2016
대 한 모 발 학 회
제15차 Hair Forum

- 일시: 2016년 8월 27일(토) 15:30-18:10
- 장소: 대전 유성 호텔 8층 스타볼룸

대 한 모 발 학 회

2016
대한모발학회 제15차 Hair Forum

2016. 8. 27(토) 오후 **유성호텔(대전) 8층 스타볼룸**

일 정 표

오후

3:30–3:40 개회사 ····· 회 장 이원수

일정소개 ····· 총무이사 최광성

진행 ····· 학술이사 김문범

제1부: 자유연제 발표 4분, 질의응답 4분

3:40–3:48 **HMGB1 and hair growth: a potential role of prostaglandin metabolism** ····· 연세의대 김도영 / 6

3:48–3:56 **Investigation on the role of PDGF-AA/PDGFR-α in human hair growth and regeneration** ····· 경북의대(면역학교실) 정현식 / 16

3:56–4:04 **화장품 헤어소재개발 연구동향과 한계** ····· 바이오스펙트럼㈜ 정은선 / 22

4:04–4:12 **Skin equivalent formation with hair follicular structure** ····· 서울의대 백승환 / 28

4:12–4:20 **Various light-emitting diode light regulates the proliferation of human outer root sheath cells via Wnt/b-catenin and ERK pathway** ····· 가톨릭의대 김정은 / 33

4:20–4:28 **Efficacy of combination therapy with diphenylcyclopropenone and anthralin in the treatment of severe alopecia areata** ···· 인하의대 이시협 / 42

4:28–4:36 **The long-term efficacy of topical diphencyprone maintenance therapy for alopecia areata: a retrospective study** ····· 연세원주의대 최승재 / 47

4:36–4:44 **Long-term prognosis of alopecia totalis and alopecia universialis** ····· 경북의대(피부과학교실) 장용현 / 57

4:44–5:05 **Coffee Break**

제2부: 주제 발표

5:05-5:30 **Alopecia project using MSC conditioned media** 메디포스트 이장영 전무 / 64

5:30-5:40 **2015 WCHR 참관기** ····· 경북의대 장용현 교수

5:40-5:50 **2016 EHRS 참관기** ····· 인하의대 최광성 교수

5:50-6:00 폐회사 ····· 회 장 이원수

6:00-6:10 기념촬영

6:10- 저녁식사

2016

대한모발학회

제15차 Hair Forum

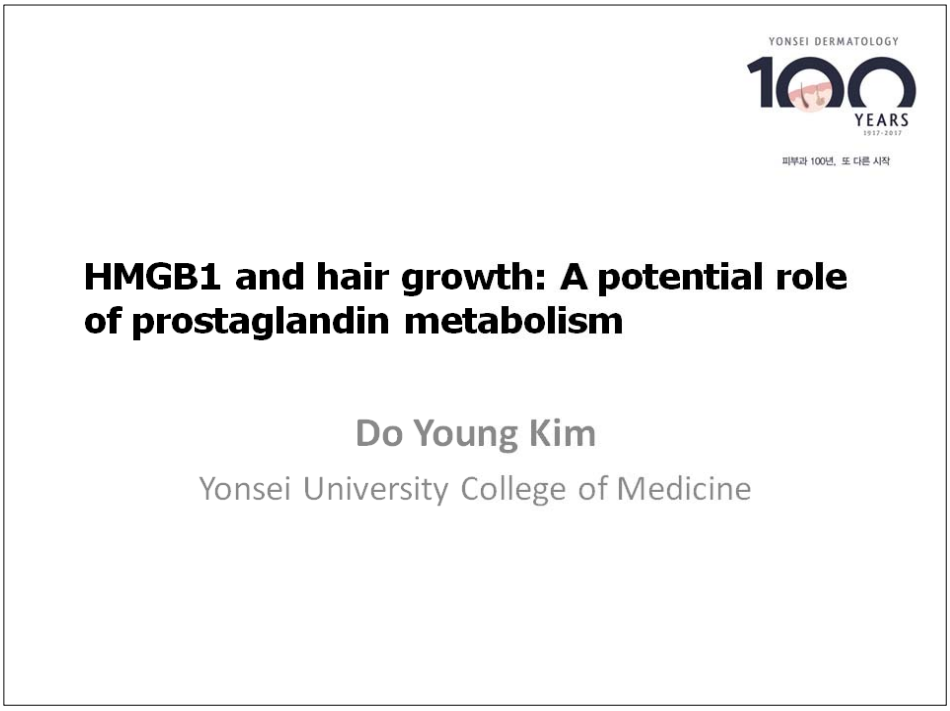
제 1 부 : 자유연제 발표

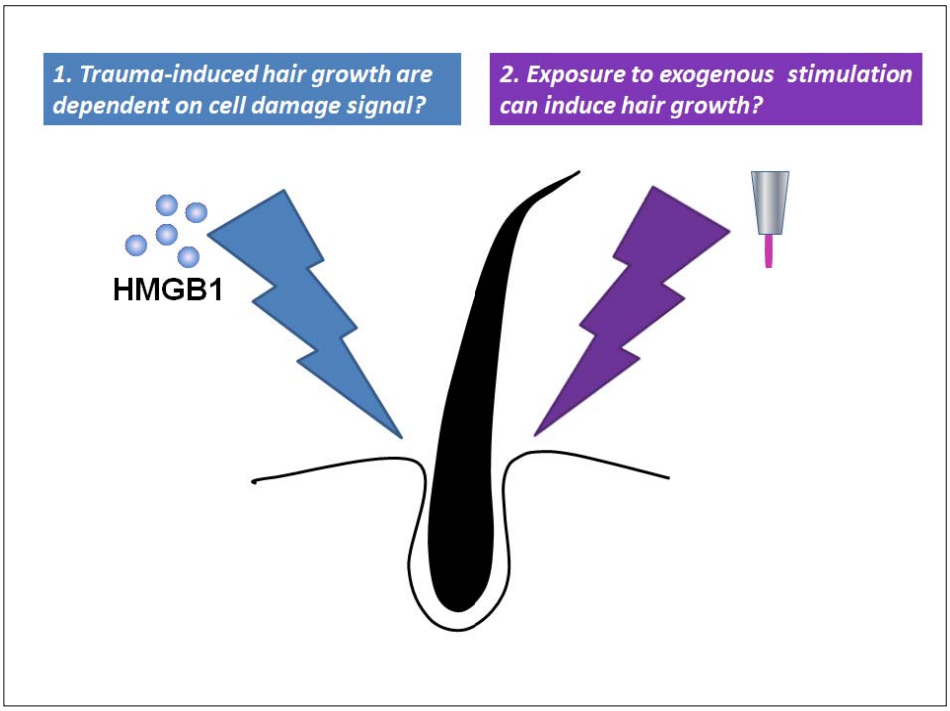
The Korean Hair Research Society

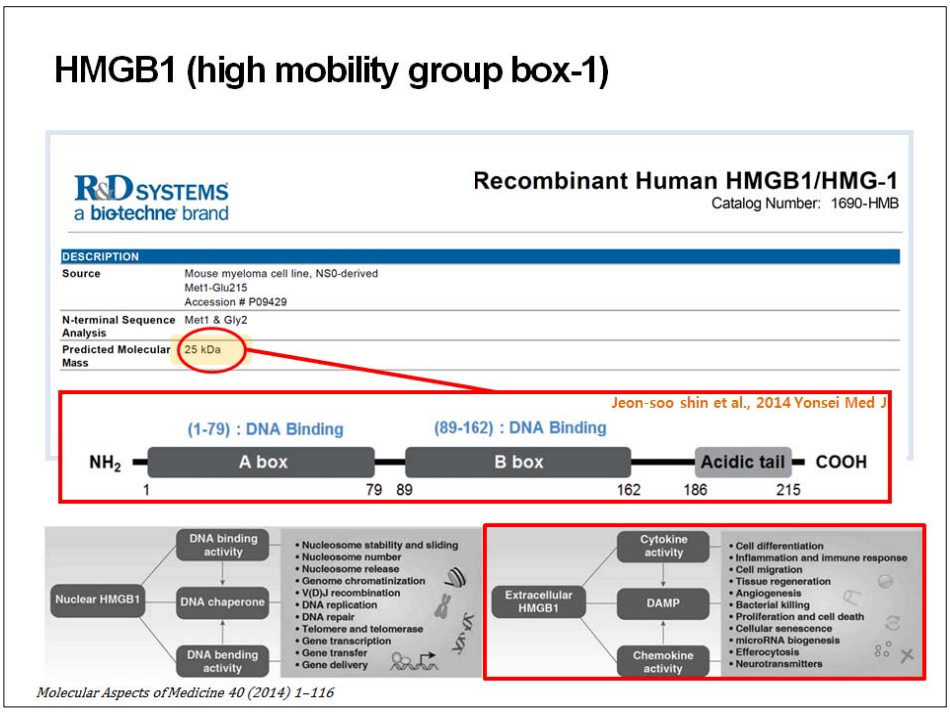
HMGB1 and hair growth: A potential role of prostaglandin metabolism

Do Young Kim

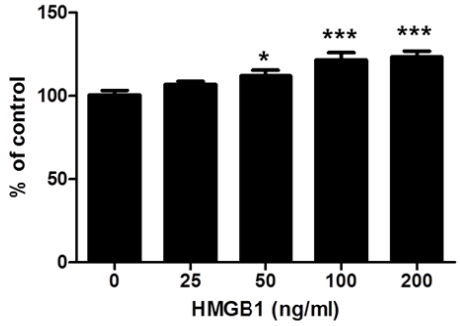
Yonsei University College of Medicine



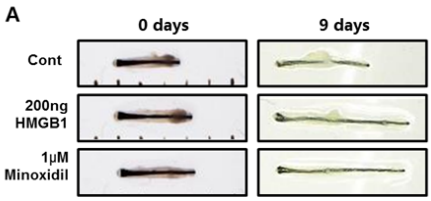

1. Trauma-induced hair growth are dependent on cell damage signal?
2. Exposure to exogenous stimulation can induce hair growth?
HMGB1

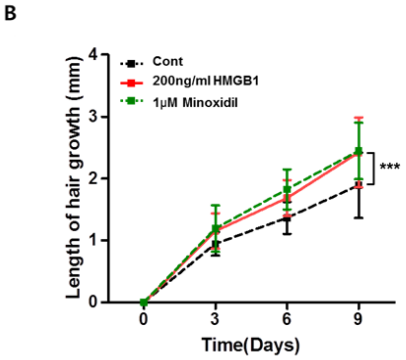

HMGB1 (high mobility group box-1)
R&D SYSTEMS
a biotechne brand
Recombinant Human HMGB1/HMG-1
Catalog Number: 1690-HMB
DESCRIPTION
Source
Mouse myeloma cell line, NS0-derived
Met1-Glu215
Accession # P09429
N-terminal Sequence Analysis
Met1 & Gly2
Predicted Molecular Mass
25 kDa
Jeon-soo shin et al., 2014 Yonsei Med J
(1-79) : DNA Binding
(89-162) : DNA Binding
NH2
A box
B box
Acidic tail
COOH
1
79
89
162
186
215
Nuclear HMGB1
DNA binding activity
DNA chaperone
DNA bending activity
• Nucleosome stability and sliding
• Nucleosome number
• Nucleosome release
• Genome chromatinization
• V(D)J recombination
• DNA replication
• DNA repair
• Telomere and telomerase
• Gene transcription
• Gene transfer
• Gene delivery
Extracellular HMGB1
Cytokine activity
DAMP
Chemokine activity
• Cell differentiation
• Inflammation and immune response
• Cell migration
• Tissue regeneration
• Angiogenesis
• Bacterial killing
• Proliferation and cell death
• Cellular senescence
• microRNA biogenesis
• Efferocytosis
• Neurotransmitters
Molecular Aspects of Medicine 40 (2014) 1–116

HMGB1 enhanced the proliferation of cultured human DPCs as determined by MTT assay

