is collected

Process
- PRP Proceeded (lyophilization, radiation)

Isolation
- PDGF/VEGF Isolation from Platelet

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PRP Isolation Processing for retrieving PDGF/VEGF

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PRP lyophilized powder and PDGF solution

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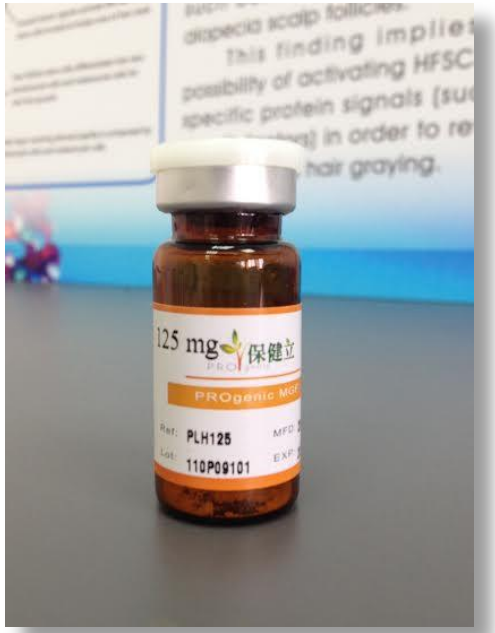
PRP powder in 60/125mg
PDGF solution in 300/600ng vial



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Tricoscopy at occipital/ crown/vertex/temporal

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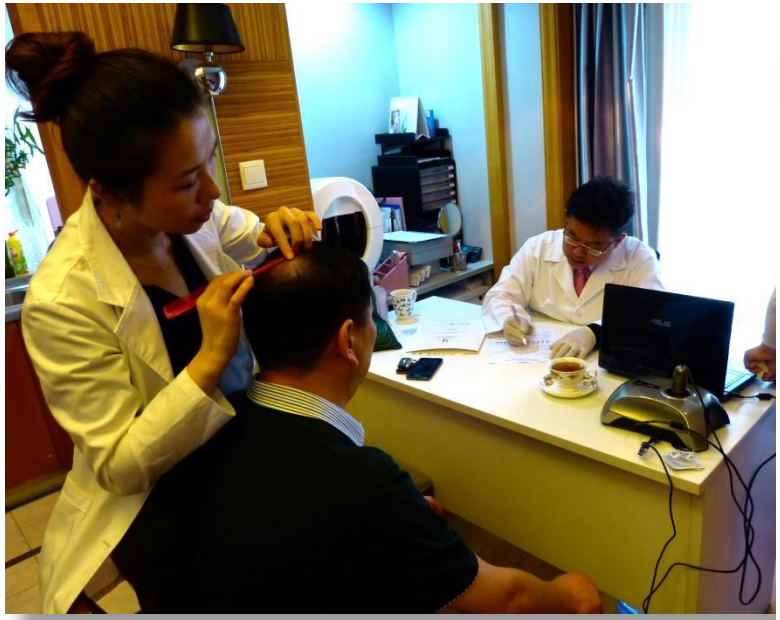

(Courtesy by Shanghai WA Antiaging Clinic)

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Hair density and terminal/vellus hairs ratio documented

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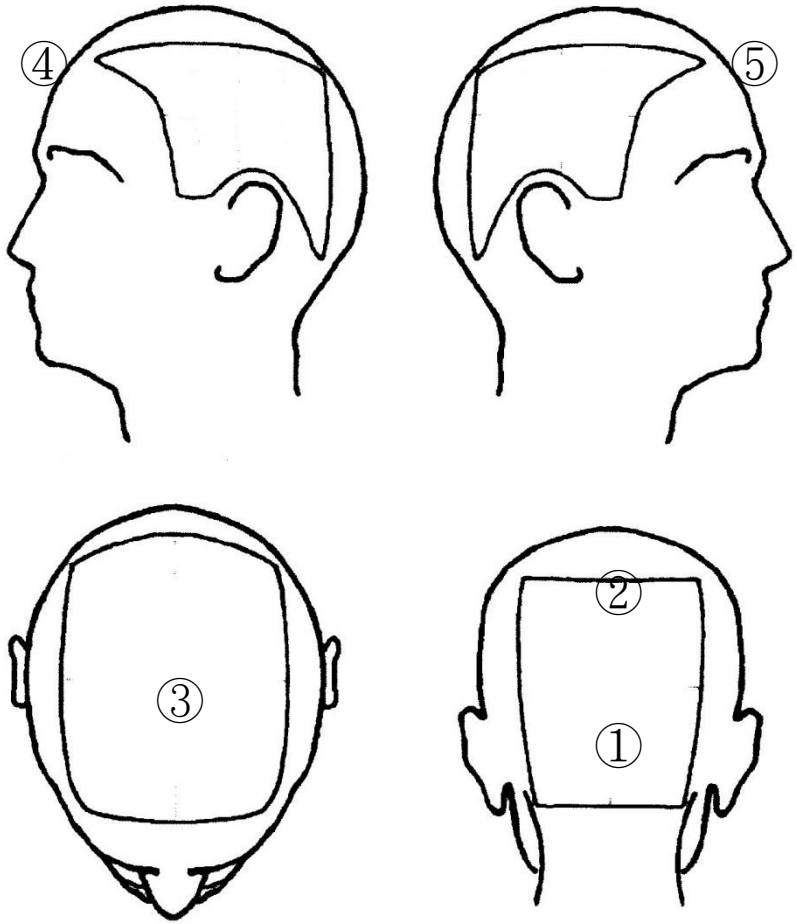
Treatment goal:

Hair density at 120 hairs /cm2
Terminal hair/vellus hair ratio improved



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PDGF solution delivered by electroporation system non-invasively

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(Courtesy by Shanghai WA Antiaging Clinic)

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Our first case AGA

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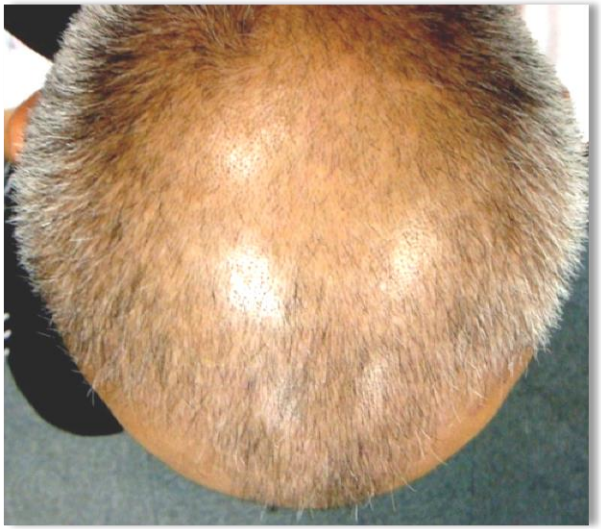
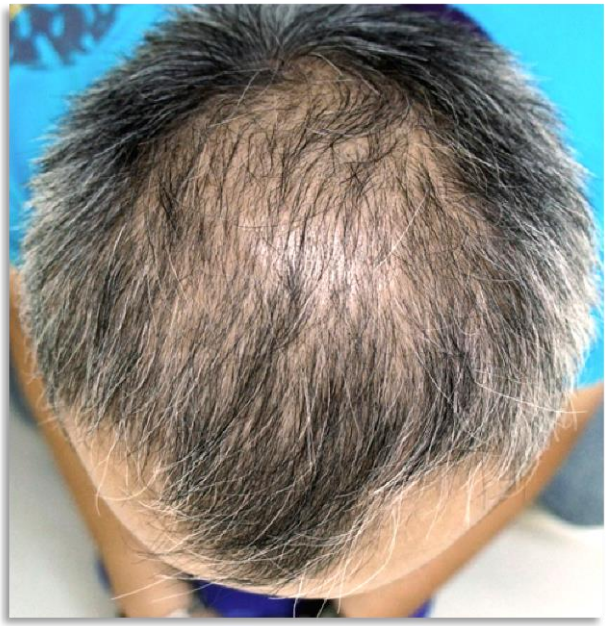
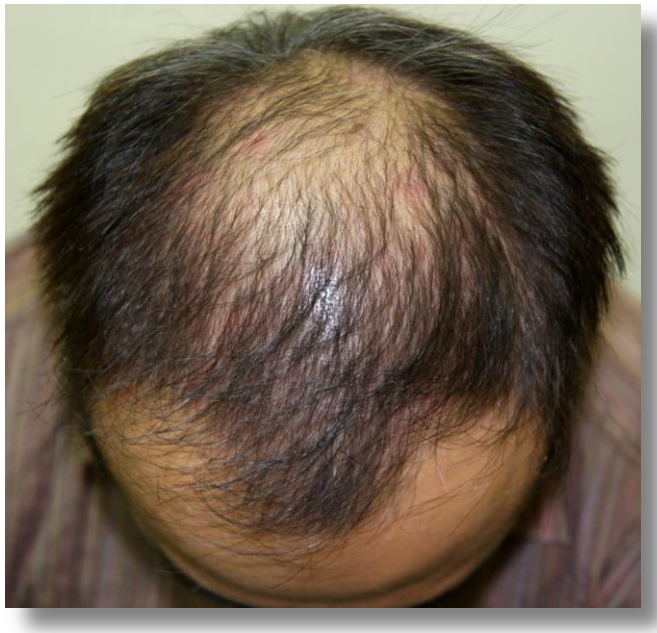
- Great hair regrowth in all regions except for crown early hair fall out caused by TGF-ß1



Before 2010.07.08



4 treatments
2010.09.08



F/U 2010.12.10

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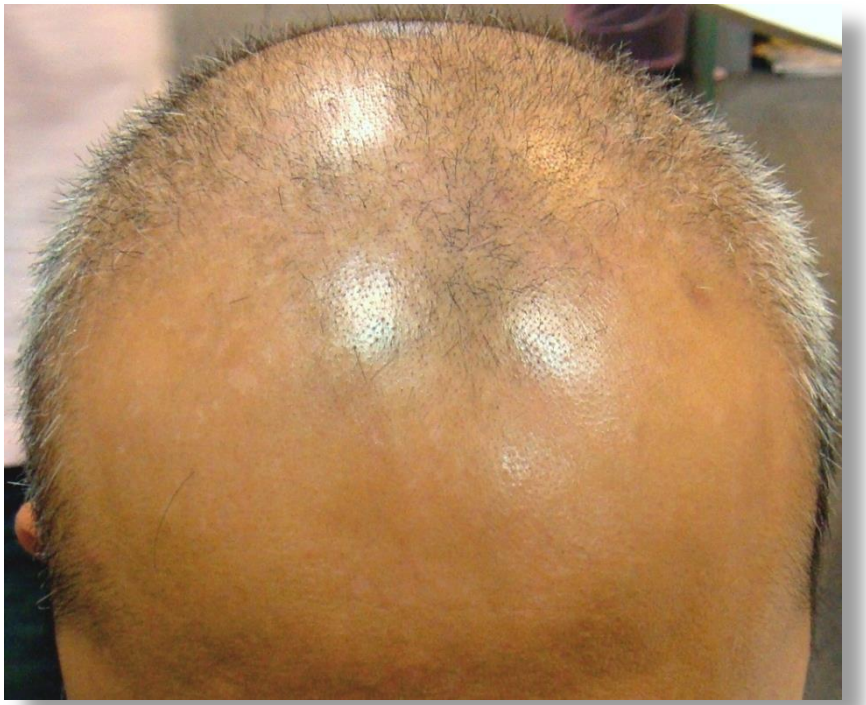
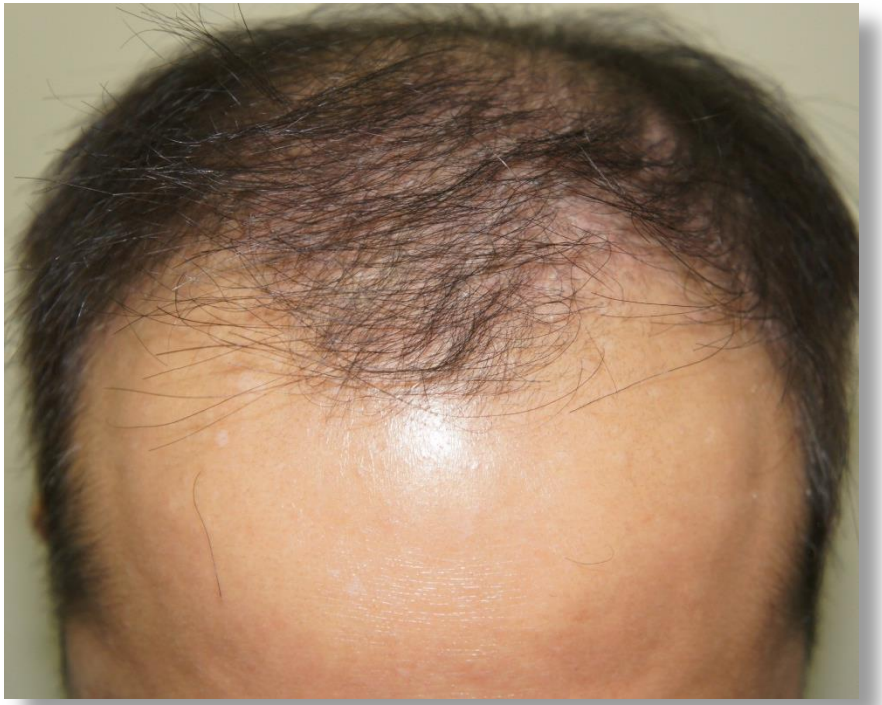
Before 2010.07.08



After 23 weeks 2010.12.08



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Great hair regrowth in occipital zone!

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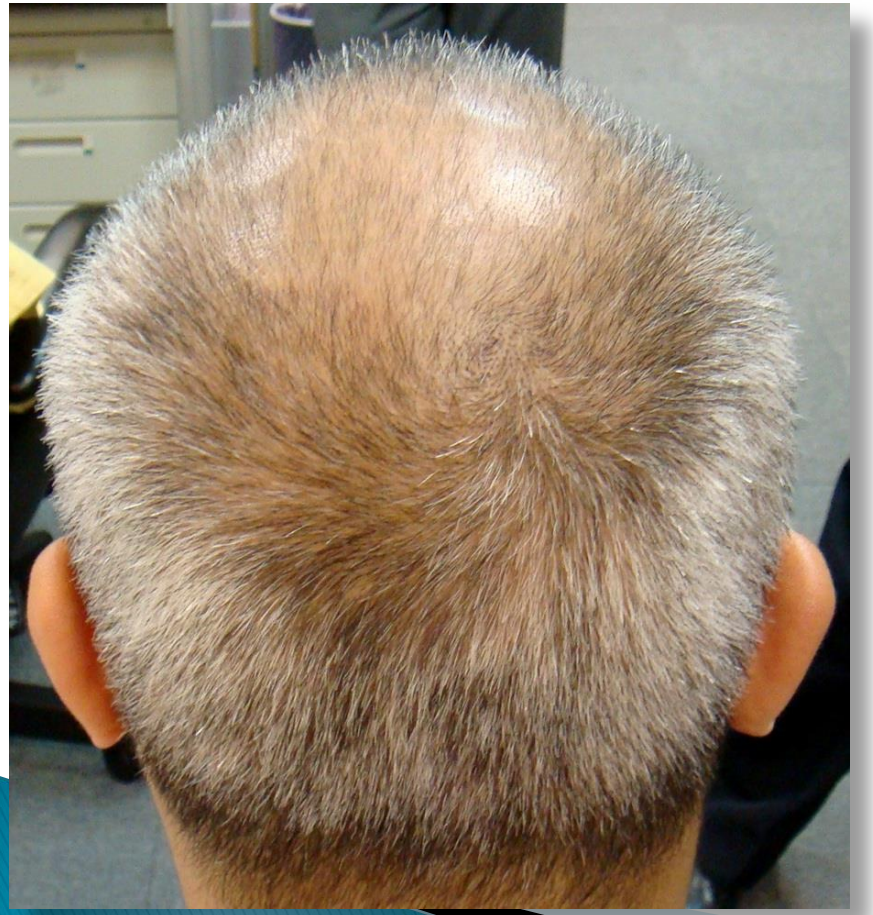
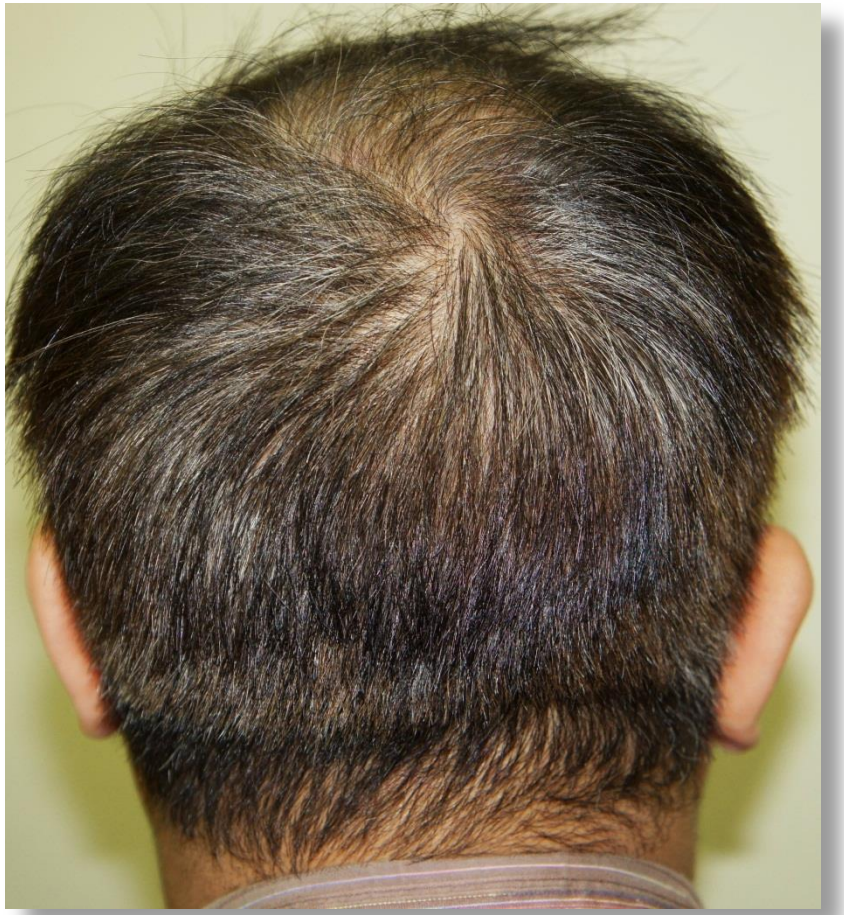
2010.07.08 使用前



2010.12.08 使用23週



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Prematured Hair Loss caused by TGF-ß1

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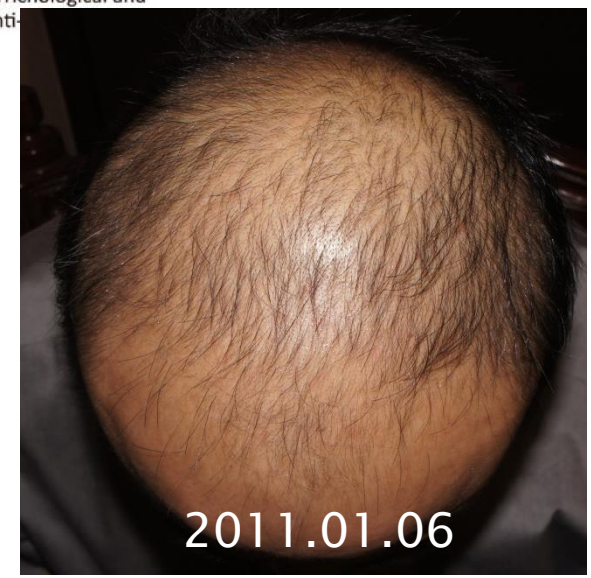

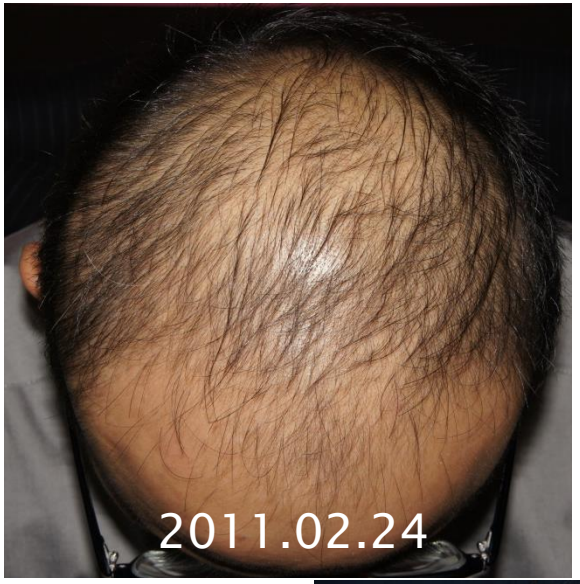

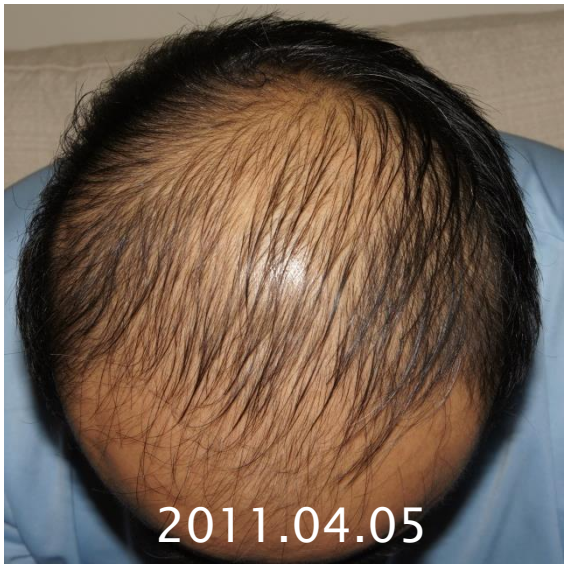

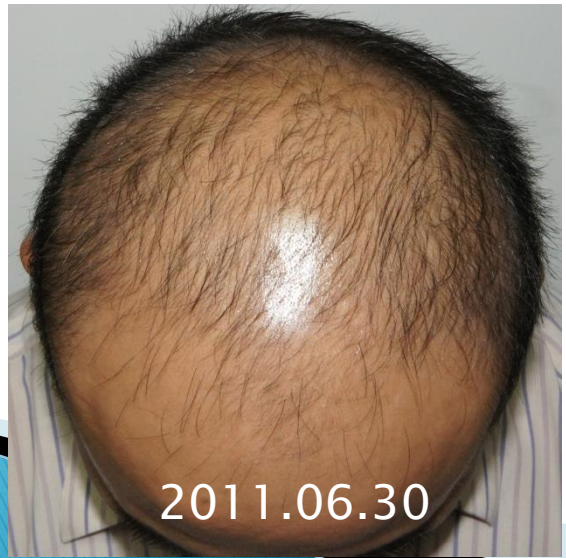

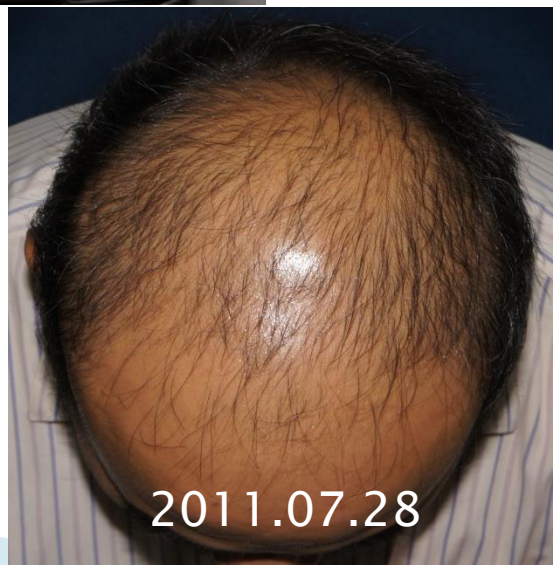

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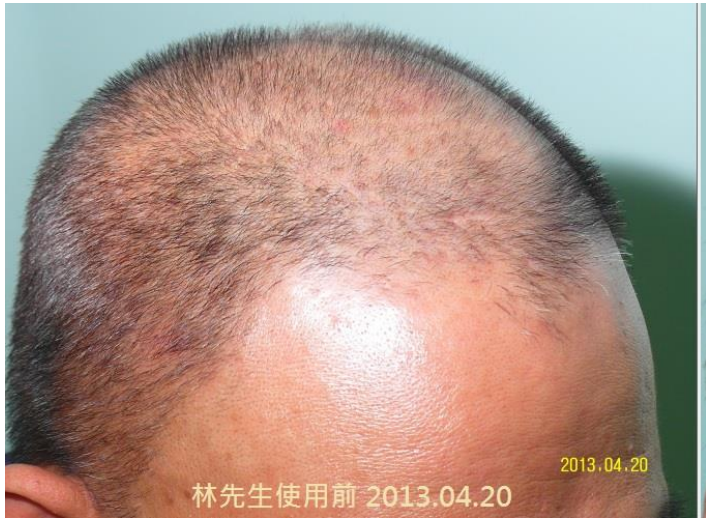