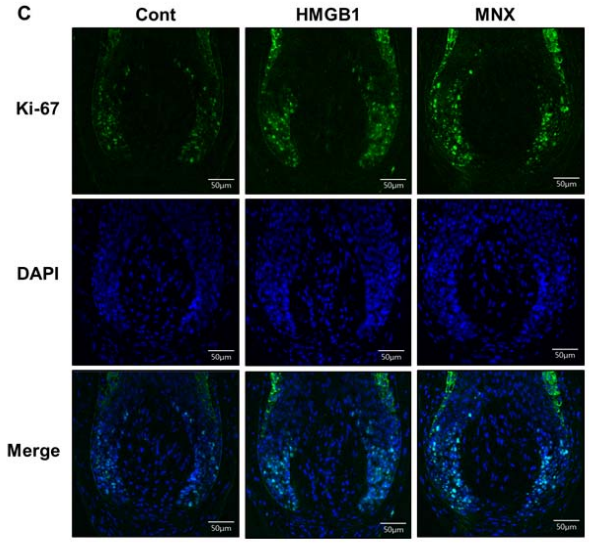


HMGB1 stimulates hair shaft elongation in organ culture model

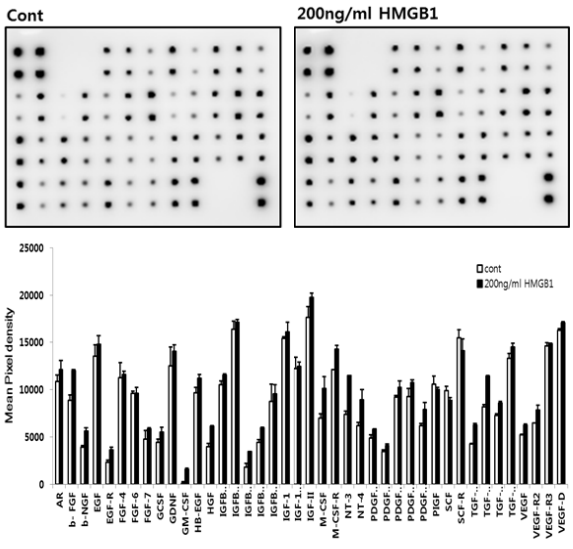




Increased Ki-67 cells in matrix after HMGB1 treatment



Mechanism study: Growth factor array

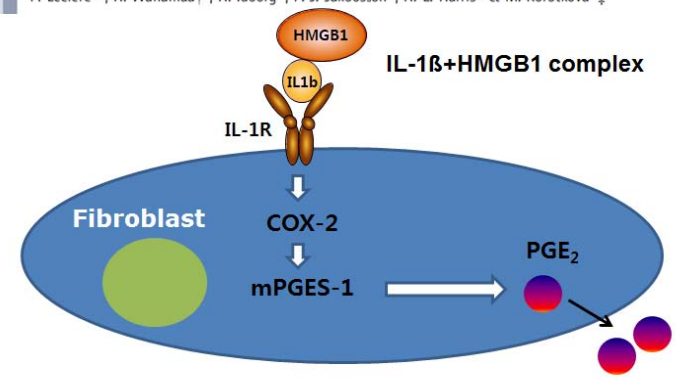


HMGB1 – PGE2 association in DPCs?

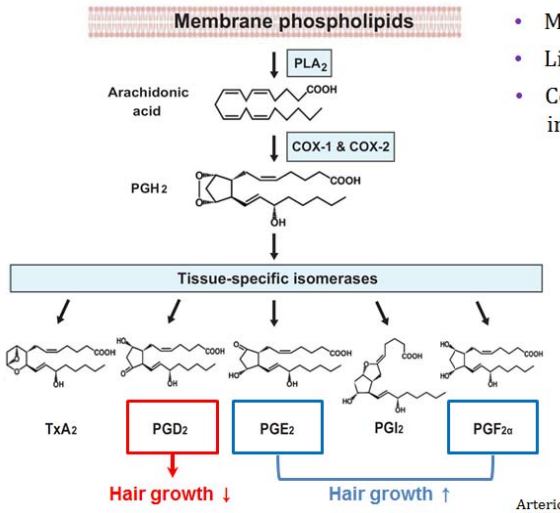
EXPERIMENTAL IMMUNOLOGY doi: 10.1111/sji.12041

IL-1β/HMGB1 Complexes Promote The PGE_2 Biosynthesis Pathway in Synovial Fibroblasts

P. Leclerc*[1], H. Wähämaa†[1], H. Idborg*, P. J. Jakobsson*, H. E. Harris* & M. Korotkova*‡



Prostaglandins (PGs)

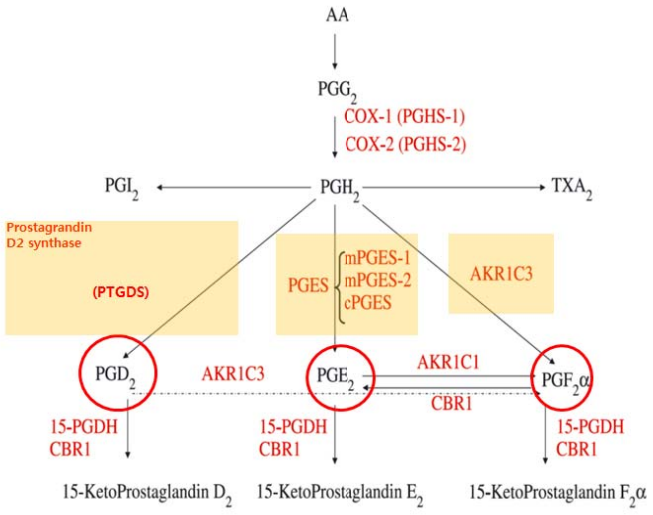


- Members of eicosanoid family
- Lipid signaling molecules
- Contains 20 carbon atoms, including a 5-carbon ring

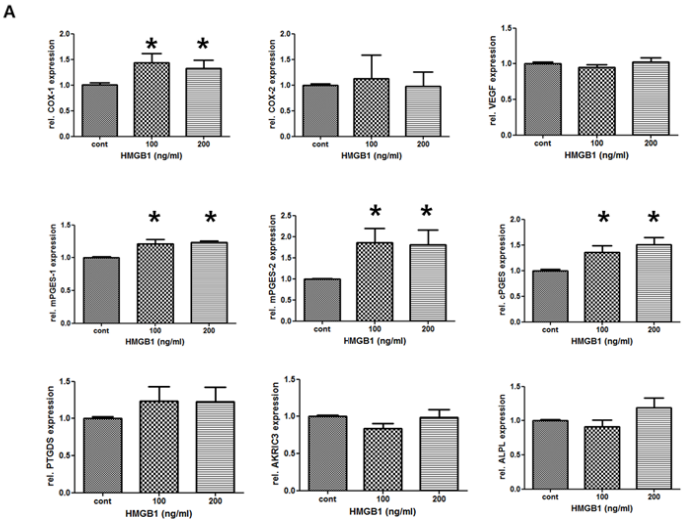
Phospholipases A_2 (PLA_2)
cyclooxygenase (COX)
thromboxane A_2 (TxA_2)
arachidonic acid (AA),
prostaglandin E_2 (PGE_2),
prostacyclin (PGI_2),
prostaglandin D_2 (PGD_2)
prostaglandin F_2 (PGF_2)

Arterioscler Thromb Vasc Biol. 2011 May;31(5):986-1000
J Invest Dermatol. 2013 Apr;133(4):881-9
Sci Transl Med. 2012 Mar 21;4(126):126-34

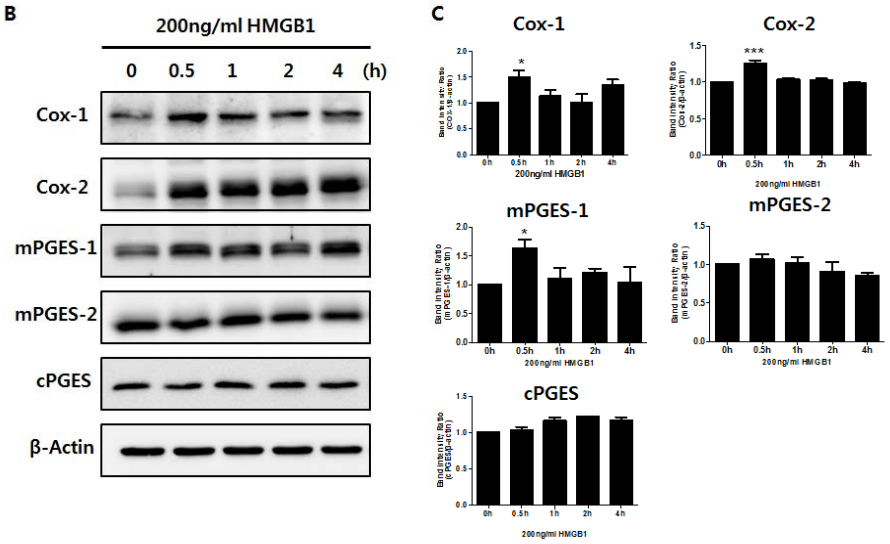
Prostaglandins (PGs)



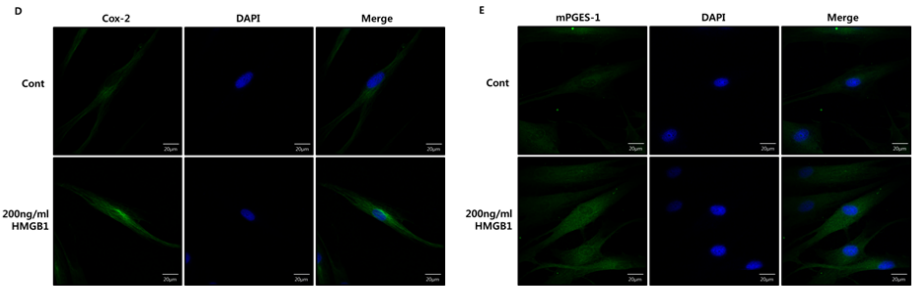
HMGB1 increases prostaglandin E synthases transcription



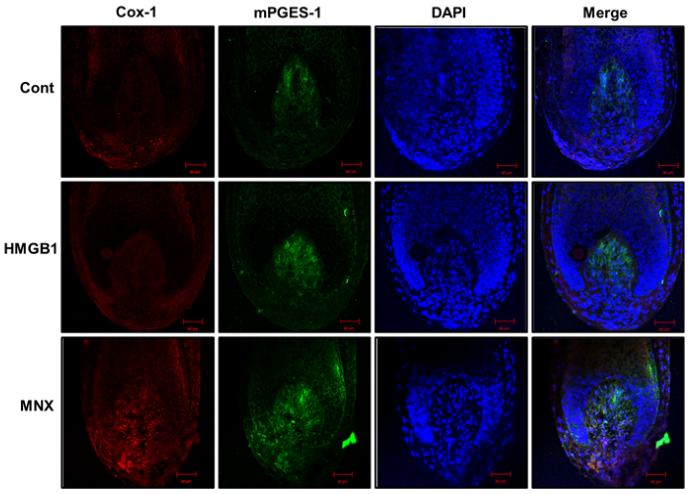
HMGB1 increases prostaglandin E synthases (WB)



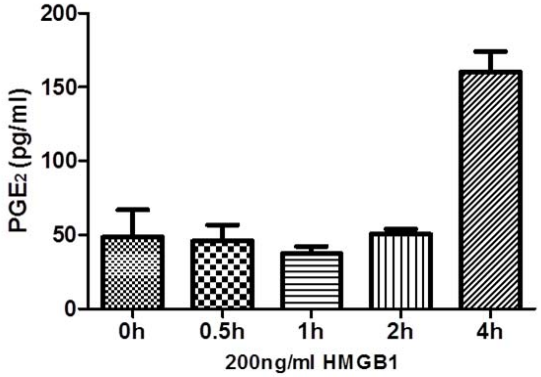
HMGB1 increases COX and mPGES-1 expression (in DPCs)



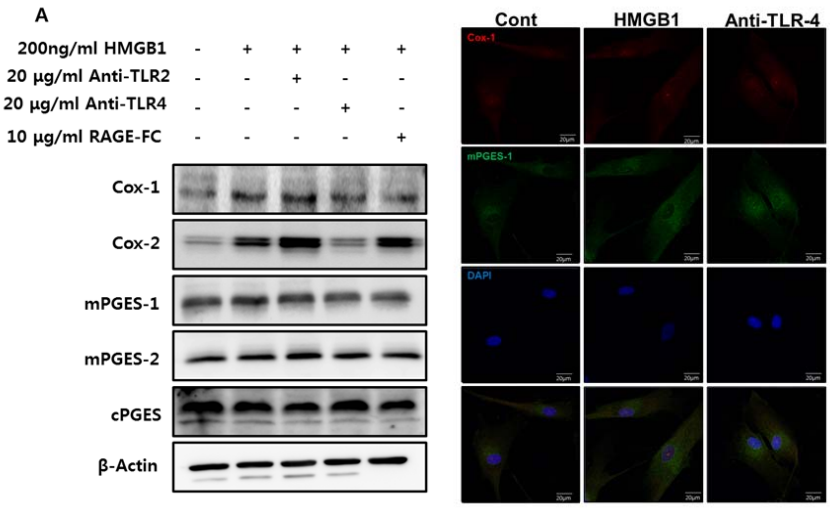
HMGB1 increases mPGES-1 expression (in DP, organ culture model)