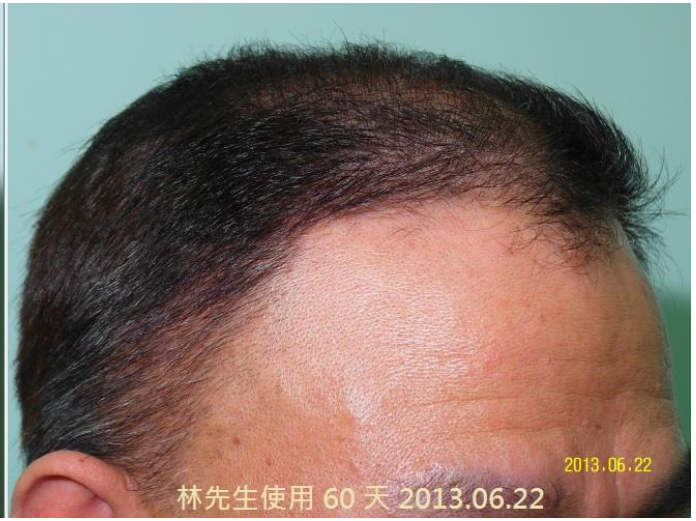

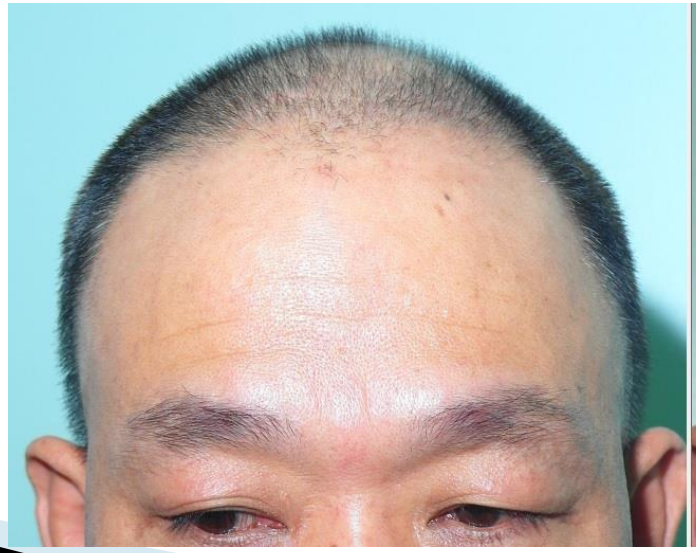

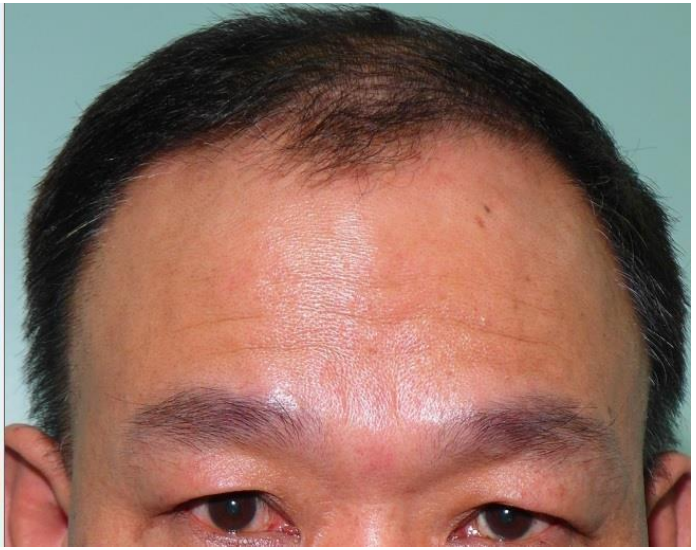

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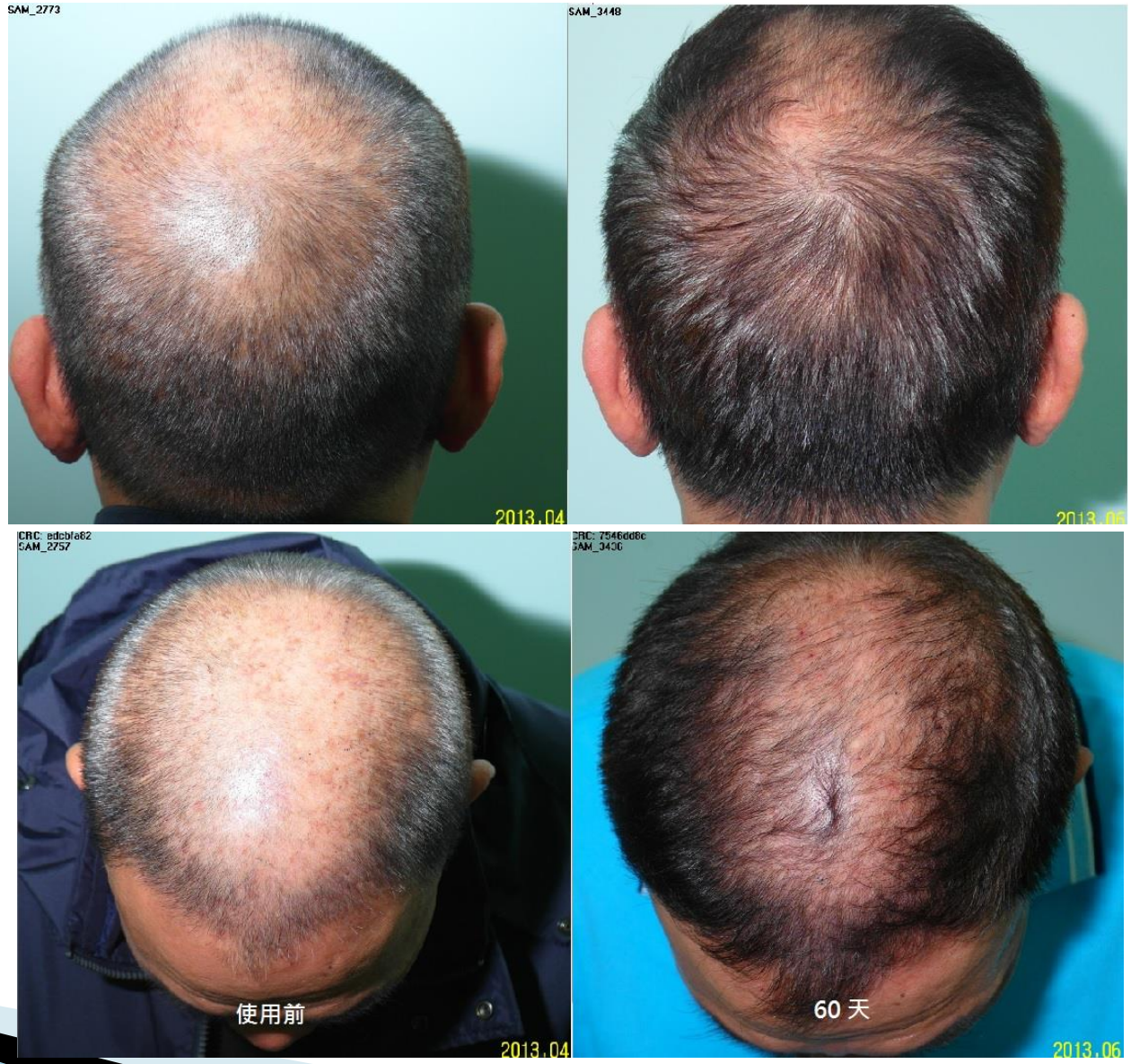

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Hair density: 68→128/ cm² @ crown

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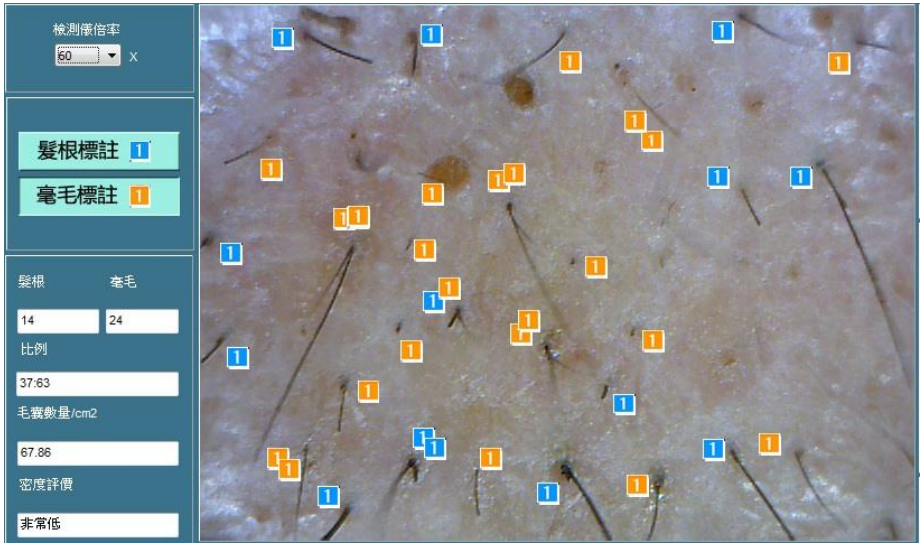
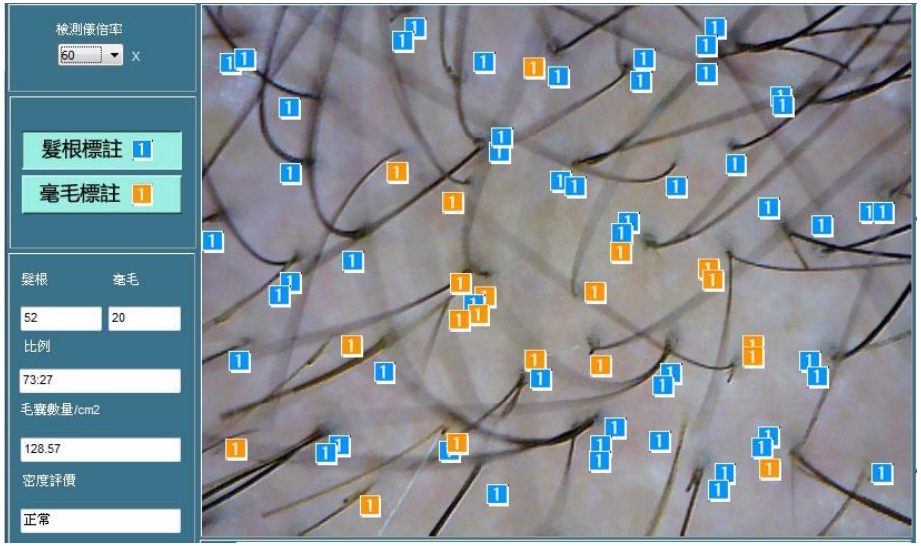
Before @ 2013.04.20



2013.06.22



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Hair density: 88→129/ cm^2 @ vertex

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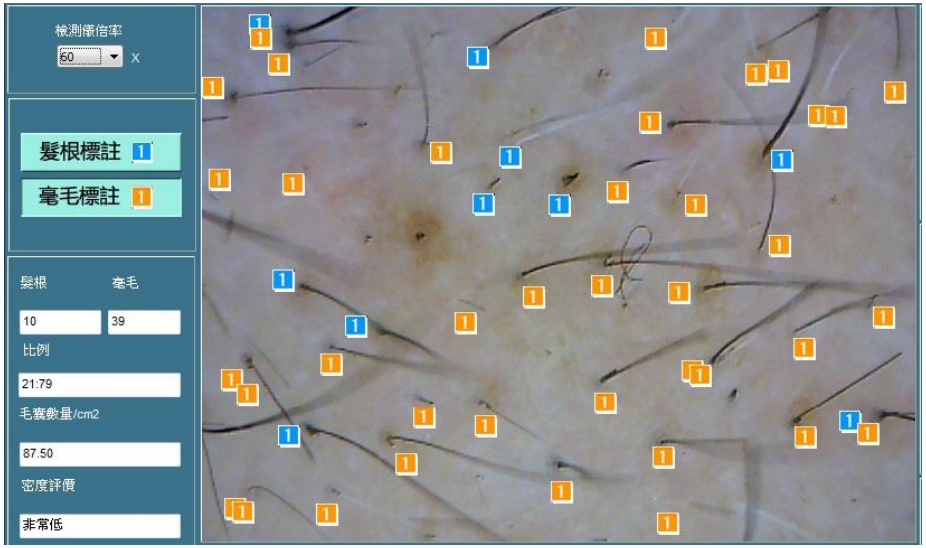
New hair gain = 40 hairs x 300cm^2 = 12,000 hairs

Before @ 2013.04.20



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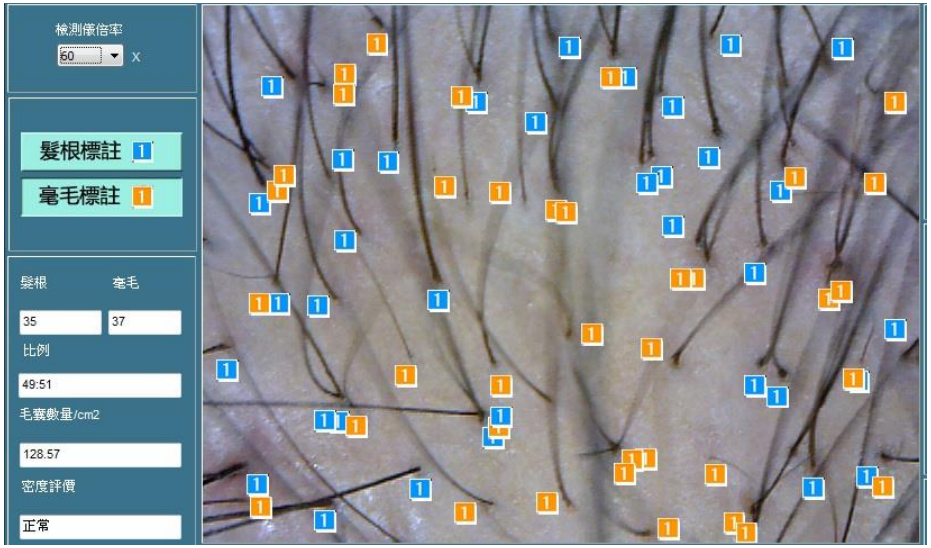

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PDGF + Antiinflammatory treatment: Great success at 75 days!

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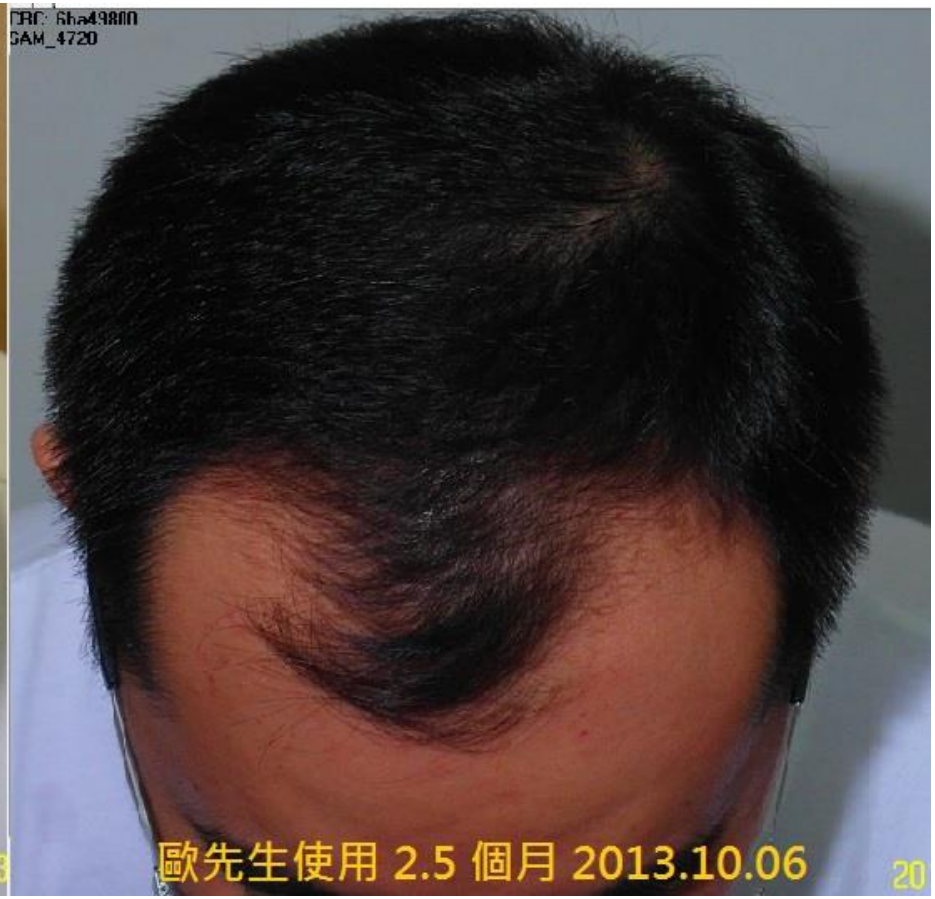

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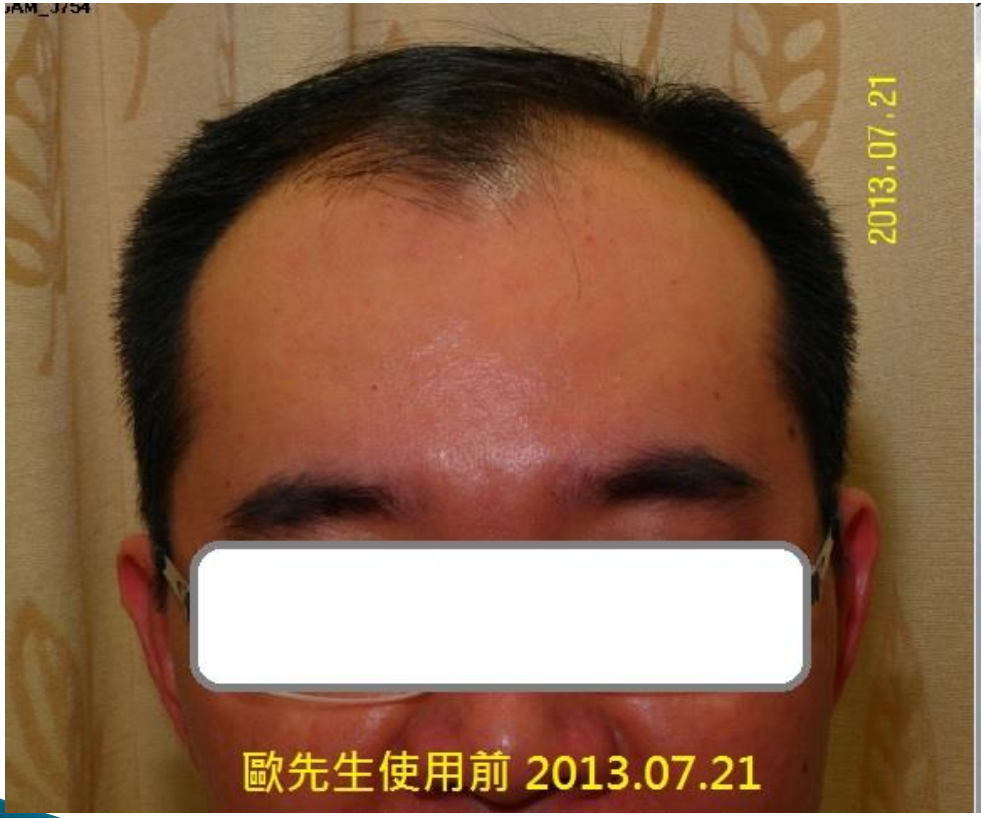

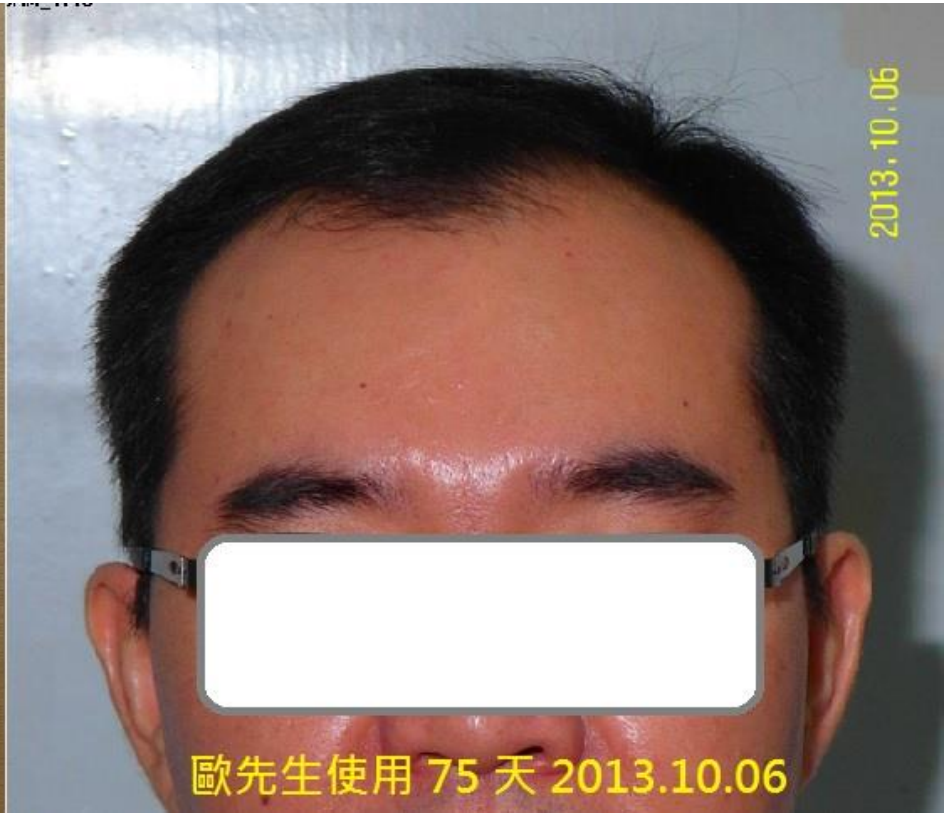

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Great recovery in occipital zone!

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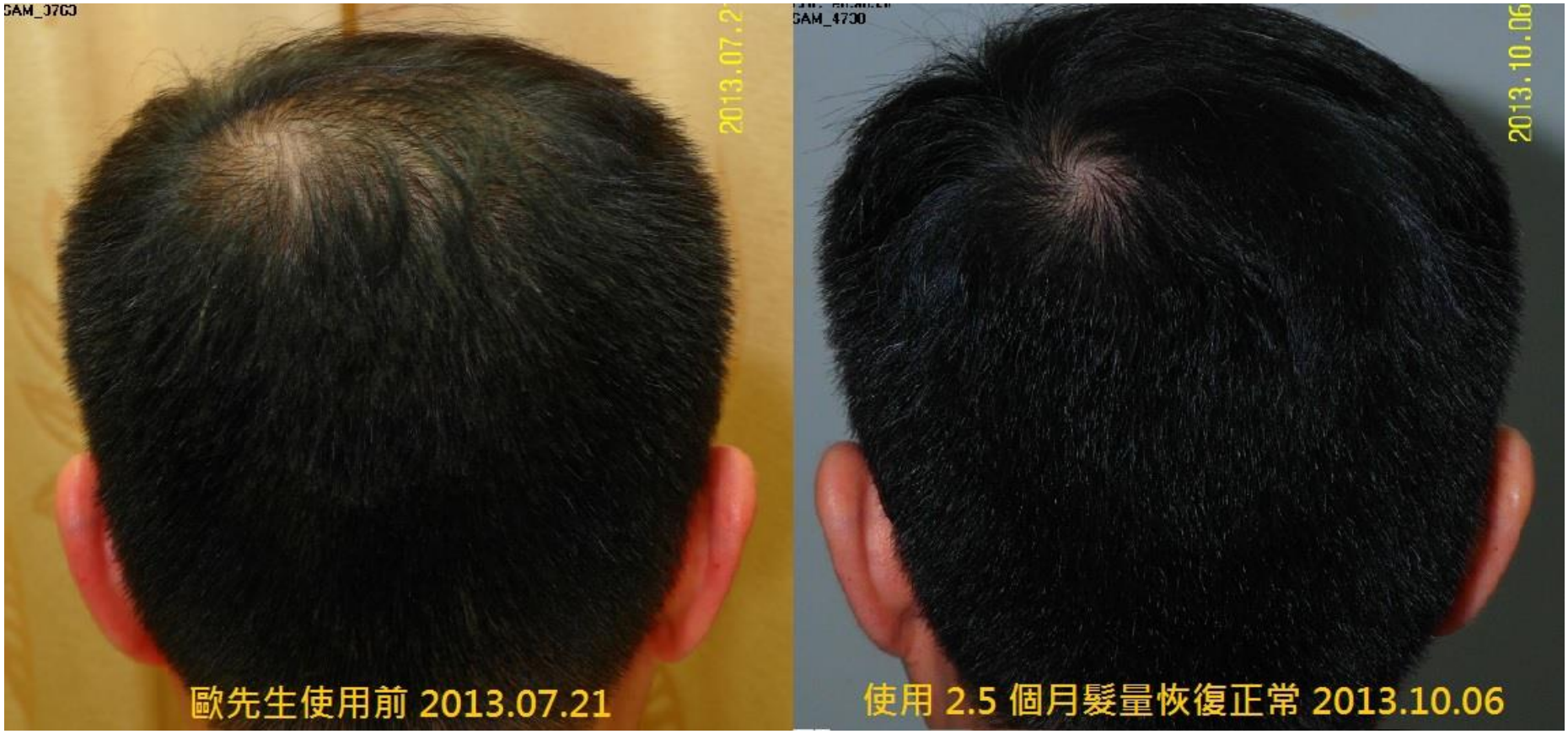

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Satisfactory outcome in crown region at 75 days

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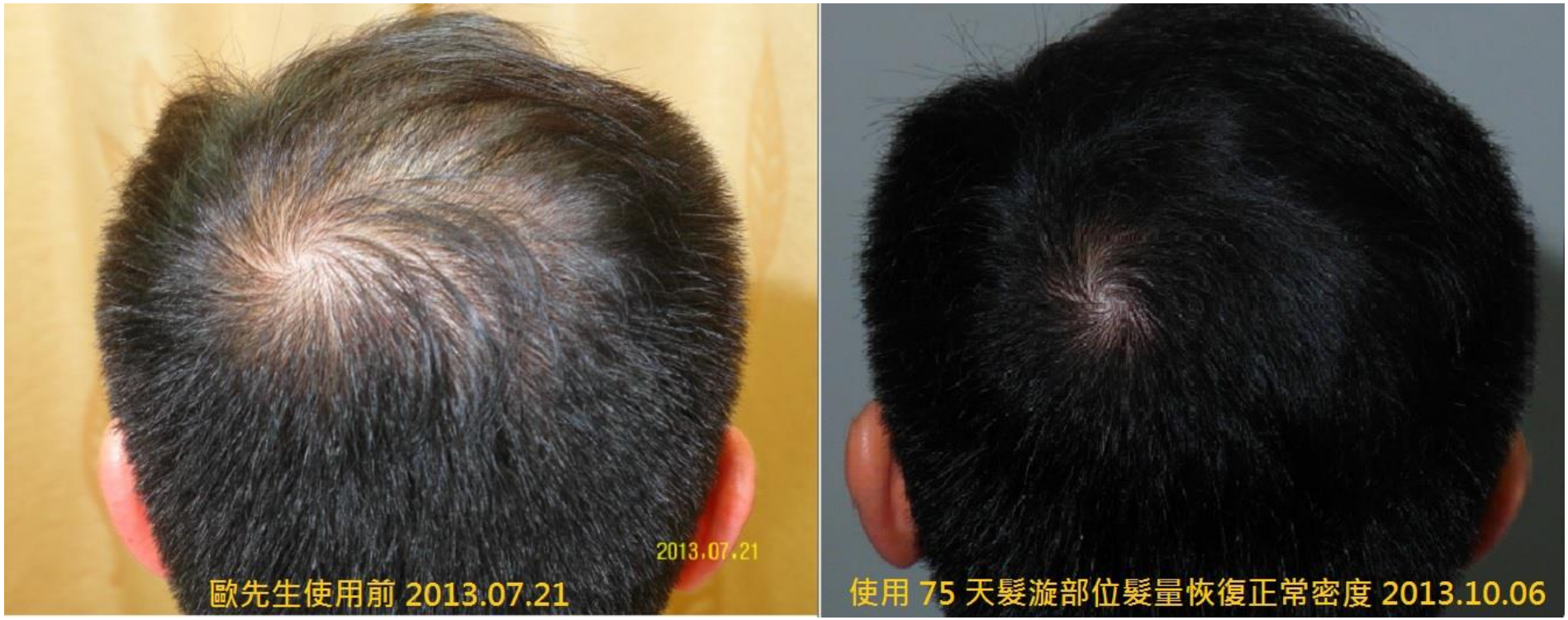

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Hair density: 139→155/ cm^2 @ crown

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Before @ 2013.07.21

高雄歐先生冠部使用前頭髮密度 139 根，粗細比 7:1
2013.07.21

2013.10.06

高雄歐先生冠部使用 75 天頭髮密度 155 根，粗細比 11:1
2014.10.06

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Hair density: 128→168/ cm^2 @ vertex

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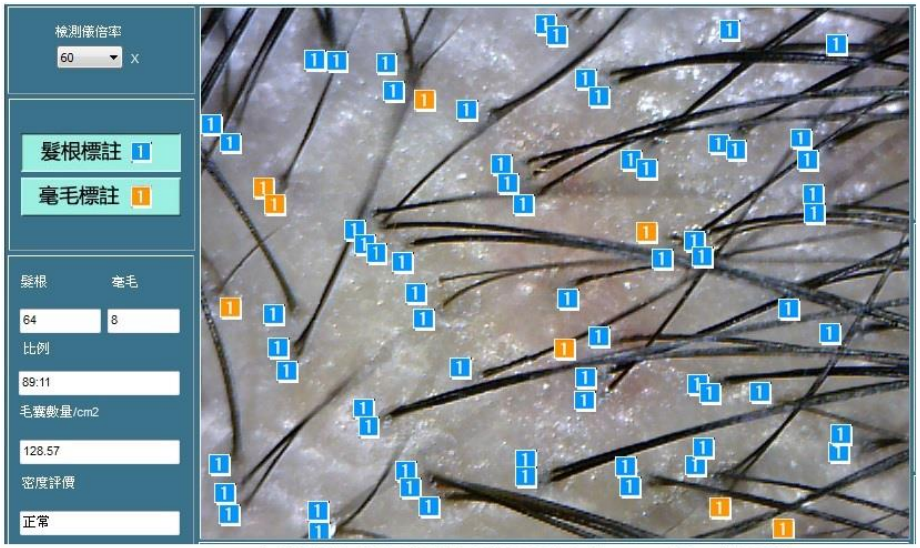
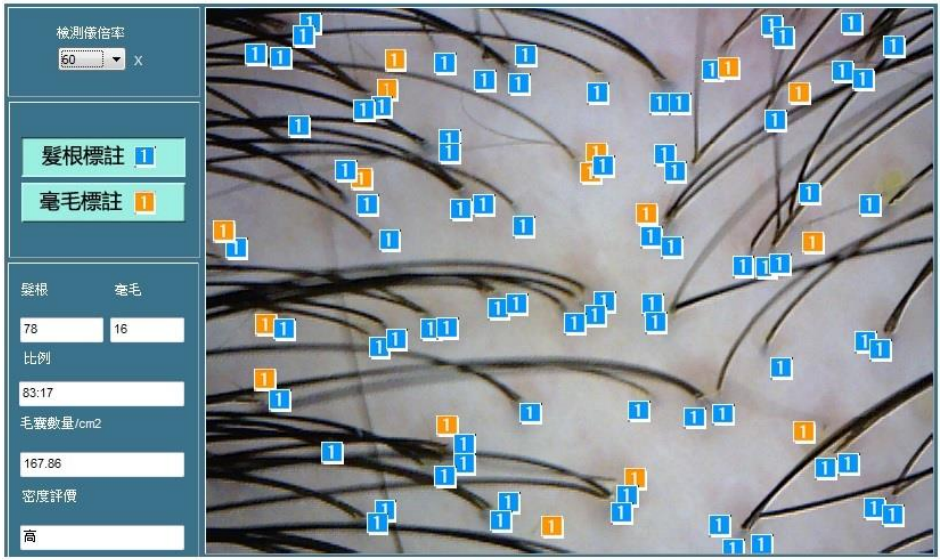
New hair gain = 30 hairs x 240cm^2 = 7,200 hairs