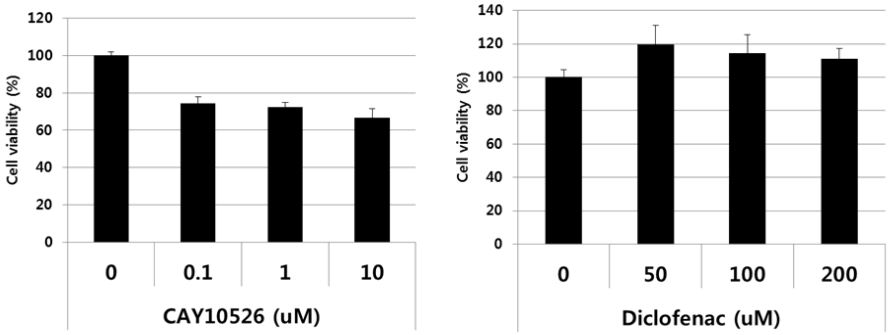
HMGB1 treated DPCs produce PGE2

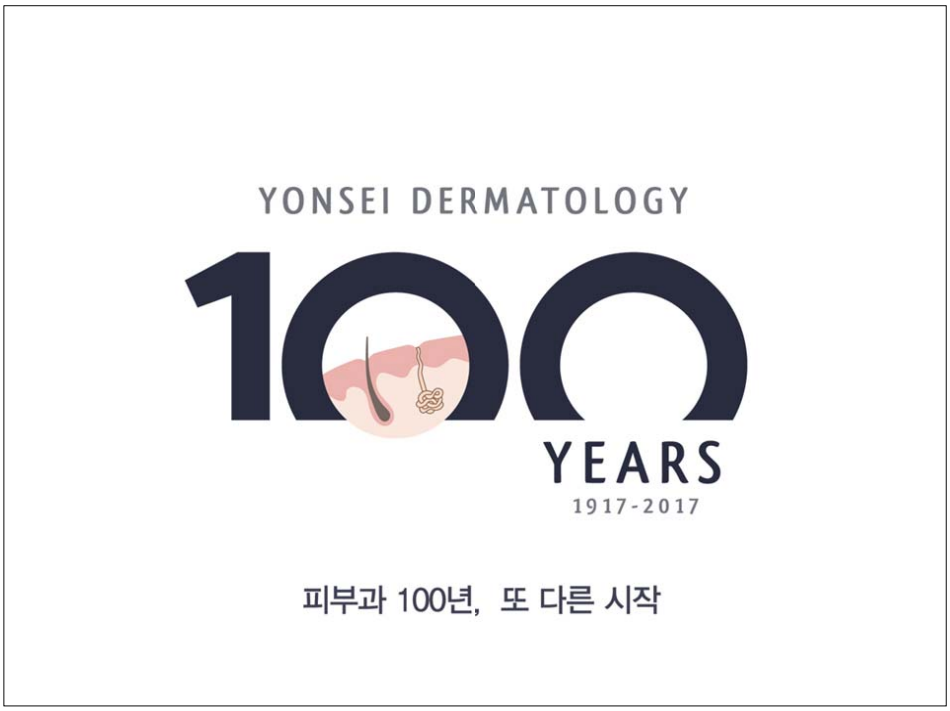


Possible action receptor for HMGB1 in DPC: TLR4?



Further study 1. PG inhibitors?




YONSEI DERMATOLOGY
100
YEARS
1917-2017
피부과 100년, 또 다른 시작

Investigation on the role of PDGF-AA / PDGFR-α in human hair growth and regeneration

Hyun-sik Jeong, Moon Kyu Kim, Jung Chul Kim, Young Kwan Sung

Department of Immunology & Hair Research Center, School of Medicine,
Kyungpook National University

Investigation on the role of PDGF-AA / PDGFR-α in human hair growth and regeneration

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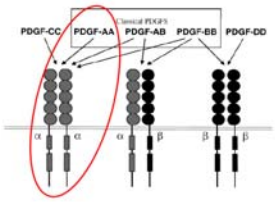
School of Medicine
Kyungpook National University

1. Introduction & Background

- PDGF(Platelet-derived growth factor)
  - One of numerous growth factors, or proteins that regulate cell growth and division
  - All PDGFs are operate as secreted form
  - play a role in blood vessel formation(angiogenesis)
- Five isoform of PDGF ligands
  - PDGF-AA, PDGF-AB, PDGF-BB, PDGF-CC, PDGF-DD
- Three different receptors
  - PDGFR-α, PDGFR-β, (PDGFR- αβ)

Types of PDGF ligands and receptors



Betsholtz et al. Bioassay(2001)

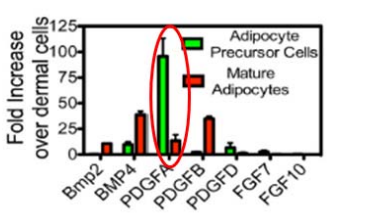
1. Introduction & Background

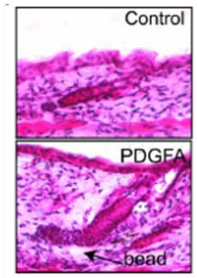
NIH Public Access
Author Manuscript
Published in final edited form as:
Cell. 2011 September 2; 146(5): 761–771. doi:10.1016/j.cell.2011.07.019.

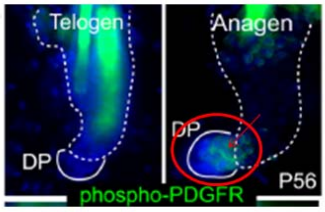
Adipocyte lineage cells contribute to the skin stem cell niche to drive hair cycling

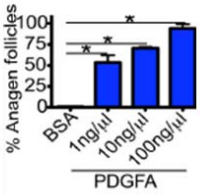
Eric Festa[1], Jackie Fretz[2], Ryan Berry[3], Barbara Schmidt[2], Matthew Rodeheffer[1,3,4], Mark Horowitz[2], and Valerie Horsley[1,4]

1. Introduction & Background









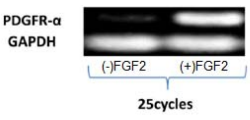
Festa et al. Cell(2011)

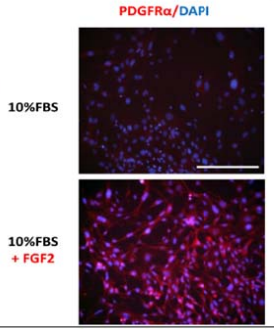
1. Introduction & Background

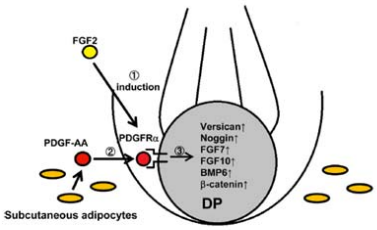
Contents lists available at ScienceDirect
Journal of Dermatological Science
journal homepage: www.jdsjournal.com

Synergistic effect of PDGF and FGF2 for cell proliferation and hair inductive activity in murine vibrissal dermal papilla in vitro

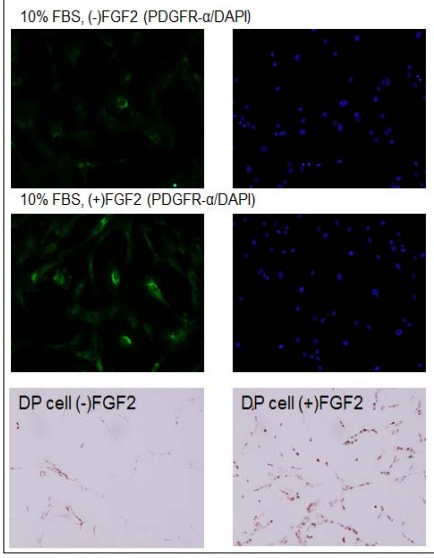
Masahiro Kiso [b], Tatsuo S. Hamazaki [a], Munenari Itoh [b], Sota Kikuchi [b], Hidemi Nakagawa [b], Hitoshi Okochi [a,*]
[a] Department of Regenerative Medicine, Research Institute, National Center for Global Health and Medicine, Japan
[b] Department of Dermatology, The Jikei University School of Medicine, Japan







2. PDGF-AA/PDGFR-α & DP cell proliferation in human HFs



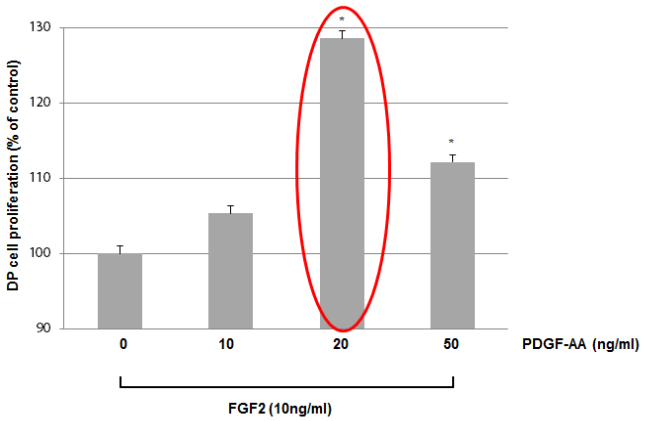
Human DP cell(P1)

Expression of PDGFR-α in RNA level(Real-time PCR)

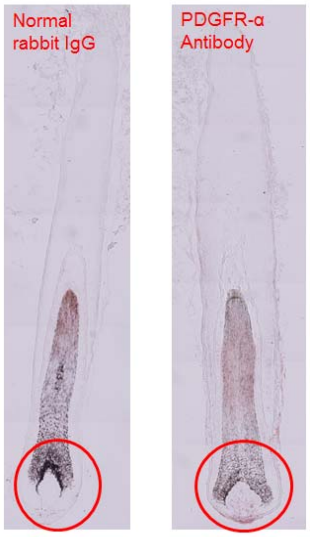
FGF2(-)	1
FGF2 10ng/ml	8.83117
FGF2 20ng/ml	7.24473
FGF2 50ng/ml	4.15108

2. PDGF-AA/PDGFR-α & DP cell proliferation in human HFs

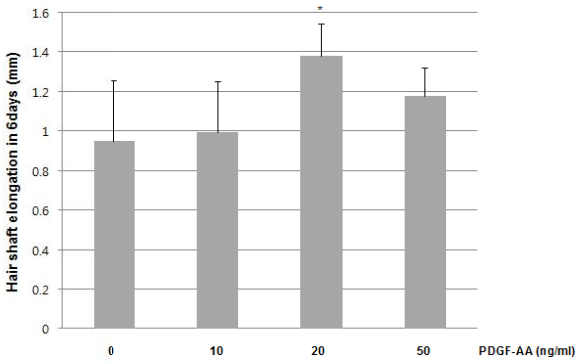
MTT assay



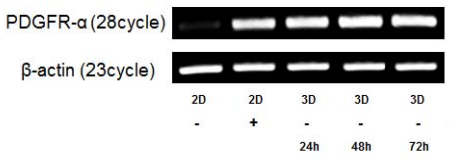
3. PDGF-AA/PDGFR-α & Hair growth in human HFs



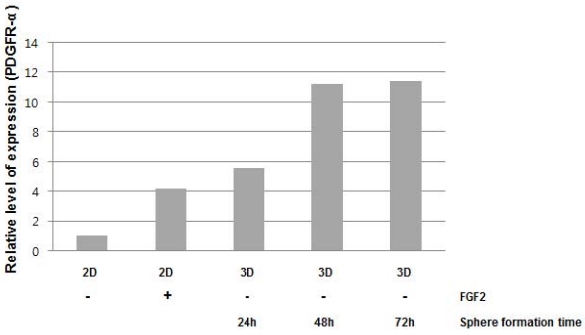
<Hair follicle organ culture>



4. PDGFR-α expression in human DP spheres

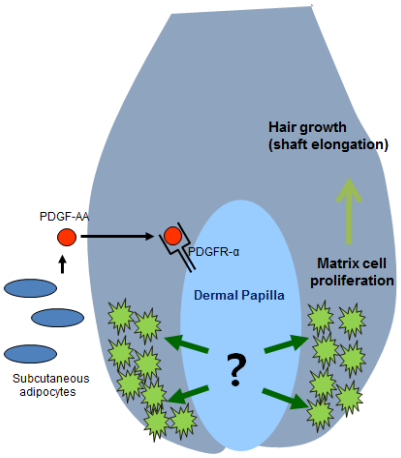


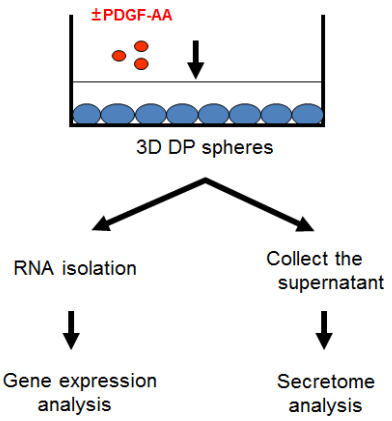
Real time PCR



Study plan

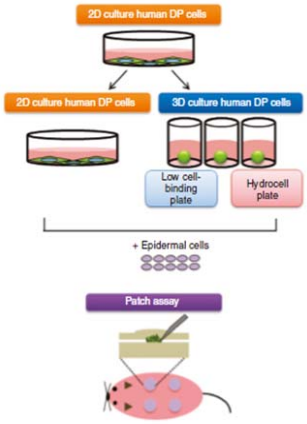
Search for PDGF-AA / PDGFR-α downstream targets using human DP spheres
(to identify genes responsible for hair growth)