Before @ 2013.07.21



高雄歐先生頂部使用前頭髮密度 128 根，粗細比 8:1
2013.07.21

2013.10.06



高雄歐先生頂部使用 75 天頭髮密度由 128 根進步到 168根
2013.10.06

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R't temporal regrowth

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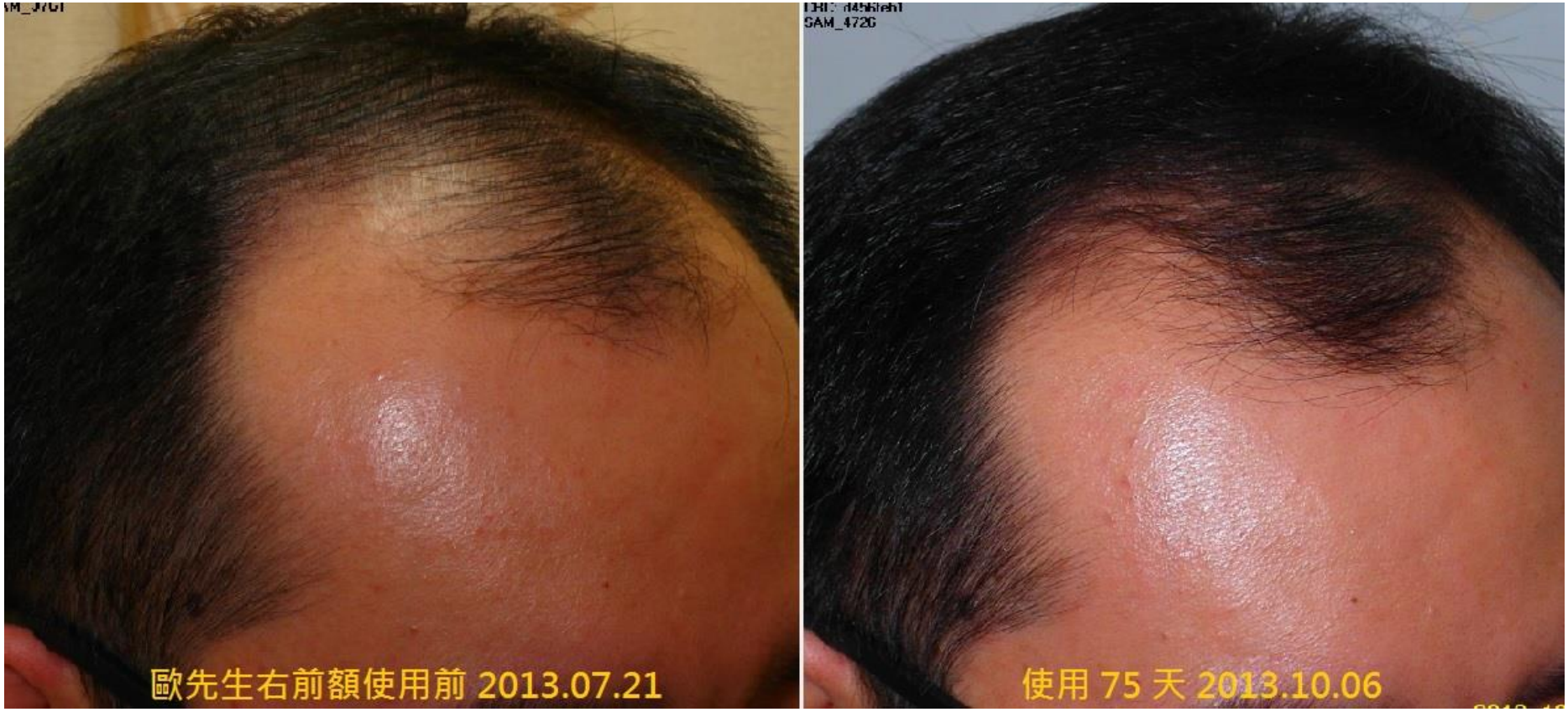

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Significant regrowth in L't temporal region

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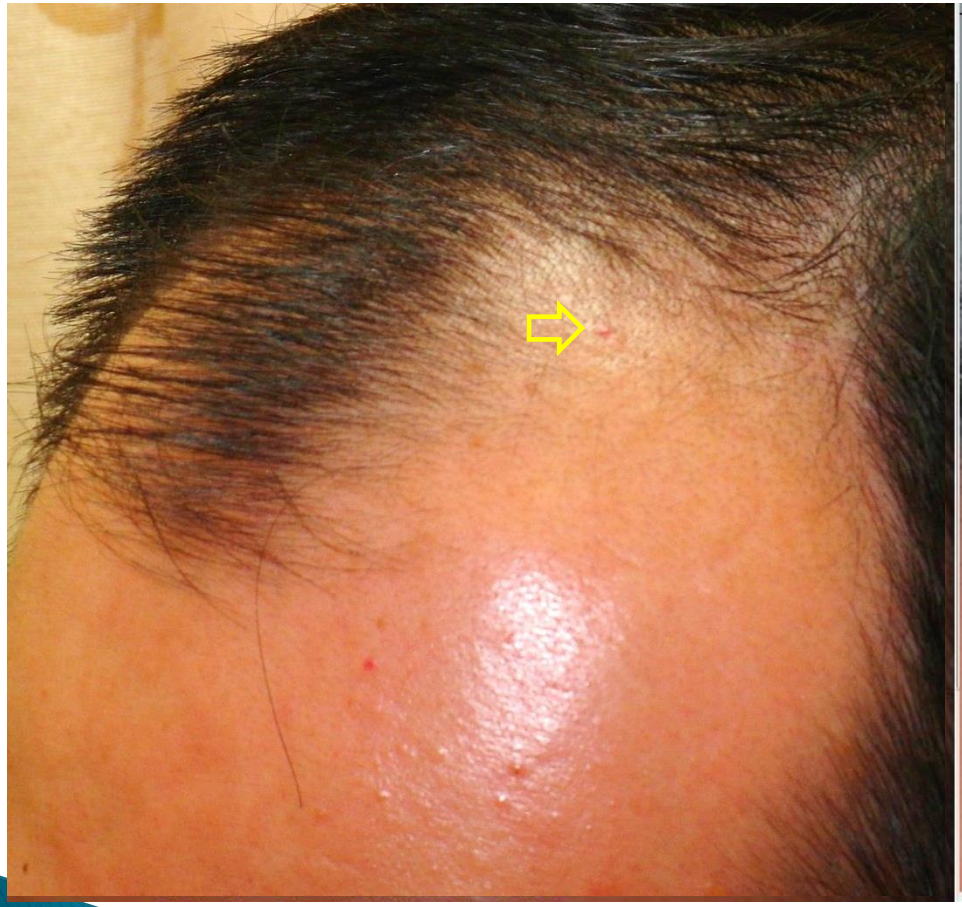

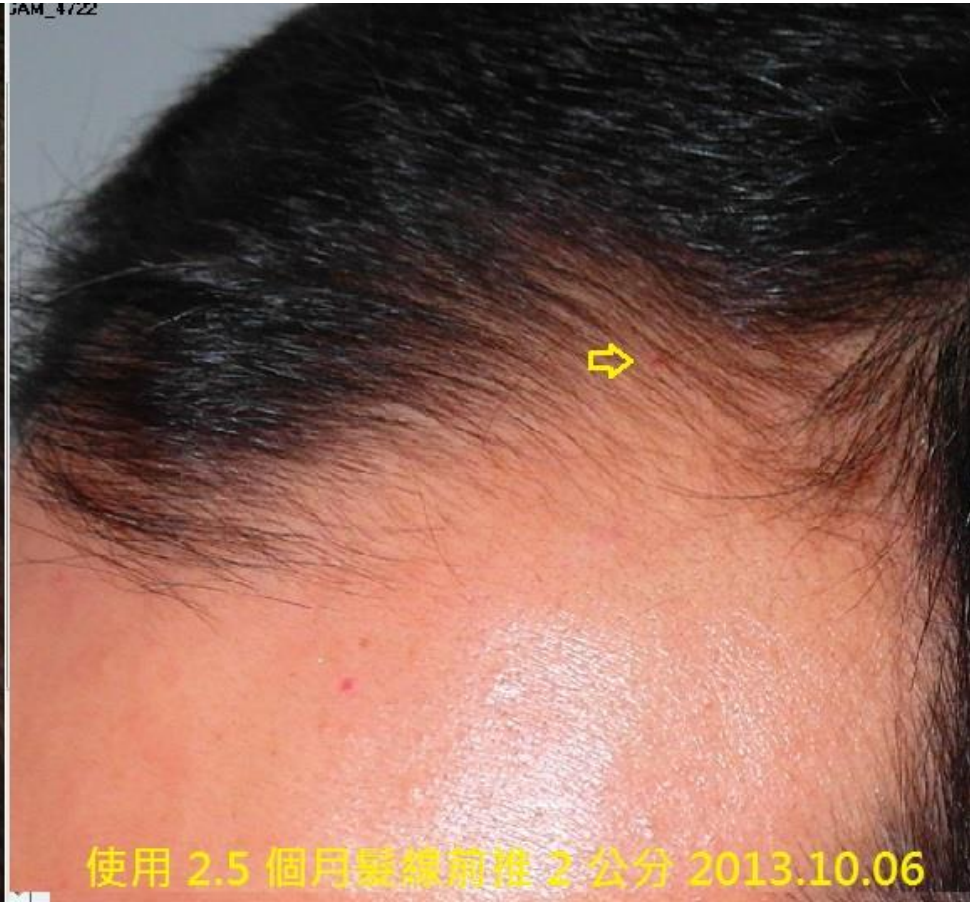

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Hair line advances by 2cm Not possible with minoxidil or finasteride!

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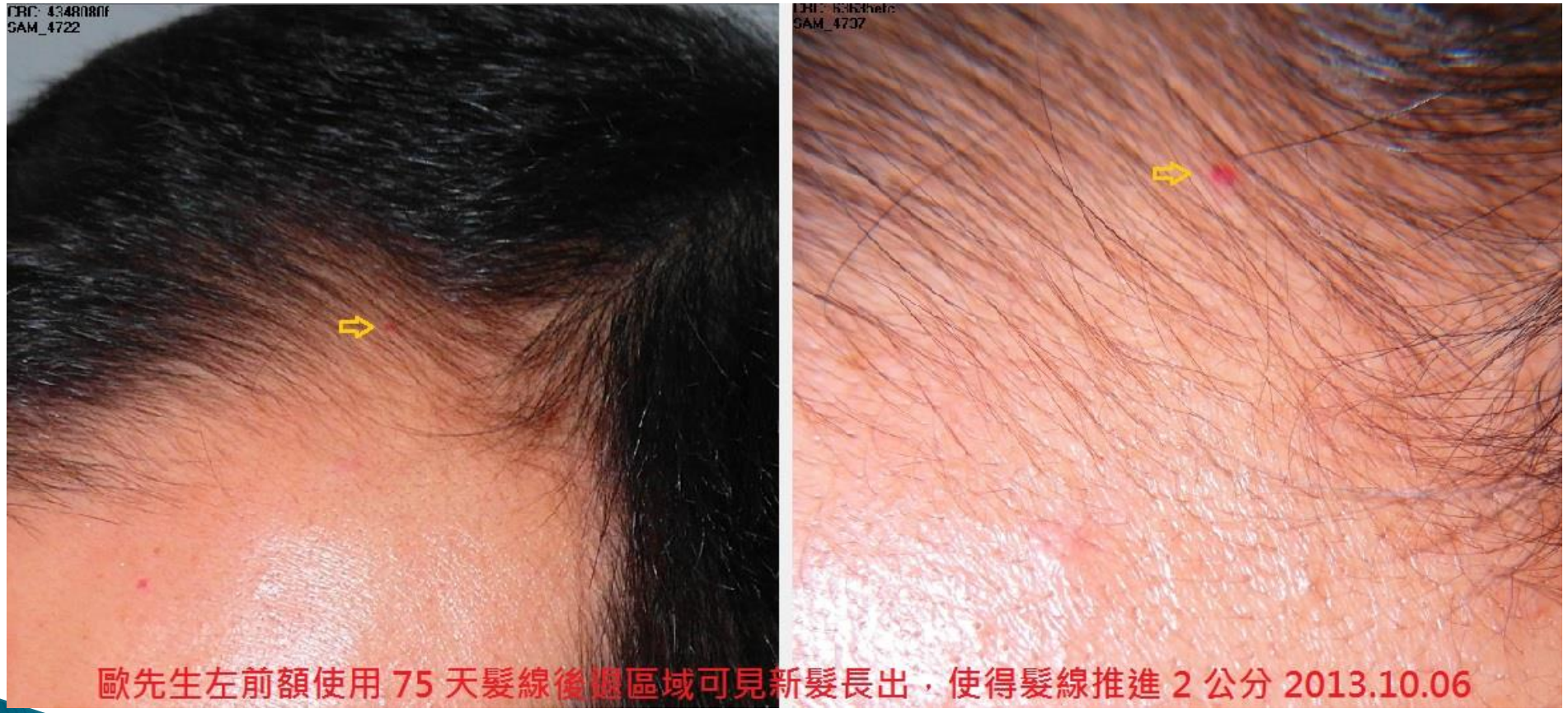

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Mr. Hsieh (Shanghai)

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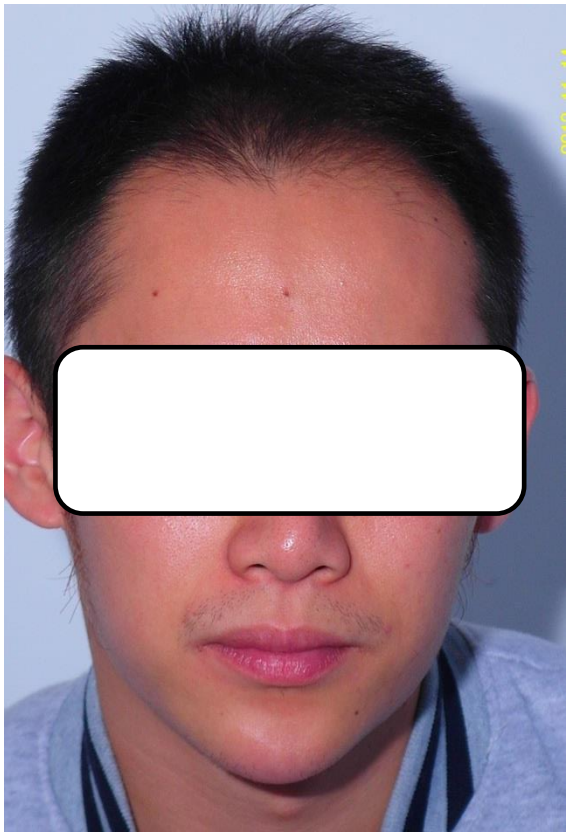
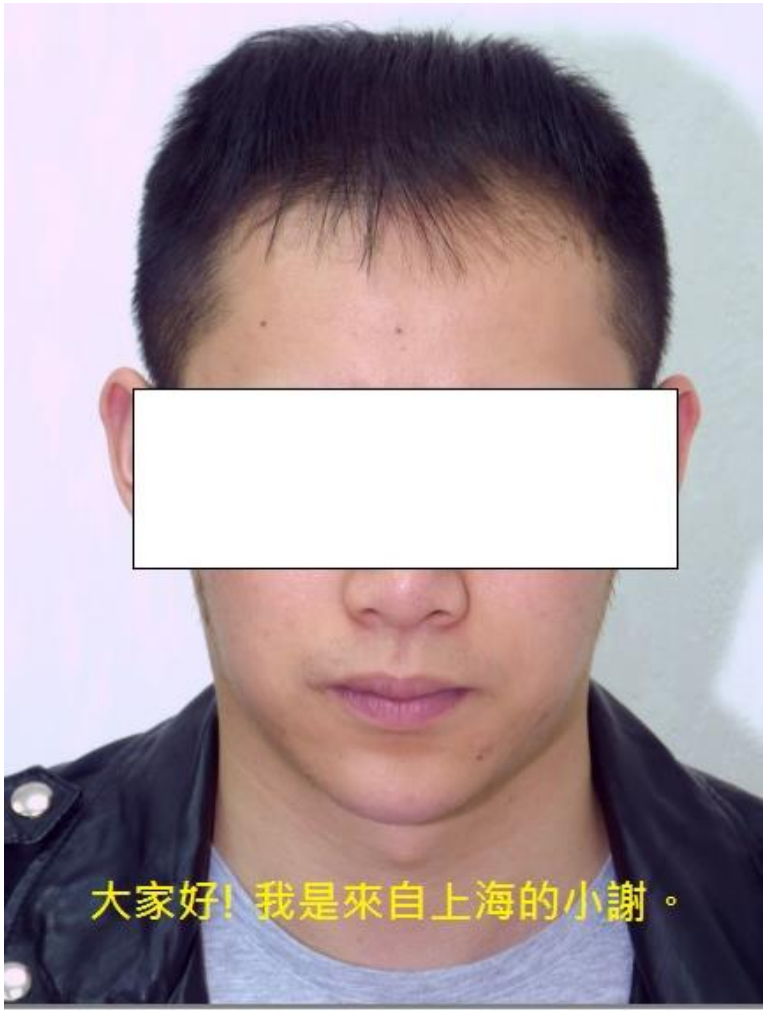
Before @ 2013.11.14



2014.05.06



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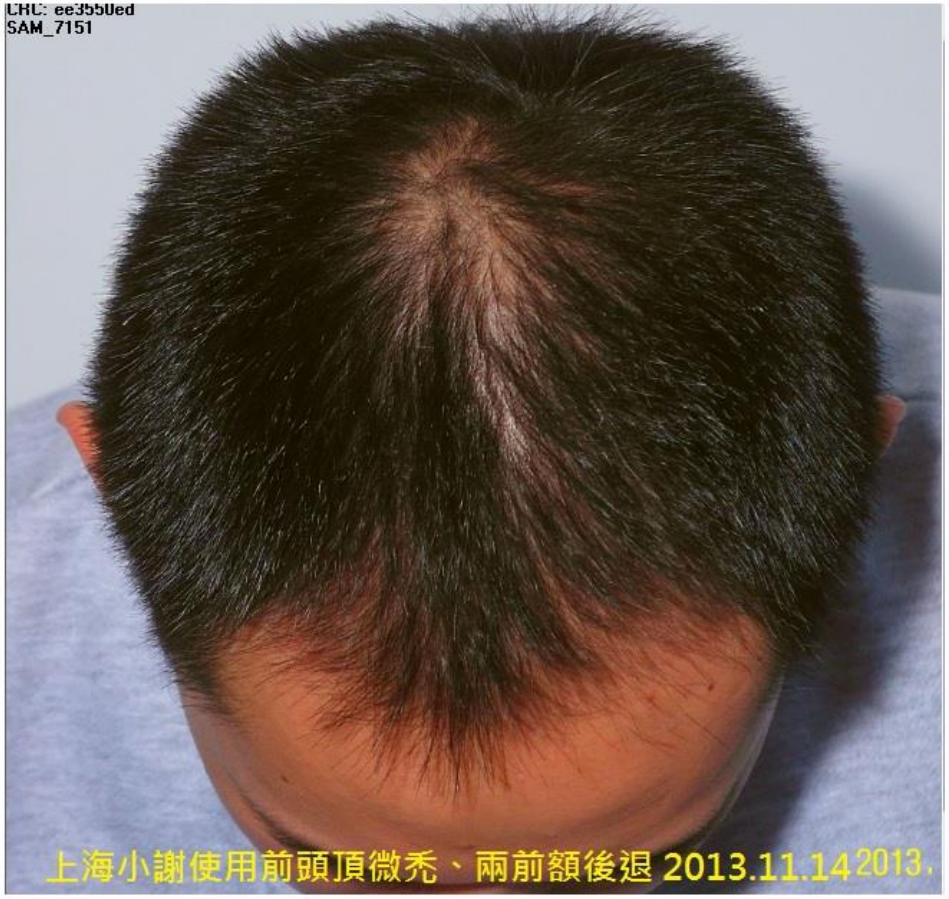
Hair density improved at vertex!!

Before @ 2013.11.14

2014.05.06



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Thicker and denser hairs at crown region!

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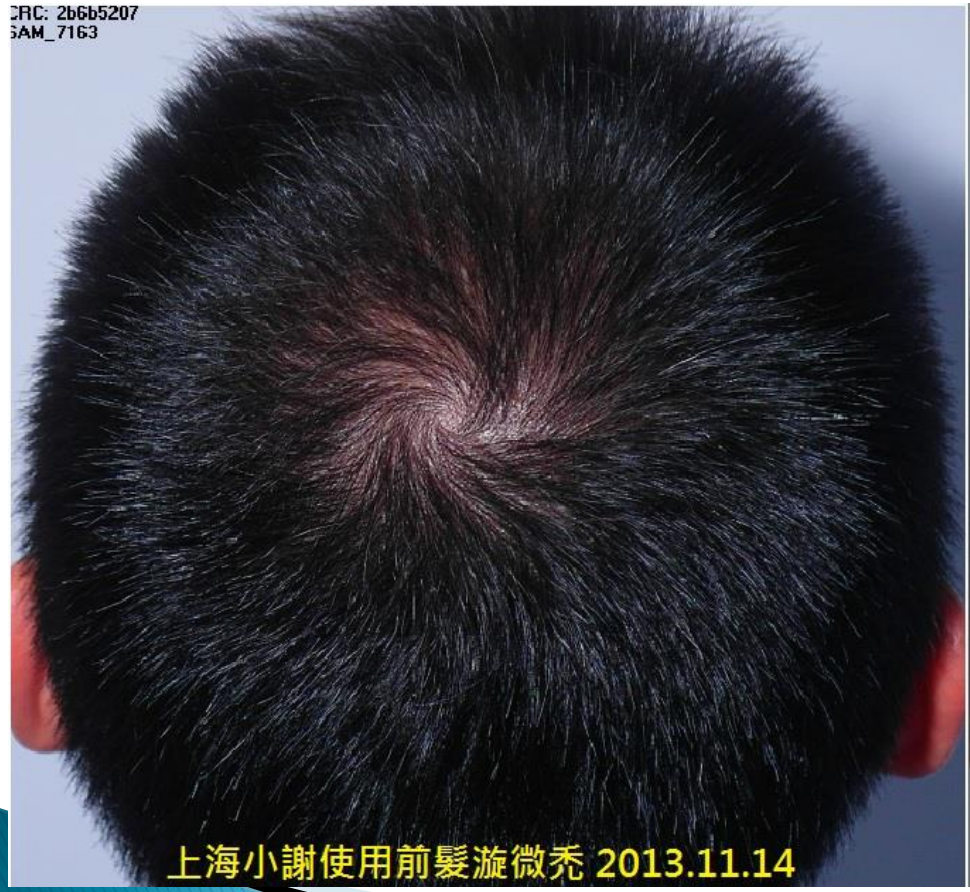
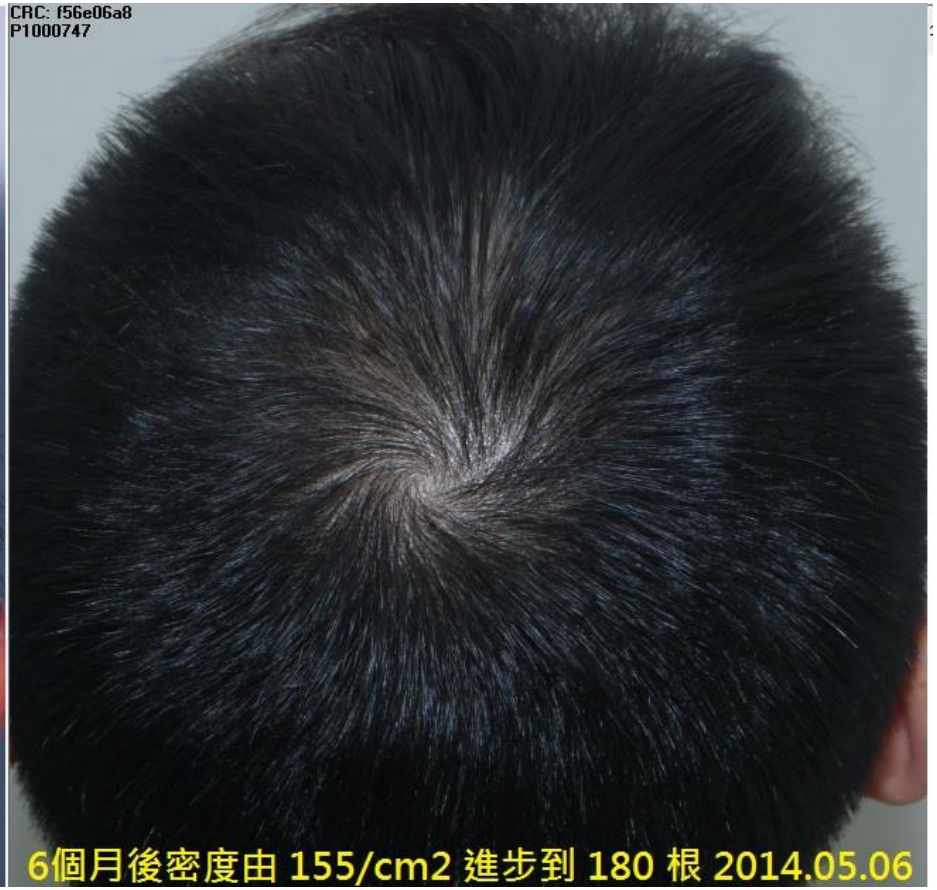
Before @ 2013.11.14

2014.05.06





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Great hair regrowth at R't temporal region !!!

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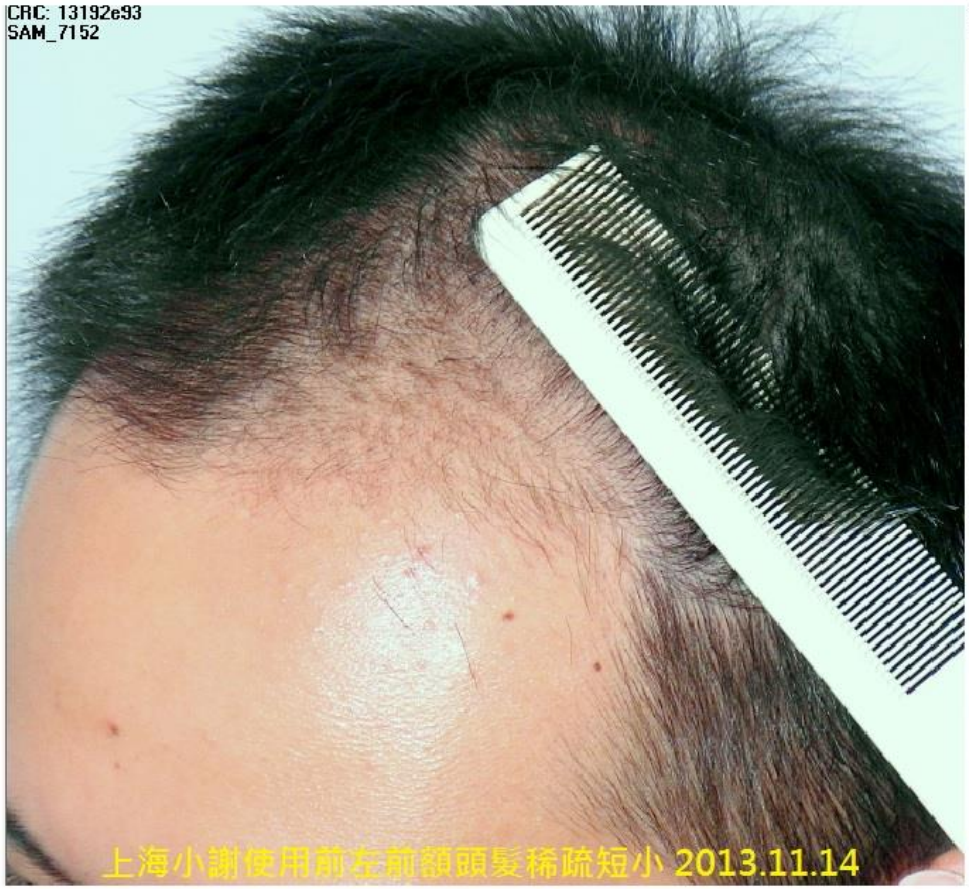
Before @ 2013.11.14



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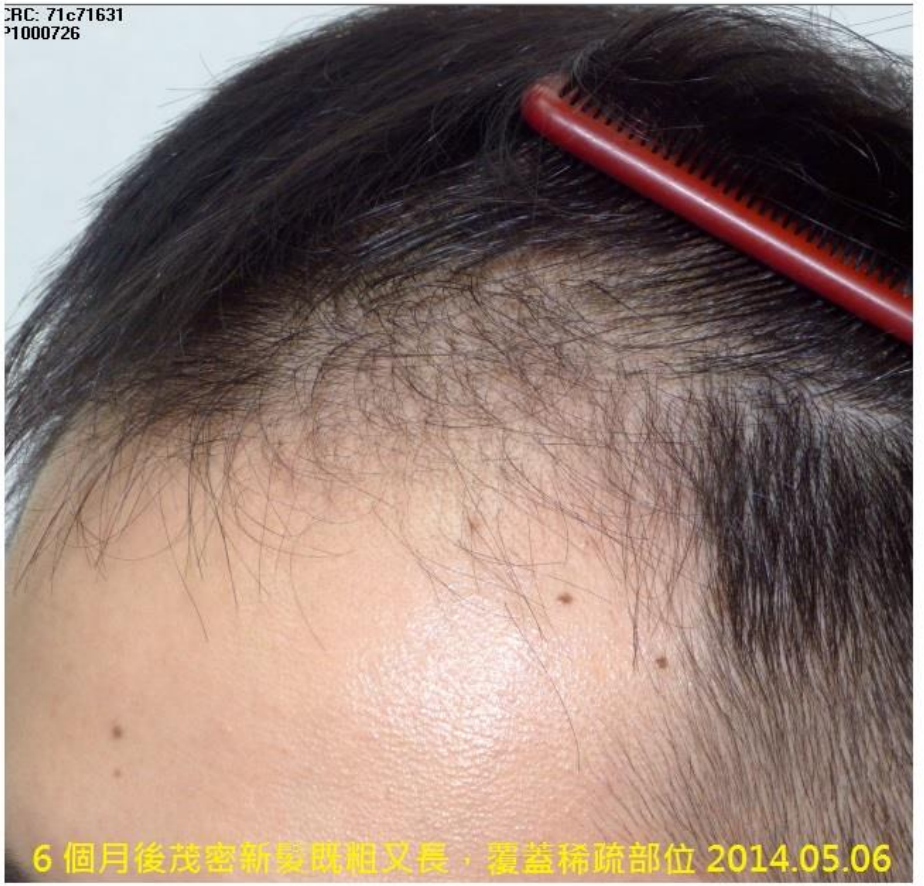

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Hair density: 155→180/ cm^2 @ crown !!!