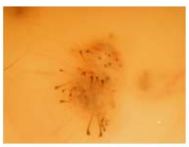


Study plan

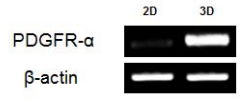
Investigate the role of PDGF-AA / PDGFR-α in hair regeneration

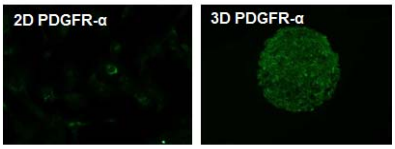


Mouse newborn epidermal cell
+ 2D cultured human DP cell



Mouse newborn epidermal cell
+ 3D human DP sphere

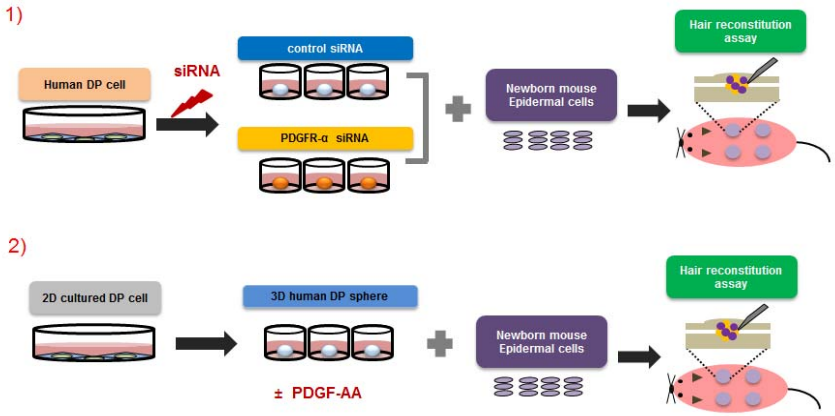




Kang et al. Journal of Investigative Dermatology (2012)

Study plan

Investigate the role of PDGF-AA / PDGFR-α in hair regeneration



Acknowledgement

- 경북의대 면역학교실

  - 지도교수 : 성 영 관

  - 박사 : 곽 미 희, 박 순 선

  - 대학원생 : 서 창 훈, 강 유 리, 김 민 규, 정 명 수, 지 상 호

- 경북대학교병원 모발센터
  - 교수 : 김 정 철, 김 문 규

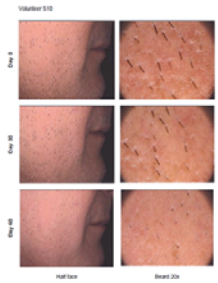
- **BK21 플러스_ KNU 의생명융복합 창의인재양성 사업단**
  (BK21 PLUS KNU Biomedical Convergence Program for Creative Talent)

Research trend of hair care cosmetics

Eunsun Jung

BioSpectrum Life Science Institute, 18FL, U-Tower, 767, Shinsu-ro, Dongchun-dong, Suji-gu, Yongin City, Gyeonggi Do, Republic of Korea

Hair care Cosmetics



식약처 기능성법

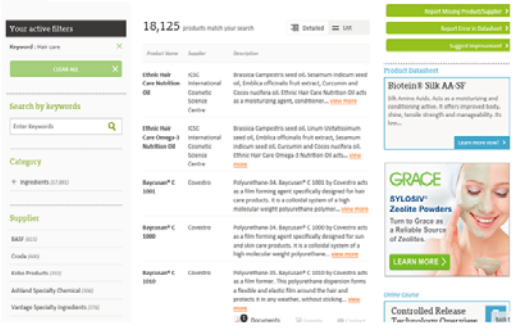
탈모방지 및 모발굵기 증가에서 탈모증상의 완화 보조로 변경

Ingredient for Hair care Cosmetics

Total : 32035

Hair care : 18,125

Anti-aging : 6,397



Claims of Hair care Cosmetic

BIOSPECTRUM

- **Natural Hair Growth Promoter :** Ginseng, Procyanidin B2, Centella asiatica, Caffeine
- **The Hair Loss Prevention**: Niacinamide, Thyme, the fruit of Corn Gluten and Vitamins B5 and B6
- **Seboreductyl :** inhibits the 5α-reductase enzyme, vitamin B groups(Pyridoxine, niacinamide, Niacinamide, Panthenol
- **FolliStem™ :** supports human hair follicle proliferation and growth,
- **Vital Hair and Scalp Complex :** anti-inflammatory/anti-oxidant, protective, smoothing and penetrating properties, Betaine, Hexapeptide-11, Hexylene glycol
- **Glycoenergizer Hair :** Acts as hair strengthening, anti-hair loss and anti-aging active
- **Thin and Dull Hair :**flowering top of Wild Thyme and the fruit of Olive Tree
- **Hair volume** : Polyurethane-34, hydroglycolic extract

Hair growth regulation

BIOSPECTRUM

RESEARCH ARTICLE

CLINICAL MEDICINE

Pharmacologic inhibition of JAK-STAT signaling promotes hair growth

Sivan Harel,[1] Claire A. Higgins,[1]* Jane E. Cerise,[1] Zhenpeng Dai,[1] James C. Chen,[1,2] Raphael Clynes,[1] Angela M. Christiano[1,2]*

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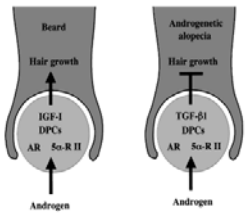
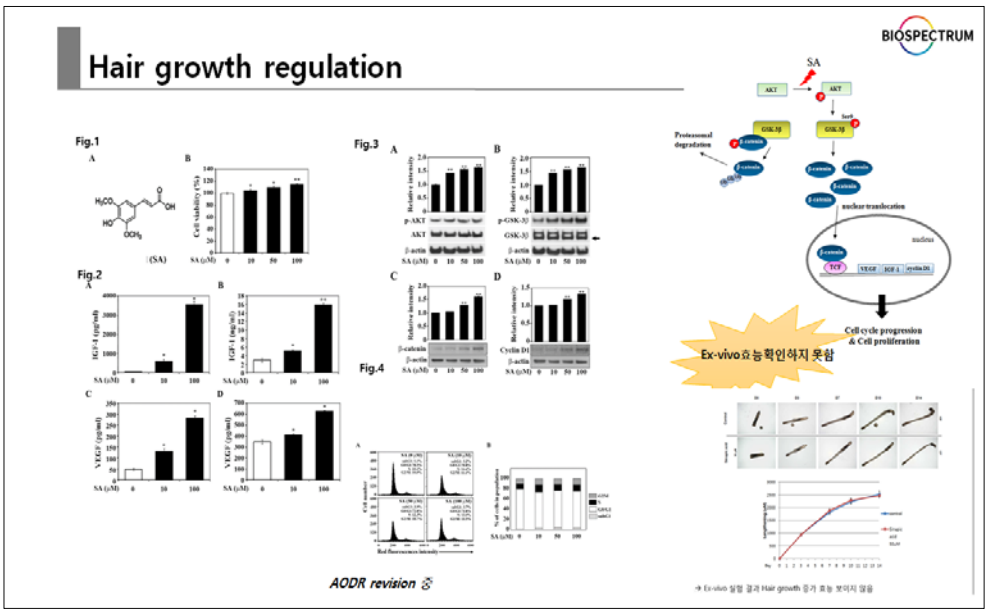
10.1126/sciadv.1500973

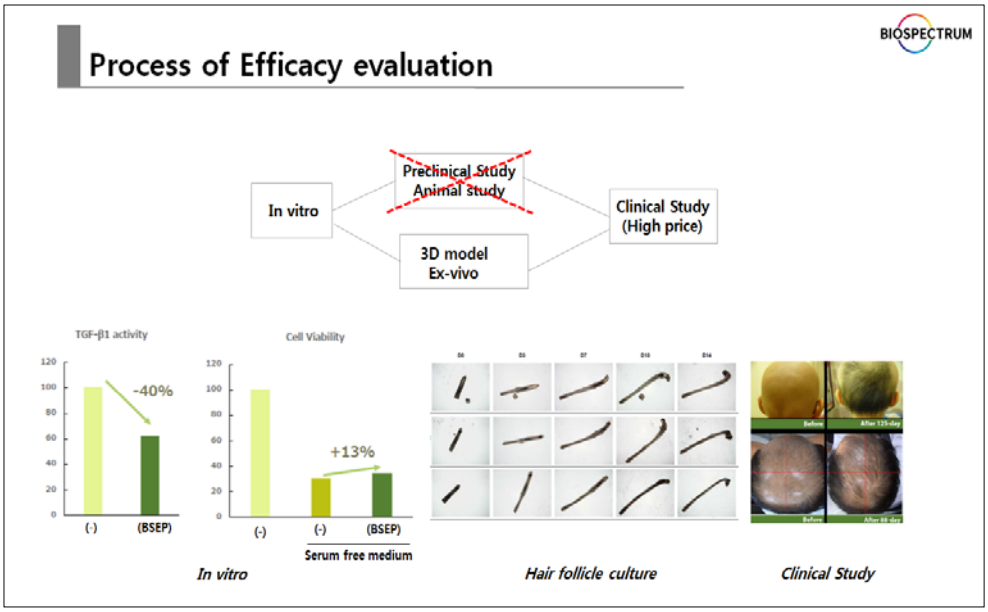
Several forms of hair loss in humans are characterized by the inability of hair follicles to enter the growth phase (anagen) of the hair cycle after being arrested in the resting phase (telogen). Current pharmacologic therapies have been largely unsuccessful in targeting pathways that can be selectively modulated to induce entry into anagen. We show that topical treatment of mouse and human skin with small-molecule inhibitors of the Janus kinase (JAK)–signal transducer and activator of transcription (STAT) pathway results in rapid onset of anagen and subsequent hair growth. We show that JAK inhibition regulates the activation of key hair follicle populations such as the hair germ and improves the inductivity of cultured human dermal papilla cells by controlling a molecular signature enriched in intact, fully inductive dermal papillae. Our findings open new avenues for exploration of JAK-STAT inhibition for promotion of hair growth and highlight the role of this pathway in regulating the activation of hair follicle stem cells.



Stimulators	Inhibitors
bFGF7(adenosine), BMP, PDGF, IGFBP (retinoid, glucortcoids), KGF, Substance P (chill pepper, capsaicin) 1,25 - dihydroxyvitamin D3(낮은농도), JAK-STAT signaling pathway, WNT ,	TGF-beta, IL-1 alpha, FGF5, EGF, Parathyroid hormone, 1,25 - dihydroxyvitamin D3 (높은농도), TRPV1, Neprilysin

*In vitro*에서 알려진 다양한 signal을 시도할 수 있으나 Ex-vivo/ animal study / 임상시험과의 연계 연구 필요


BIOSPECTRUM
Hair growth regulation
Fig.1
Fig.2
Fig.3
Fig.4
SA
Ex-vivo효능확인하지 못함
AODR revision &

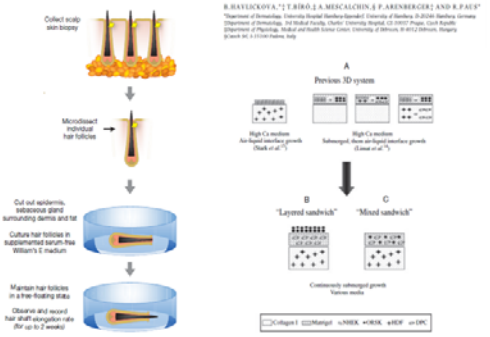

BIOSPECTRUM
Process of Efficacy evaluation
In vitro
Preclinical Study
Animal Study
3D model
Ex-vivo
Clinical Study
(High price)
TGF-β1 activity
-40%
(-)
(BSEP)
Cell Viability
+13%
(-)
(-)
(BSEP)
Serum free medium
In vitro
Hair follicle culture
Clinical Study

Hair 연구_3D culture

BIOSPECTRUM

Cutaneous Biology

Towards optimization of an organotypic assay system that imitates human hair follicle-like epithelial–mesenchymal interactions



Ji Won Oh et al., JID, (2013), Volume 133, 1-4

Sphere Formation Increases the Ability of Cultured Human Dermal Papilla Cells to Induce Hair Follicles from Mouse Epidermal Cells in a Reconstitution Assay

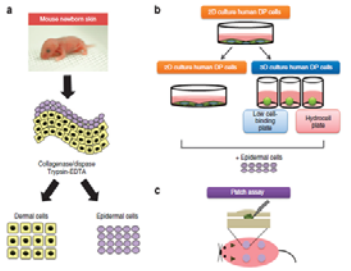
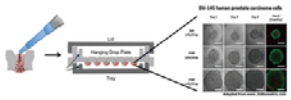


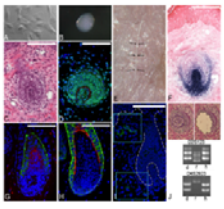
Figure 1. Diagram of experiments conducted in this study. Mouse dermal and epidermal cells were freshly isolated from C57BL/6 mouse neonates (P0-P1) and were used for control experiments (a). Human dermal papilla (DP) spheres were prepared from two-dimensional (2D) cultured DP cells by using either low cell-binding plate or hydrocell plate and combined with freshly isolated mouse epidermal cells for implantation (b). Scheme of patch assay (c).