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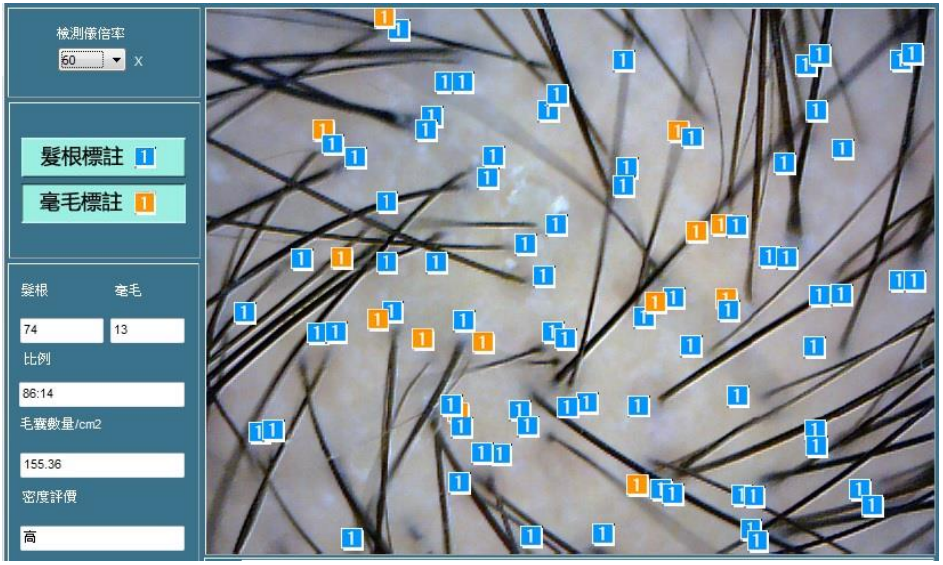
Before @ 2013.11.14



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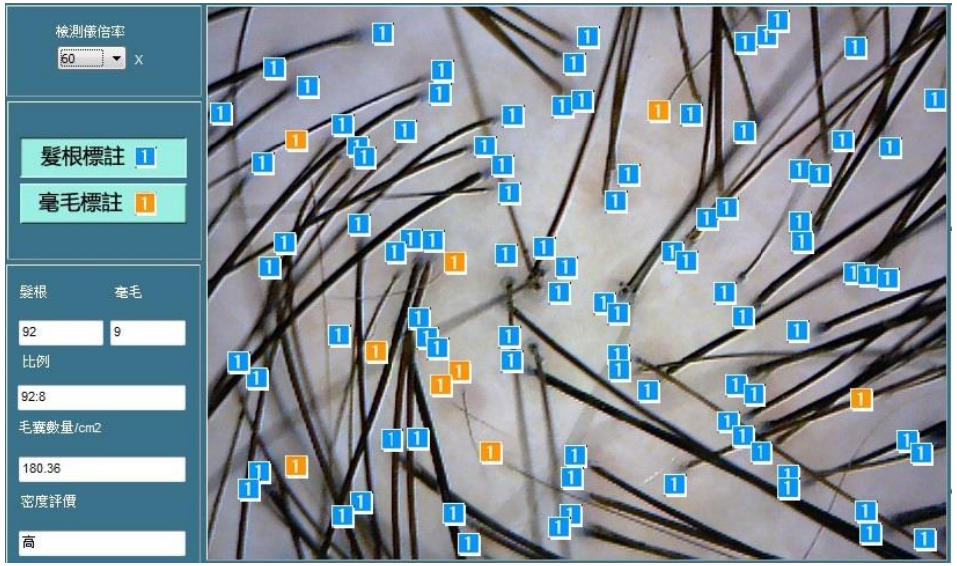

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Hair density: 142→159/ cm^2 @ vertex

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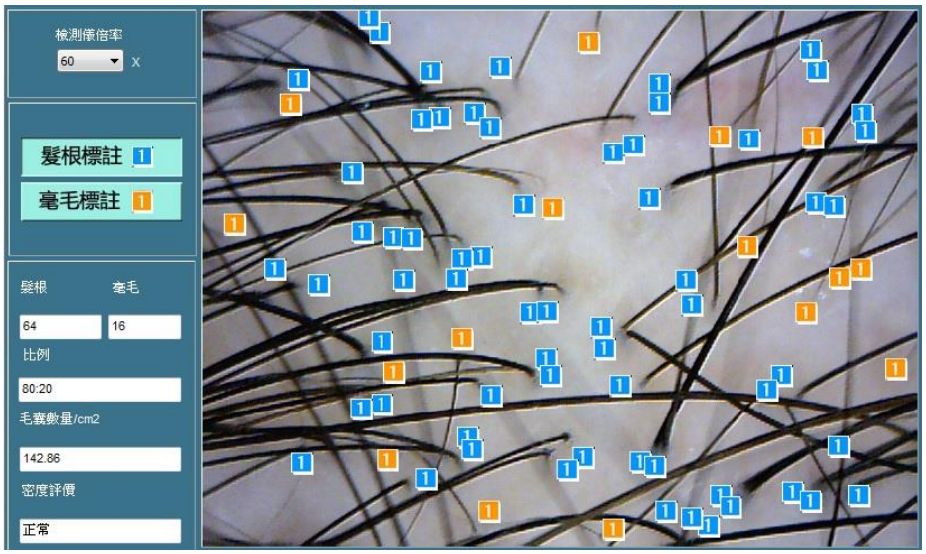
New hair gain = 17 hairs x 200cm^2 = 3,400 hairs

Before @ 2013.11.14



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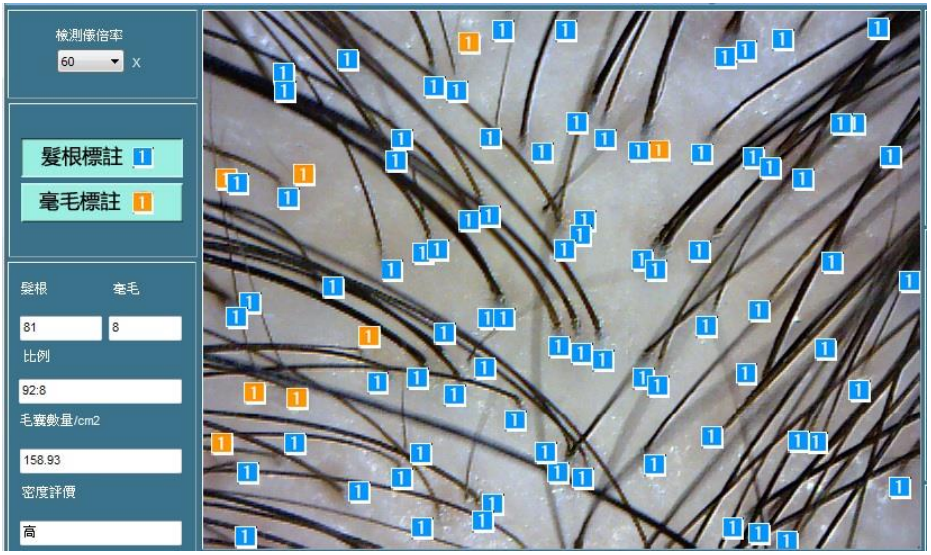

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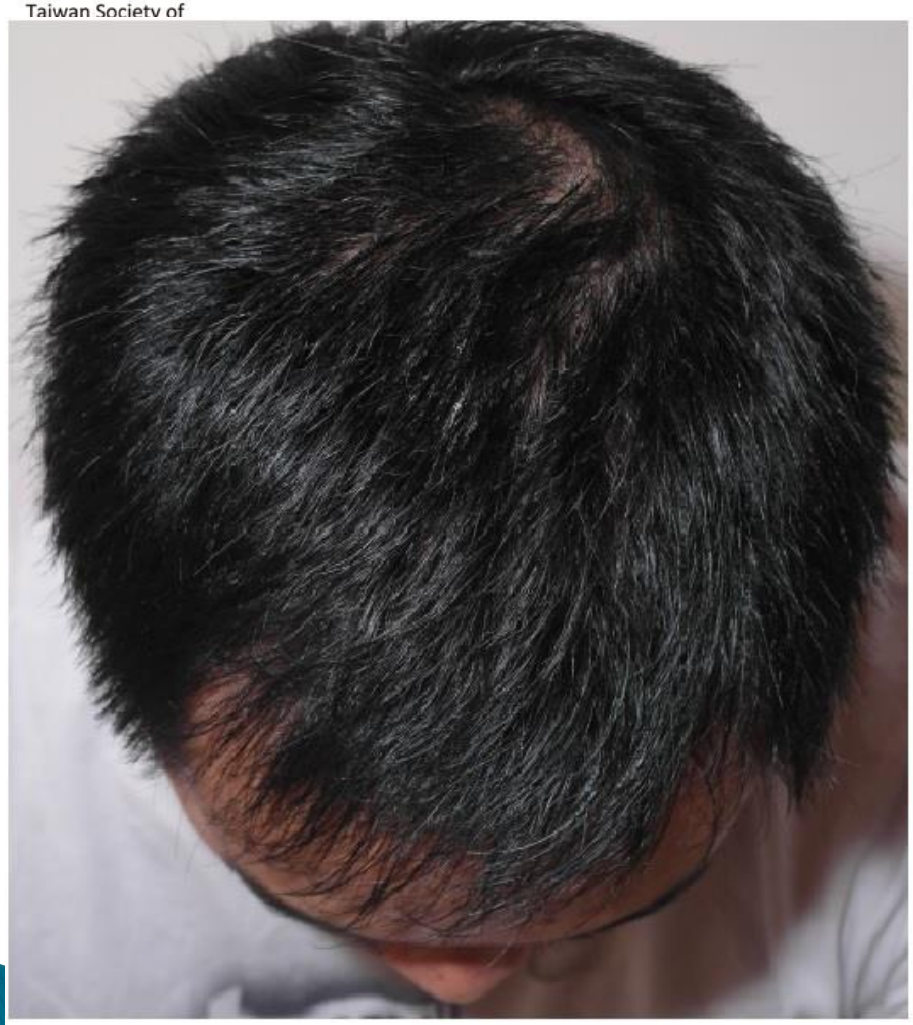
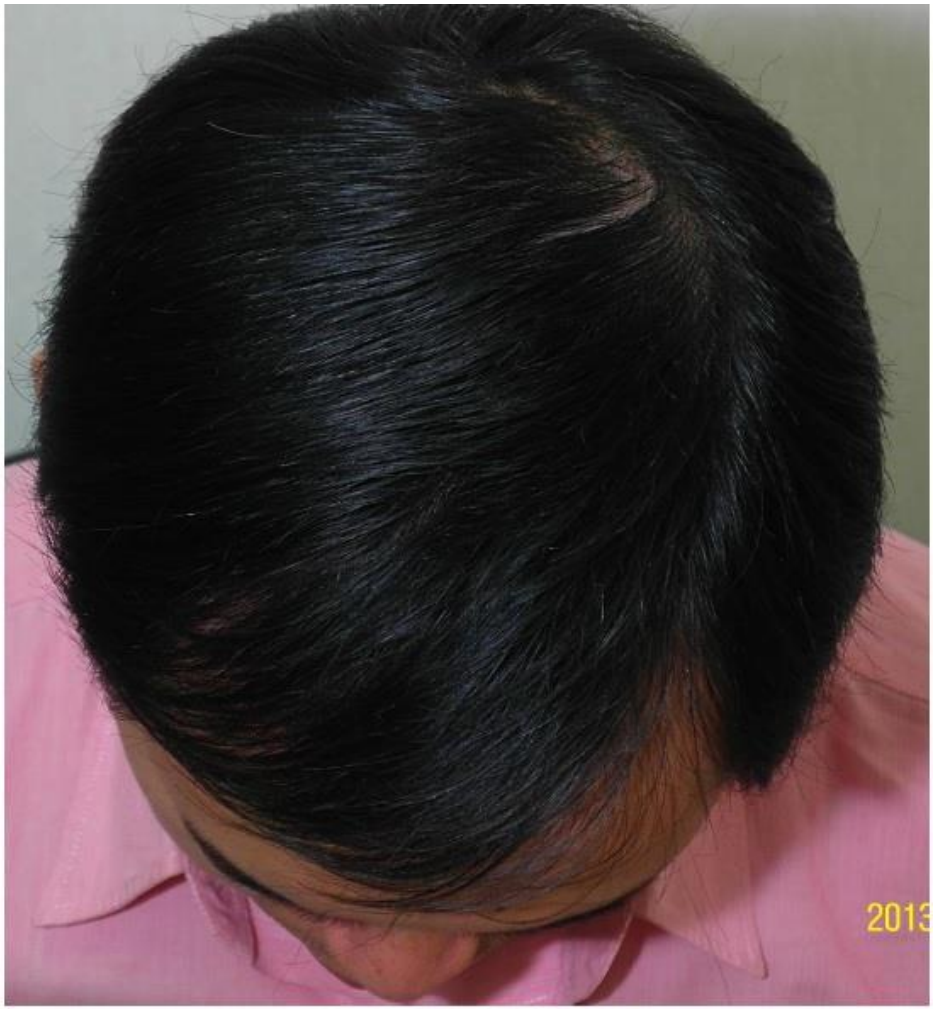