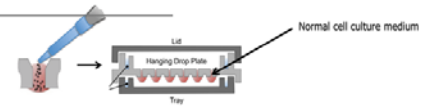
Hair 연구_3D culture

BIOSPECTRUM

Microenvironmental reprogramming by three-dimensional culture enables dermal papilla cells to induce de novo human hair-follicle growth





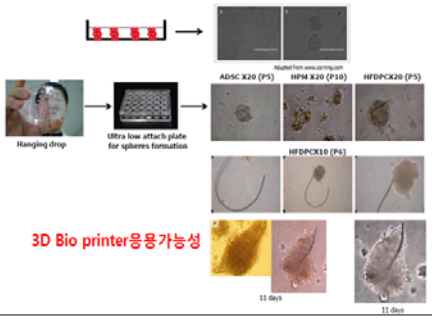


-> HF, ADSC, melanocyte (5x10⁵cells/ml) with each 20ul /one drop and adherent cell culture with same cell numbers

-> 3-6 days culture (3days in this time)

-> collect all spheres and then transfer into Ultra-low attachment plate

-> culture spheres in Ultra-low attachment plate until adherent cells are arrested
(4 days more culture in low-attachment plate)



3D Bio printer응용가능성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Heartfelt GREEN satisfaction to customers
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BIOSPECTRUM

Skin equivalent formation with hair follicular structure

Paik SH, Choi SJ, Jo SJ, Kim KH, Kwon O

Department of Dermatology, Seoul National University College of Medicine, Seoul, Republic of Korea
Institute of Human-Environment Interface Biology, Seoul National University, Seoul, Republic of Korea.

Skin equivalent formation
with hair follicular structure

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National University, Seoul, Republic of Korea.

BRUSSELS BUREAU 3 years ago

EU extends ban on animal-tested cosmetics

last updated: 11/03/2013

Euronews

Aa Aa

A full ban on cosmetics that have been tested on animals entered into force across the EU on Monday.

The ban, announced by the European Commission, extends previous restrictions and now outlaws the sale of products tested on animals outside Europe.

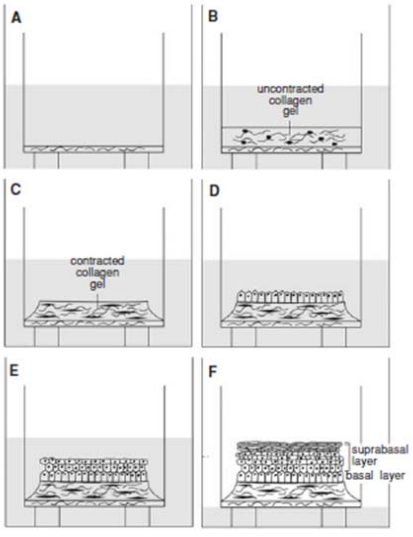
Firms had gotten around an earlier ban by having tests carried out outside the EU, and therefore out of regulators' reach.

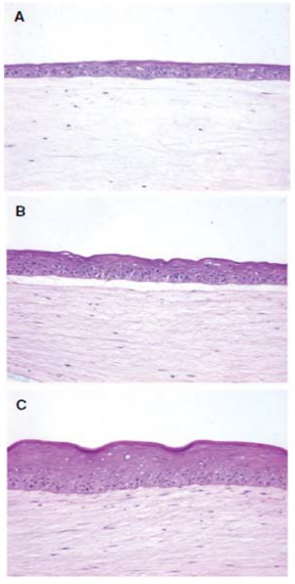
The EU banned animal testing of finished cosmetic products since 2004.

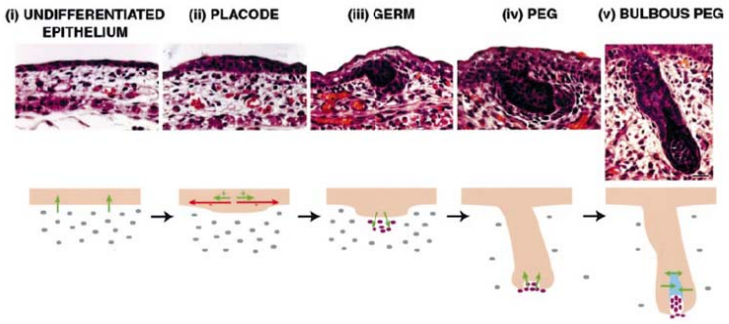
The ban on cosmetics containing animal-tested ingredients was first agreed in 2009.

Yet many loopholes remained in place after intensive lobbying by the cosmetics industry.

However, products that use ingredients tested on animals before the ban can remain on the shelves.

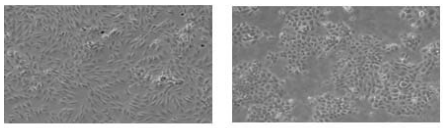




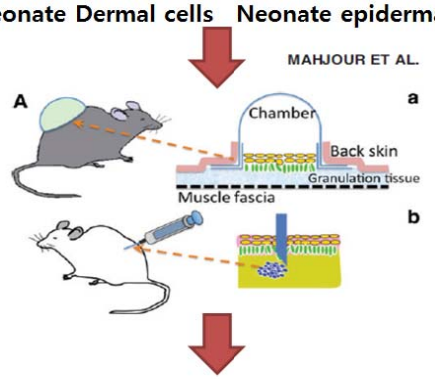


Ectoderm → Epithelial cell ↔ Dermal papilla cell ← Mesoderm

neonate mouse

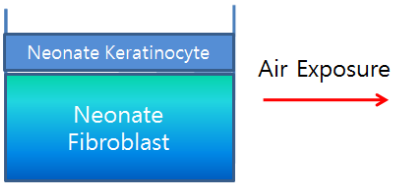


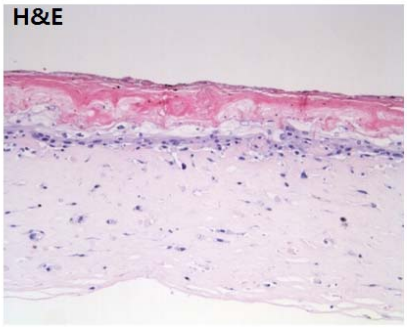
Neonate Dermal cells Neonate epidermal cells

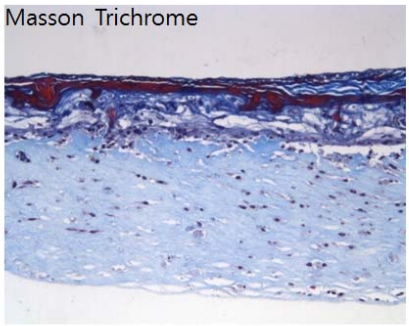


Hair follicle formation *in vivo*

3D equivalent 3- Control CMI15-6494







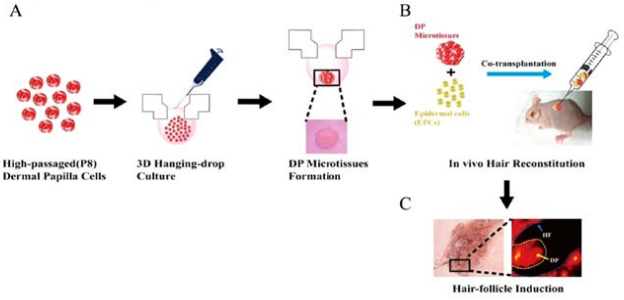
ACS APPLIED MATERIALS & INTERFACES — Research Article — www.acsami.org

Surface Tension Guided Hanging-Drop: Producing Controllable 3D Spheroid of High-Passaged Human Dermal Papilla Cells and Forming Inductive Microtissues for Hair-Follicle Regeneration

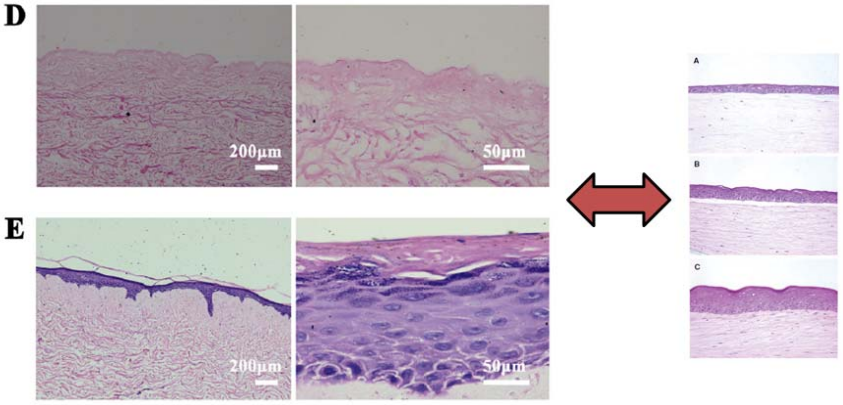
Bojie Lin,[†,‡,§] Yong Miao,[†] Jin Wang,[†] Zhexiang Fan,[†] Lijuan Du,[†] Yongsheng Su,[†] Bingcheng Liu,[†] Zhiqi Hu,[*,†] and Malcolm Xing[*,‡,§]

ACS Applied Materials & Interfaces — Research Article

Scheme 1. Formation of High-Passaged (P8) DP Microtissues Based on Surface Tension Fabrication Technique and Their Further Application for Hair-Follicle Induction[a]



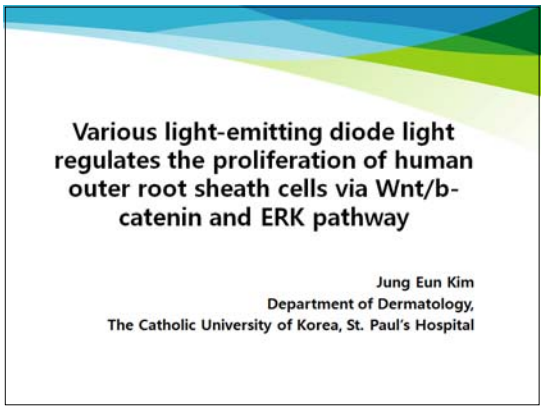
DED(Deepidermized dermis)



Various light-emitting diode light regulates the proliferation of human outer root sheath cells via Wnt/b-catenin and ERK pathway

Jung Eun Kim

Department of Dermatology, The Catholic University of Korea, St. Paul's Hospital



Introduction

- Human Outer Root Sheath Cells (hORSCs)
  - ORSCs play an essential role to support hair follicle.
  - ORSCs located in the bulge have several properties with the stem cells
- The effect of LED irradiation on ORSCs survival and growth promotion and it's mechanism is not well known.

Objectives

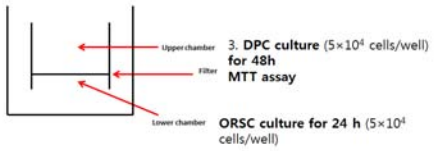
- We aimed to investigate the effects of LLLT irradiation on
  - cell viability and migration of hORSCs
  - ERK/MAPK signaling pathway in hORSCs
  - β-catenin/Wnt signaling pathway in ORSCs
  - hair stem cell markers in ORSCs
  - Cytokines and Growth factors in ORSCs
  - LED-irradiated ORSCs on the proliferation of DPCs

Methods

- **LED irradiations**
  - Wavelengths 415 nm, 525 nm 660nm and 830nm (1,3,5,10J)
- **Cell culture and cell proliferation assay**
  - hORSCs, passage 4-5, MTT assay
- **Real time-PCR**
  - Target genes : VEGF, IGF-1, β-Catenin, Wnt5a, Axin2, Lef1, Sox9, Bcl-2/Bax, FGF2, IFN receptor, IL-6, IL-18, TGFβ1, TGFβ2
- **Western blot assay**
  - ERK, AKT, JNK, p38, c-Jun and β-catenin antibodies
  - PD98059 (MAPK inhibitor) treatment for 1 h before LED irradiation

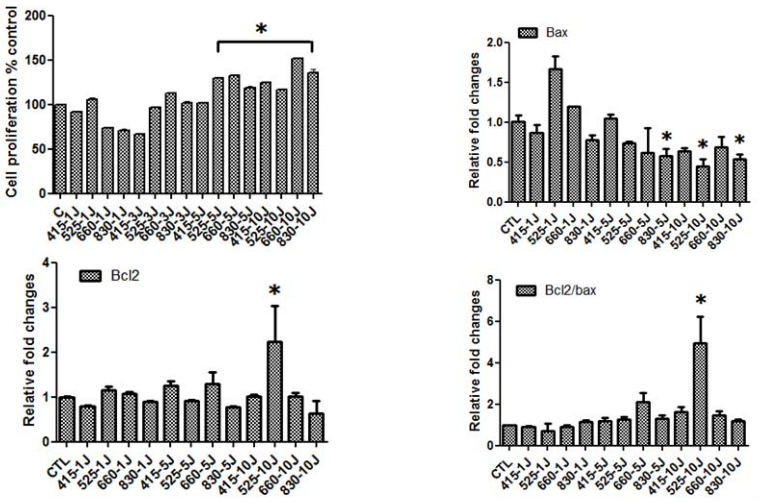
Methods

- **Migration assay**
  - Migration of hORSCs was measured in transwell plates (8 mm pore size). media was added to the lower chamber.
- **Co-culture with hORSCs and hDPCs**