使用前 Before treatment 2012.08.02



療程後 12 個月 12 M after treatment 2013.12.03

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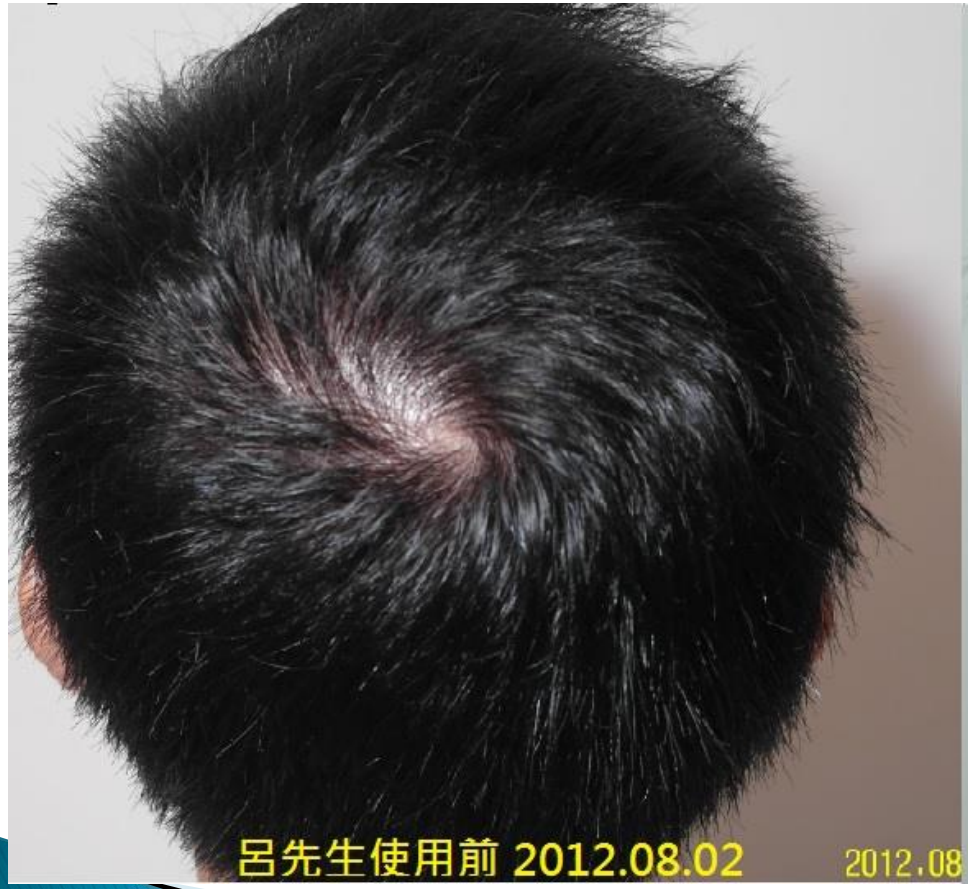

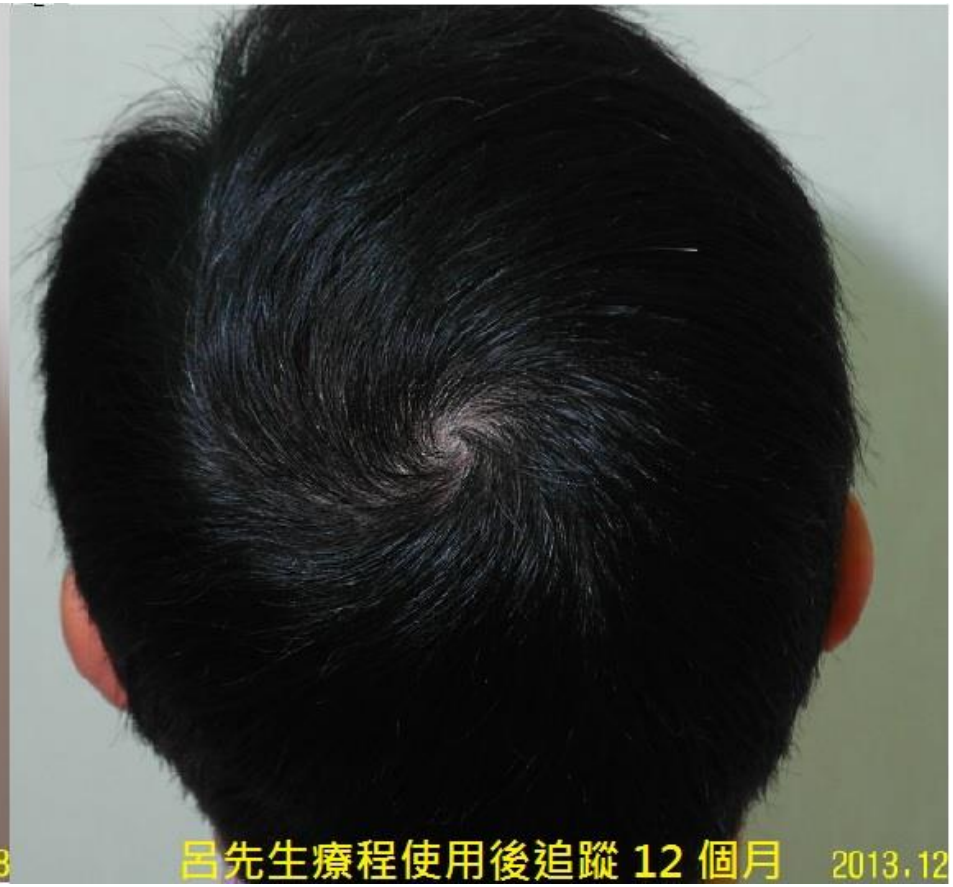

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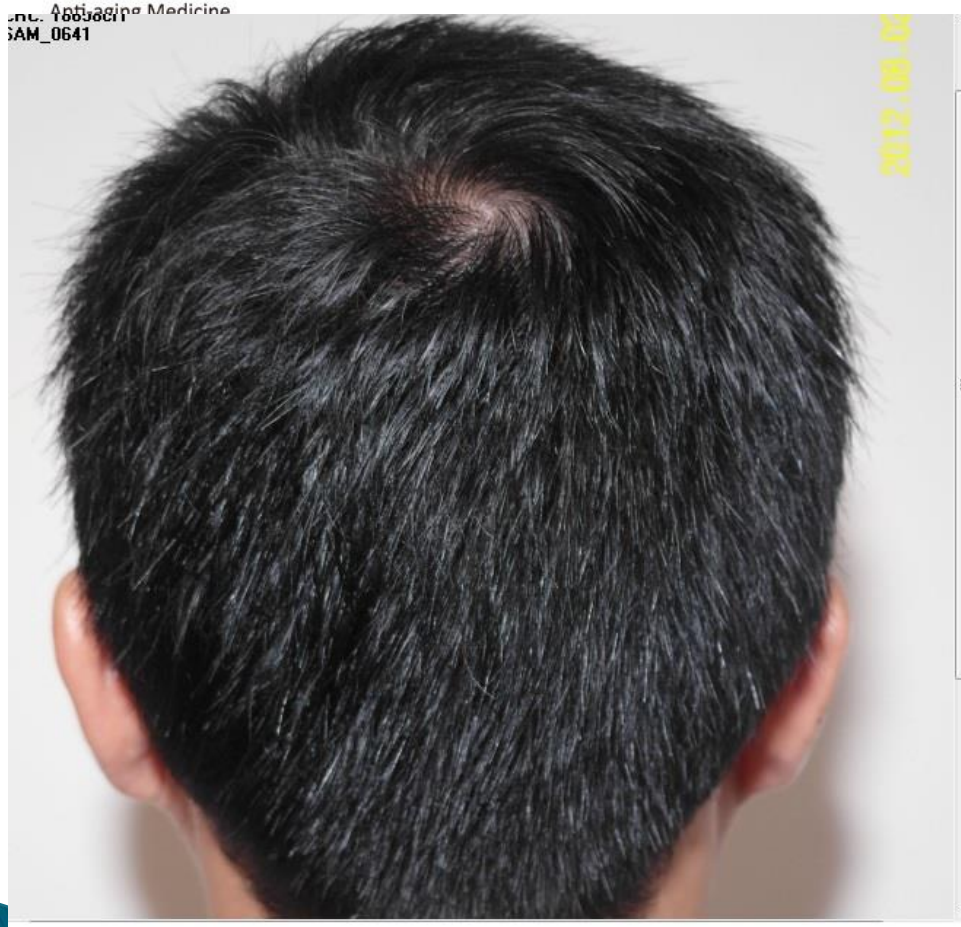
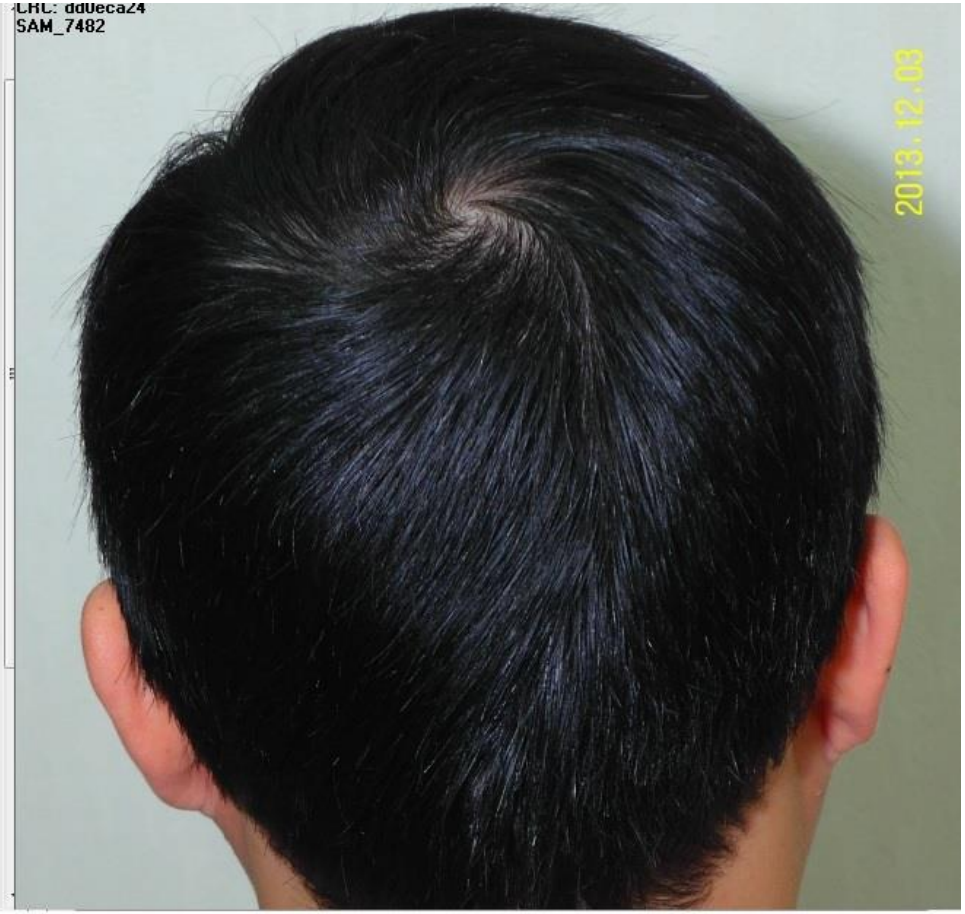


使用前 Before treatment 2012.08.02



使用後 12 個月追蹤 After 12 months 2013.12.03

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Vertex hair density increase from 129 hairs to 154 hairs/cm²

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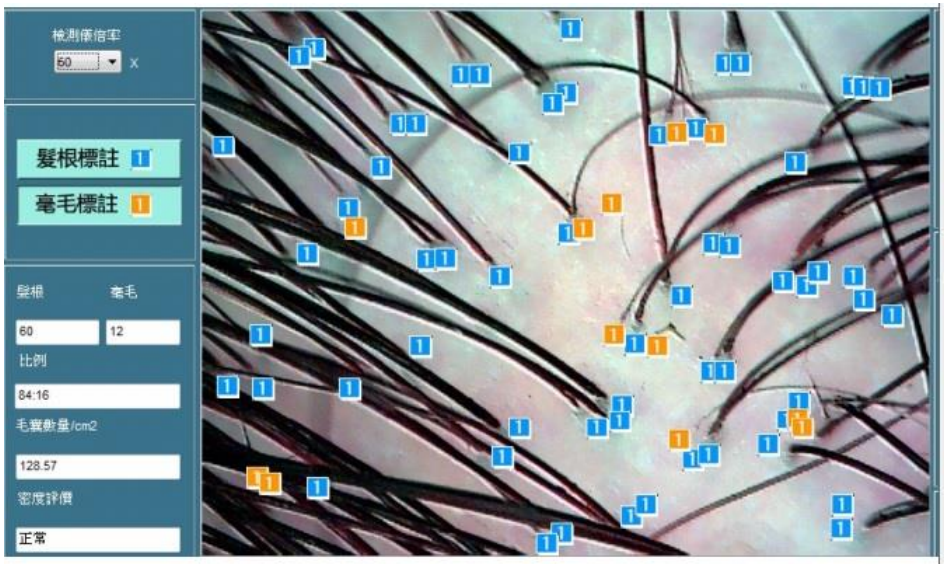
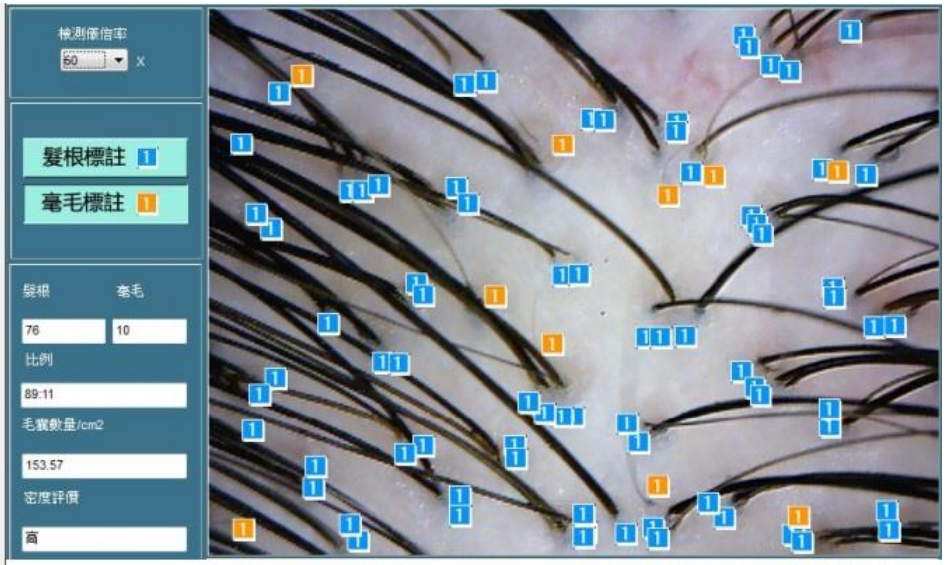
New hair gain = 25 hairs x 200cm² = 5,000 hairs



Before treatment hair density 129 hairs/cm2
T/V ratio 5:1 2012.08.02



12 months after treatment hair density 154 hairs
T/V ratio 7.6:1 2013.12.03

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Conclusions

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- PDGF is effective in activating hair follicle stem cells to initiate hair follicle regeneration
- Dose dependant
- Monthly treatment
- TGF-ß1 causes prematured hair loss as early as 4 months by inducing follicles into catagen
- Anti-inflammatary agent provides satisfactory bitemporal regrowth at 60 days when used with PDGF
- Hair care tonic containing azelaic acid, saw plametto extract, green tea extract, provides satisfactory outcome in terms of inhibition of microinflammation, TGF-ß1 and 5-αreductase.

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Conclusions

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- Hair regrowth treatment with PDGF delivery and supporting therapies proves effective
- May replace most hair transplant procedures in AGA cases.

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