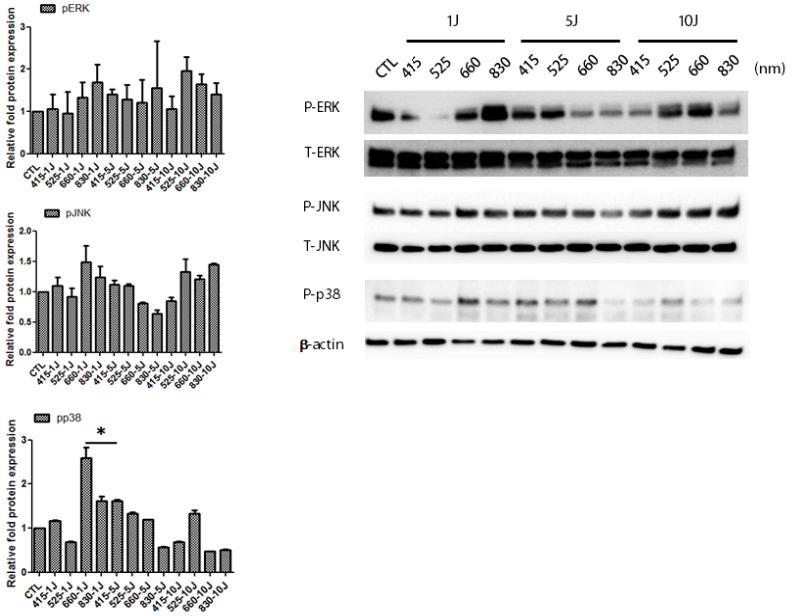
RESULTS

The effects of LED lights on the ORSC viability and apoptosis



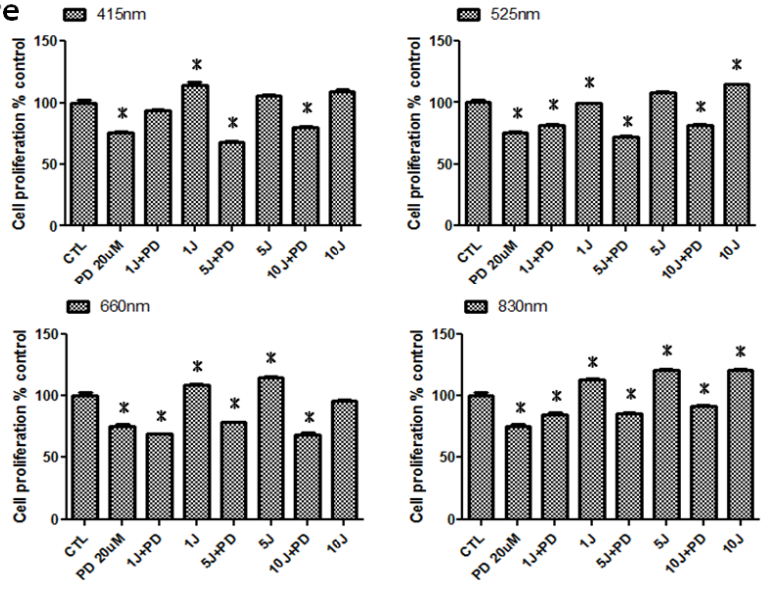
*p< 0.05

Changes in protein levels of ERK/MAPK signaling pathway



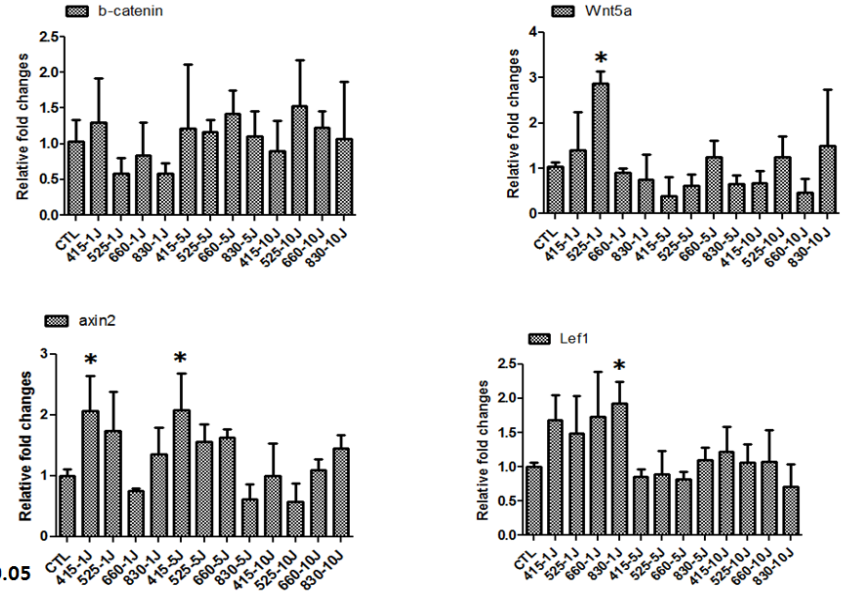
*p< 0.05

Changes in LED-induced ORSCs proliferation by pretreatment with ERK inhibitor(PD) before LED light exposure



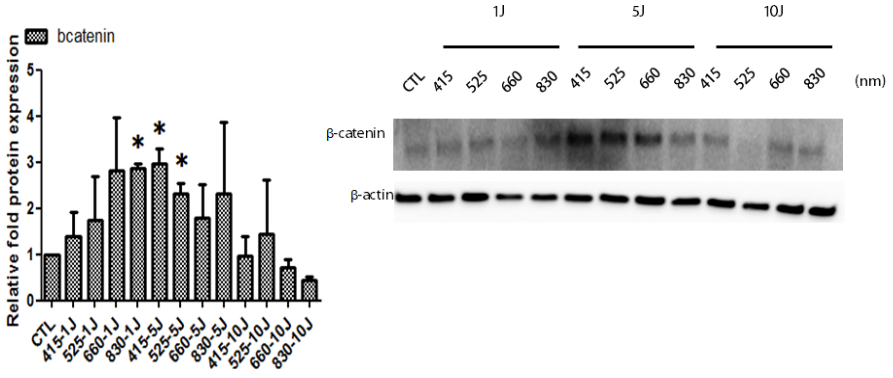
*: p< 0.05

The effects of LED irradiation on the β-catenin/Wnt signaling pathway mRNA expression

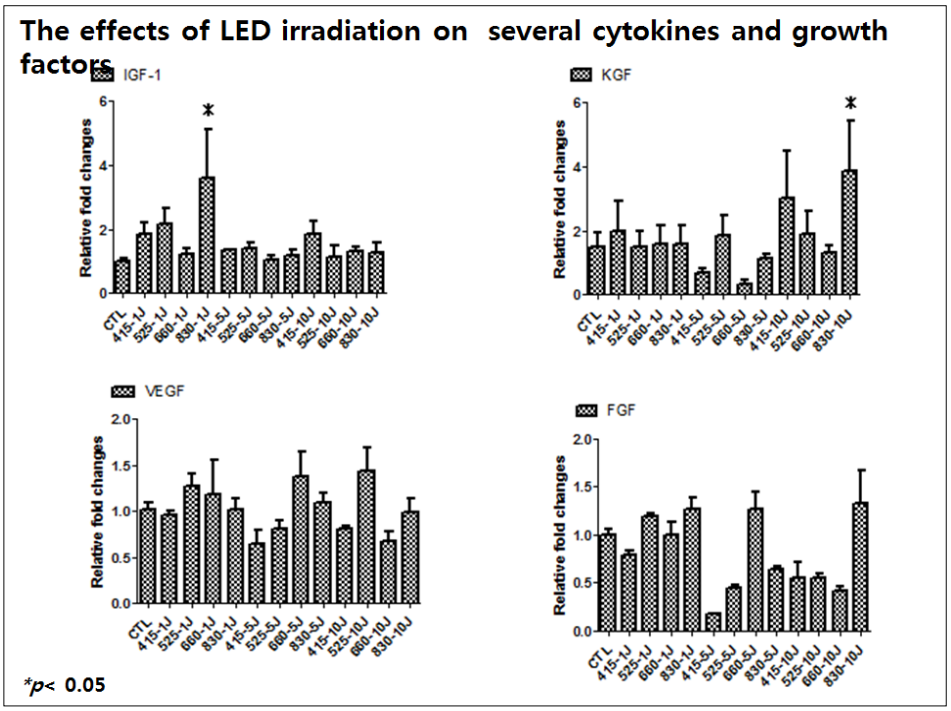


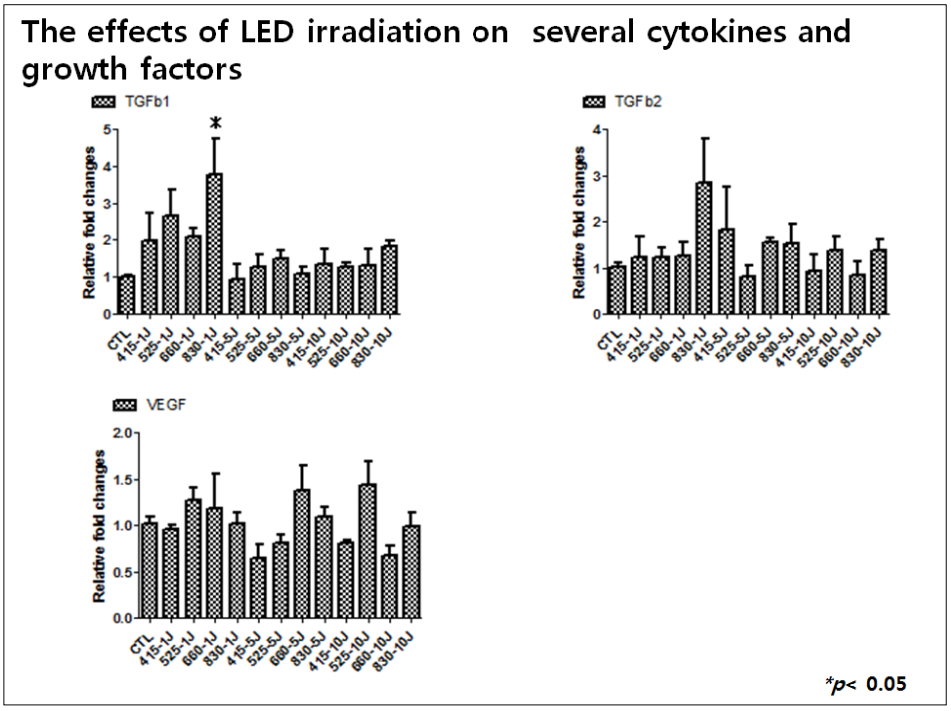
*: $p < 0.05$

The effects of LED irradiation on the β-catenin/Wnt signaling pathway

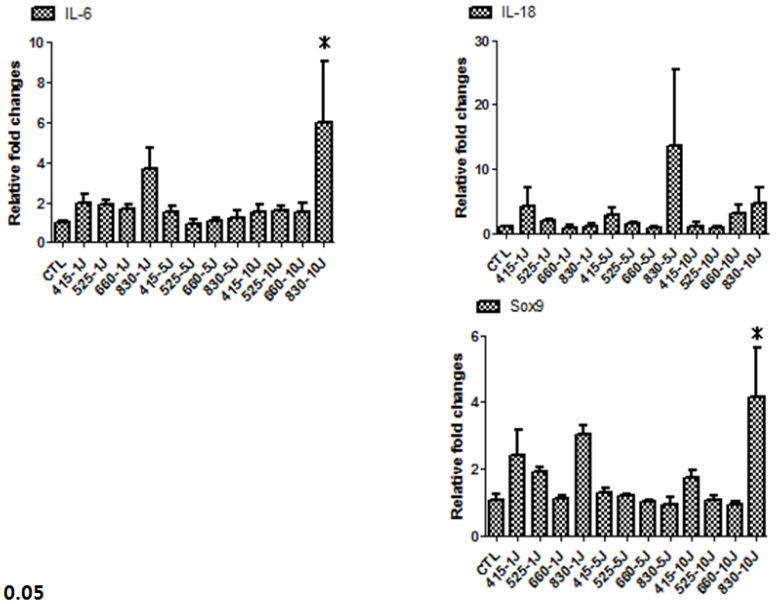


*$p < 0.05$


The effects of LED irradiation on several cytokines and growth factors
IGF-1
KGF
VEGF
FGF
Relative fold changes
CTL
415-1J
525-1J
660-1J
830-1J
415-5J
525-5J
660-5J
830-5J
415-10J
525-10J
660-10J
830-10J
*p< 0.05

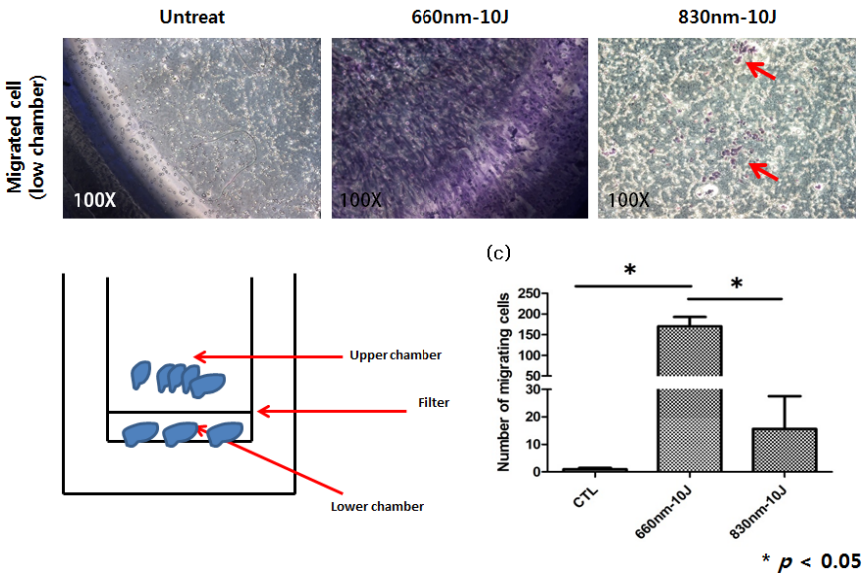

The effects of LED irradiation on several cytokines and growth factors
TGFb1
TGFb2
VEGF
Relative fold changes
CTL
415-1J
525-1J
660-1J
830-1J
415-5J
525-5J
660-5J
830-5J
415-10J
525-10J
660-10J
830-10J
*p< 0.05

The effects of LED irradiation on several cytokines and growth factors

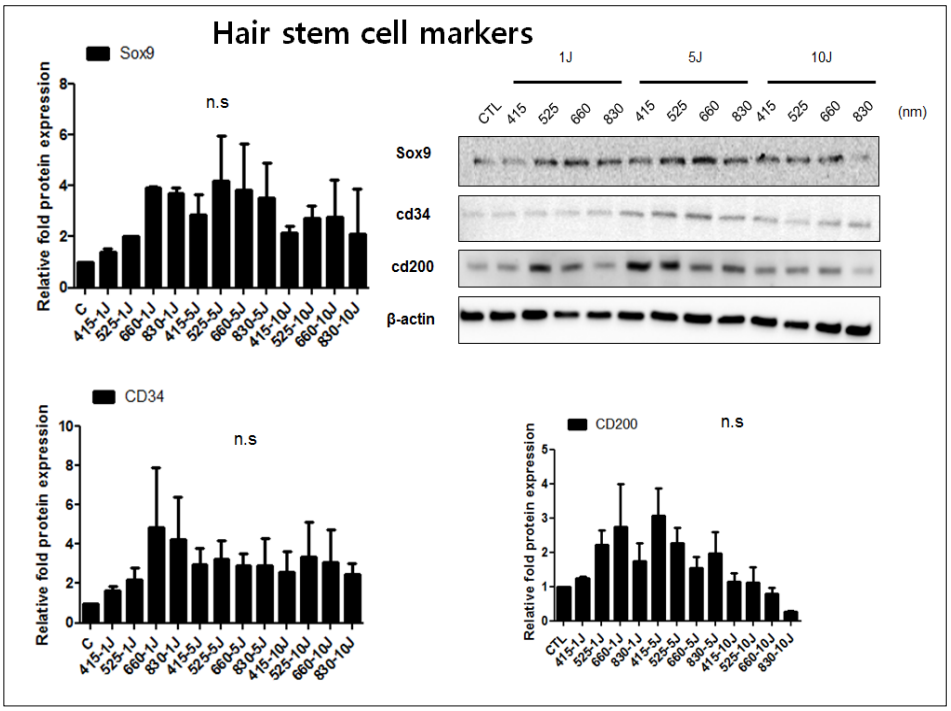


*p< 0.05

Effects of LED irradiation on hORSCs migration



* p < 0.05


Hair stem cell markers
Sox9
n.s
Relative fold protein expression
C
415-1J
525-1J
660-1J
830-1J
415-5J
525-5J
660-5J
830-5J
415-10J
525-10J
660-10J
830-10J
1J
5J
10J
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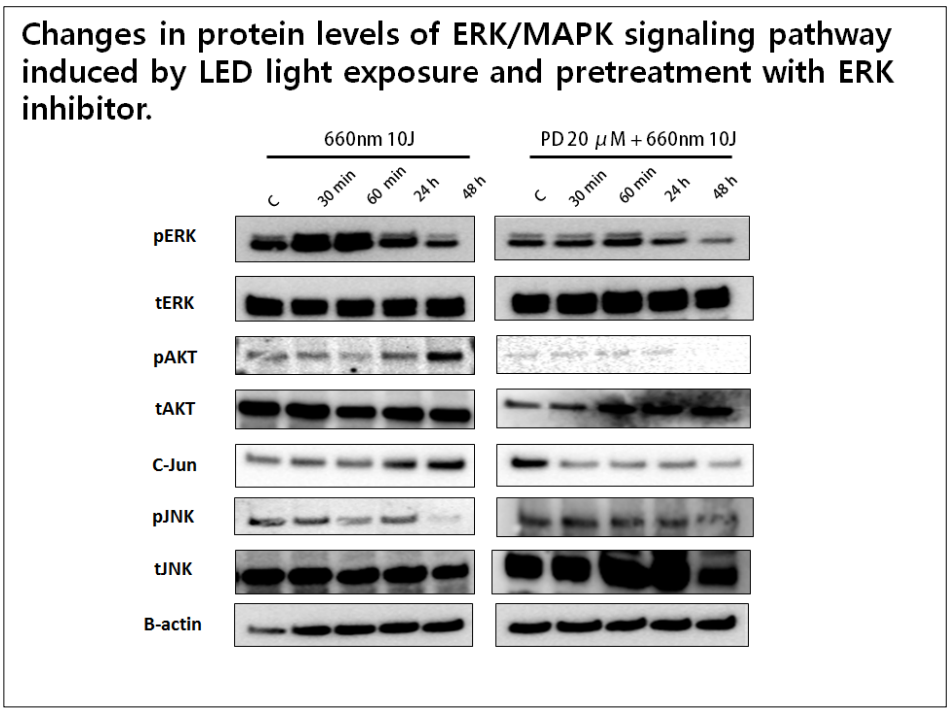
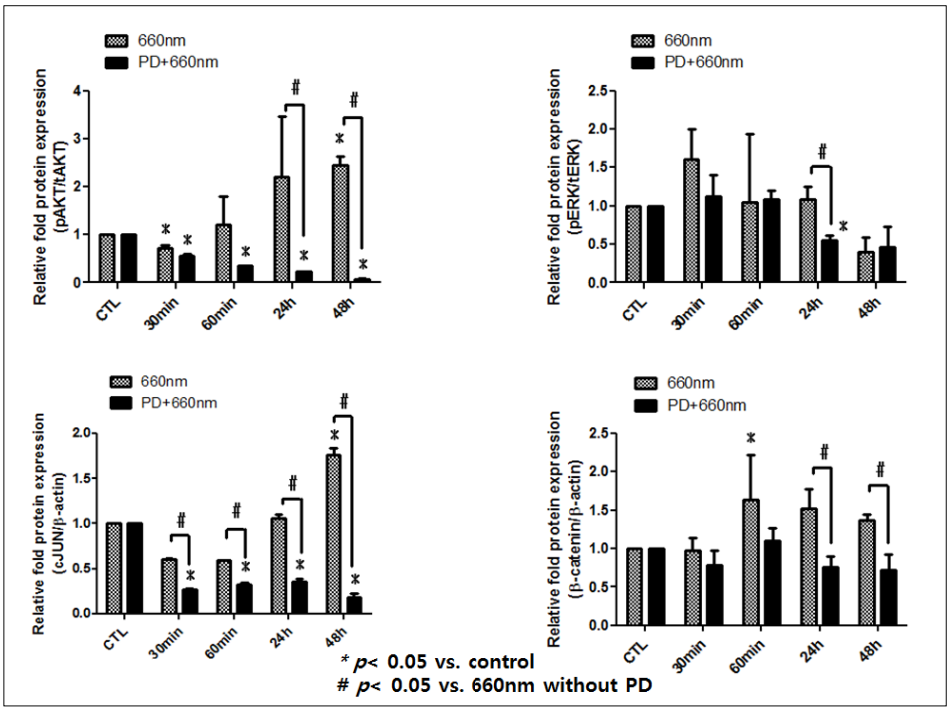
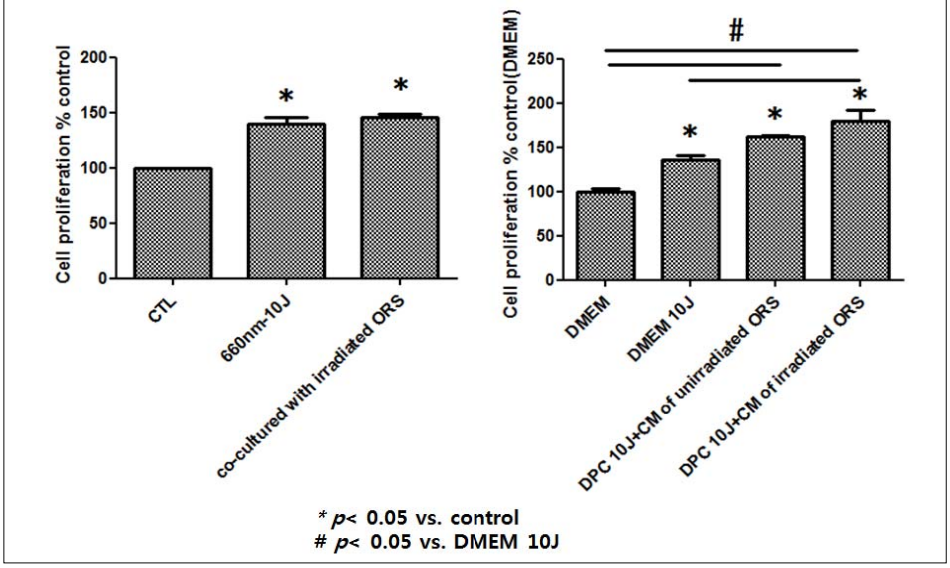
830
(nm)
Sox9
cd34
cd200
β-actin
CD34
n.s
CD200
n.s


Changes in protein levels of ERK/MAPK signaling pathway induced by LED light exposure and pretreatment with ERK inhibitor.
660nm 10J
PD 20 μM + 660nm 10J
C
30 min
60 min
24 h
48 h
pERK
tERK
pAKT
tAKT
C-Jun
pJNK
tJNK
B-actin

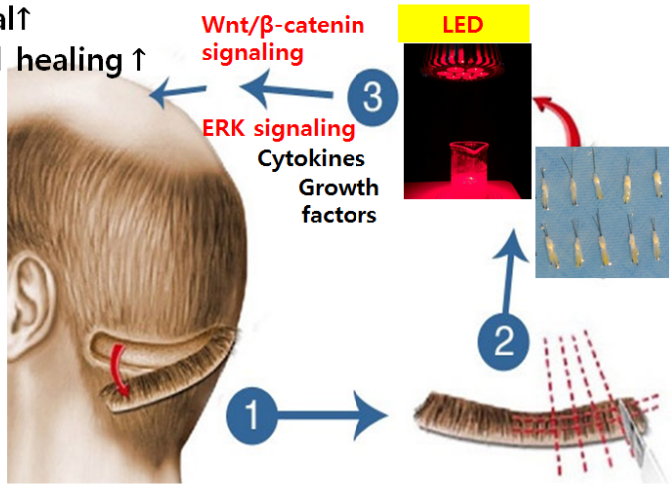


LED irradiation on ORSCs could stimulate DPC proliferation when ORSCs and DPCs are co-cultured.



Discussion

Trasplanted hair survival↑
wound healing ↑



Conclusion

- Our results emphasize the ORSC-growth promoting effect of LED irradiation appears to be associated with the direct stimulation of the Wnt/β-catenin signaling pathway as well as activating ERK signaling.

Efficacy of combination therapy with diphenylcyclopropenone and anthralin in the treatment of severe alopecia areata

Si Hyub Lee, Hee Seong Yoon, Seung Dohn Yeom, Hye Soo Ko, Ji Won Byun , Jeonghyun Shin, Gwang Seong Choi

Department of Dermatology, Inha University School of Medicine

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Department of Dermatology, Inha University School of Medicine

Background

- Treatment of alopecia totalis, alopecia universalis, and widespread multifocal patchy alopecia areata is very difficult.
- In chronic, treatment-refractory extensive alopecia areata (AA), topical immunotherapy with diphenylcyclopropenone (DPCP) is recommended.
- Previous study reported combination therapy with DPCP and anthralin was superior to DPCP alone in chronic extensive AA.

Background

Efficacy and safety of diphenylcyclopropenone alone or in combination with anthralin in the treatment of chronic extensive alopecia areata: A retrospective case series

Murat Durdu, MD,[a] Deren Özcan, MD,[b] Mete Baba, MD,[b] and Deniz Seçkin, MD[b]
Adana and Ankara, Turkey

Background: Some patients with chronic extensive alopecia areata (AA) may be refractory to topical immunotherapy. Combination therapy is recommended for such patients. Efficacy and safety of a combination therapy with diphenylcyclopropenone (DPCP) and anthralin in chronic extensive AA is unknown.

Objective: We sought to determine whether the combination therapy of DPCP and anthralin is superior to DPCP alone in chronic extensive AA.

Methods: We retrospectively analyzed the efficacy, side effects, and relapse rates of DPCP (alone or with anthralin) in chronic extensive AA.

Results: A total of 47 patients (22 were treated only with DPCP and 25 with DPCP and anthralin for at least 30 weeks) were evaluated. Complete hair regrowth was observed in 36.4% and 72% of the patients who received DPCP and combination therapy, respectively ($P = .03$). Hair regrowth duration was shorter with combination therapy ($P = .03$). Regrowth rates of the eyebrows, eyelashes, and beard in patients on combination therapy were higher than those in patients on DPCP ($P = .01$). Side effects such as folliculitis, hyperpigmentation, and staining of skin, hair, and clothes were more common in combination therapy group.

Limitations: The retrospective design and small number of patients are limitations.

Conclusion: Combination therapy with DPCP and anthralin is superior to DPCP alone in chronic extensive AA. (J Am Acad Dermatol 2015;72:640-50.)

Objective

- We sought to identify the efficacy of combination therapy with DPCP and anthralin in the treatment severe AA.

Methods

- **Retrospective case series of 10 patients with severe (>50% scalp hair loss) and/or treatment-resistant AA**

Demographic features	
Mean age, year (range)	19.3 (8-48)
Male / Female	5/5

Previous treatments, n (%)	
Topical corticosteroids	7 (70)
Intralesional injection	3 (30)
Topical minoxidil	2 (20)
Systemic corticosteroids	8 (80)
DPCP	3 (30)
Herb medicine	4 (40)

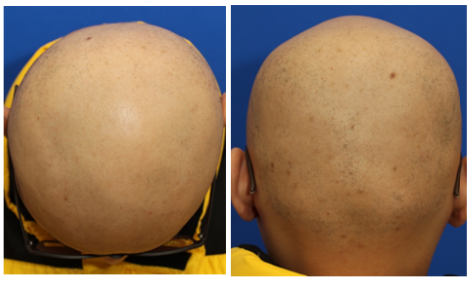
Subtypes, n (%)	
Multifocal patchy AA	3 (30)
Alopecia totalis	4 (40)
Alopecia universalis	3 (30)

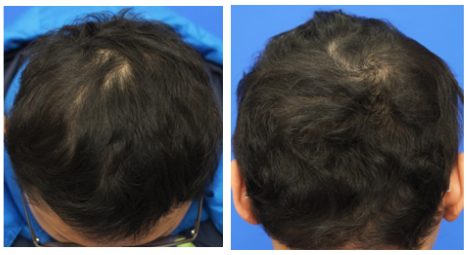
Scalp involvement, n (%)	
S1 (<25% hair loss)	-
S2 (26-50% hair loss)	-
S3 (51-75% hair loss)	2 (20)
S4 (76-99% hair loss)	6 (60)
S5 (100% hair loss)	2 (20)

Methods

	Sex/Age	Severity	SALT score	AA Type	DPCP before combination (months)	Combination with DPCP & Anthralin (month)
#1	F/8	S4 (76-99%)	85.8	AT	-	8 m
#2	M/18	S4 (76-99%)	87.2	AT	6 m	11 m
#3	M/18	S3 (51-75%)	57.6	patchy AA	17 m	11 m
#4	F/48	S4 (76-99%)	93.8	AT	2 m	10 m
#5	M/39	S4 (76-99%)	93.8	AT	-	6 m
#6	F/15	S4 (76-99%)	96.6	AU	2 m	3 m
#7	F/10	S5 (100%)	100	AU	-	6 m
#8	M/9	S5 (100%)	100	AU	-	10 m
#9	F/13	S3 (51-75%)	62	patchy AA	-	8 m
#10	M/15	S4 (76-99%)	84.8	patchy AA	-	6 m

#2 DPCP → DPCP + Anthralin





#2 (M/18)
S4 (76-99%)
SALT score 87.2

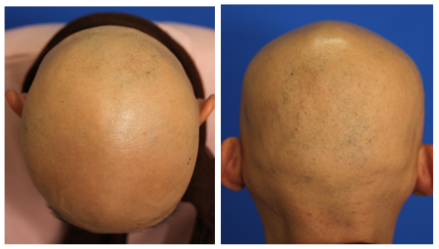
2015.02.~

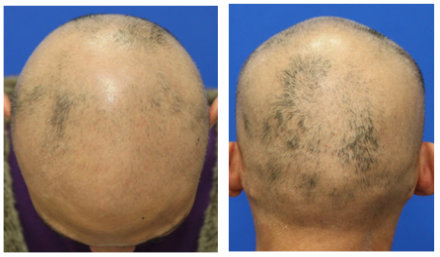
DPCP for 6 months
DPCP + Anthralin for 11 months

DPCP (0.25%)
Anthralin (0.2%)

Clinical response :
A4 (76-99%)

#5 DPCP + Anthralin





#5 (M/39)
S4 (76-99%)
SALT score 93.8

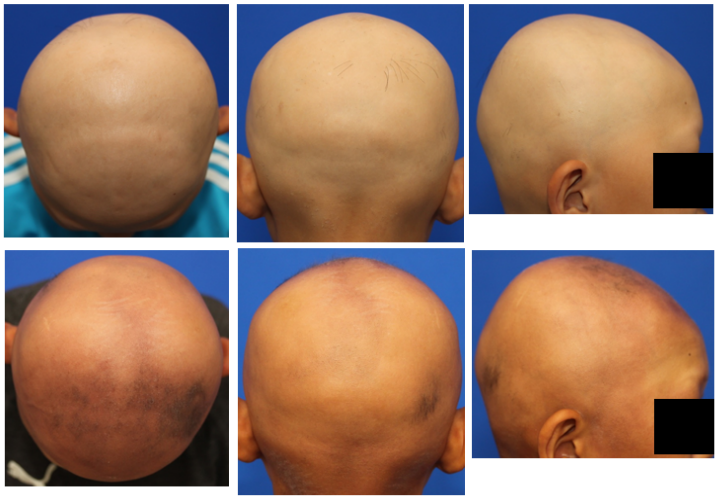
2015.11.~

DPCP + Anthralin for 6 months

DPCP (0.0005%)
Anthralin (0.2%)

Clinical response :
A1 (<25%)

#8 DPCP → DPCP + Anthralin



#8 (M/9)
S5 (100%)
SALT score 100

2015.9.~

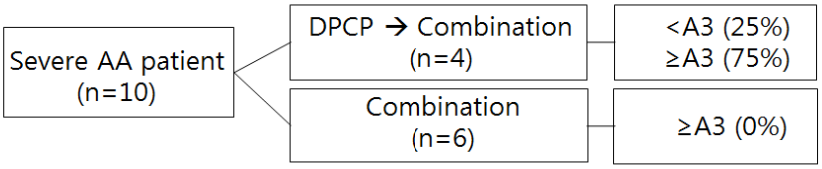
DPCP + Anthralin
for 10 months

DPCP (0.01%)
Anthralin
(0.2% → 0.5%)

Clinical response :
A1 (<25%)

Results

HAIR REGROWTH, n (%)		DPCP → Combination, n (%)	Combination, n (%)
A0 (0%)	3 (30)	1 (25)	2
A1 (<25%)	4 (40)	-	4
A2 (26%-50%)	-	-	-
A3 (51%-75%)	1 (10)	1 (25)	-
A4 (76%-99%)	1 (10)	1 (25)	-
A5 (100%)	1 (10)	1 (25)	-
>50% Hair regrowth	**3 (30)**	**3 (75)**	-
>75% Hair regrowth	**2 (20)**	**2 (50)**	-



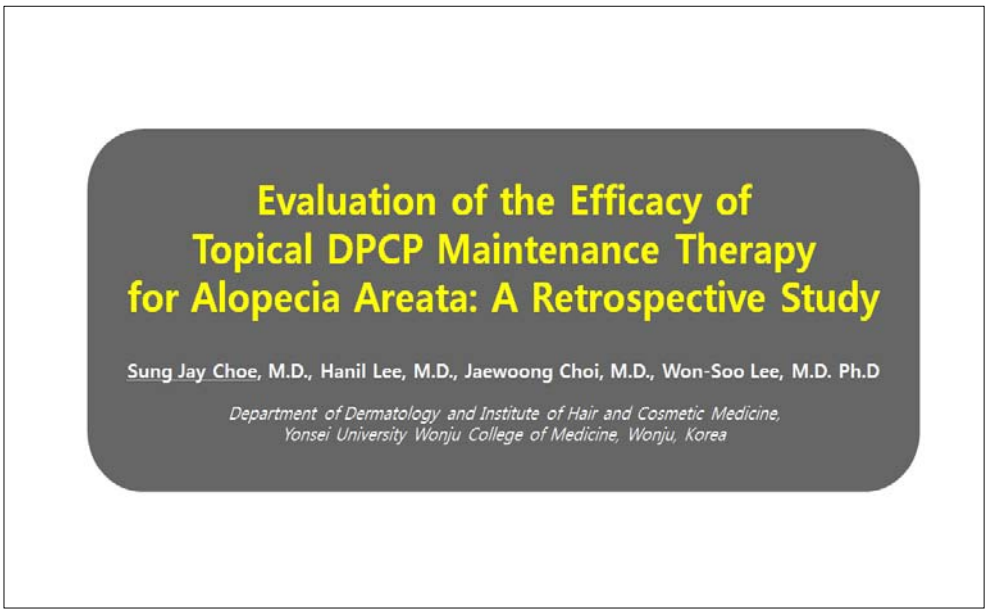
Discussion

- DPCP treatment in chronic extensive AA has some limitations.
- In AU & AT, the complete hair regrowth rate is reported to between 17% ~ 50%.
- In our case series, a synergistic effect has not been observed with DPCP and anthralin in patients with therapy-resistant extensive AA.

Evaluation of the efficacy of topical DPCP maintenance therapy for alopecia areata: a retrospective study

Sung Jay Choe, Hanil Lee, Jaewoong Choi, Won-Soo Lee

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



Background

A few studies only reported about maintenance treatment of alopecia areata patient. At the aspect of treatment response of alopecia areata, some authors have reported that the use of topical DPCP immunotherapy will maintain AA patient in good condition. However, other studies have not shown this benefit.

Chinese Experience in the Treatment of Alopecia Areata with DPCP

- Maintanence treatment: Complete Response에 도달한 환자를 대상 (1-4weeks interval)
- Relapse : > 25% Regrowth hair loss
- 14명의 환자
- Average follow up : 10.5 months
- Relapse rate : 57.1% (maintenance O) / 85.7% (maintenance X)
- Mean time to relapse 8.16mon (maintenance O) / 4.17mon (maintenance X)

J Dermatol. 2015;42(2):220-221.

Background

Efficacy and Safety of DPCP alone or in combination with Anthralin in the Treatment of Chronic Extensive Alopecia Areata: A retrospective Case Series

- DPCP or DPCP + Anthralin 을 받은 환자를 대상
- 1-4 week interval follow up [6-9개월까지 follow up]
- **26명**의 환자 (8명 - DPCP / 18명 - DPCP+Anthralin)

- **Mean time to relapse -** 40weeks (DPCP) / 50weeks (DPCP+Anthralin)
  (No statistical significance due to Low relapse rate)
- **Relapse rate:**
  DPCP - 13.6% : Regrowth after 12-14 weeks (weekly DPCP)
  DPCP+Anthralin - 16% : Regrowth after 8-14 weeks (weekly DPCP+Anthralin)

J Am Acad Dermatol. 2015;72(4):640-650

Background

Five-year Experience in the Treatment of Alopecia Areata with DPC

- 총 46명의 환자를 follow up
- Maintenance treatment: 39명(1-4weeks interval)
- Relapse : > 25% Regrowth hair loss
- 7명은 치료를 중단하고 2-20개월까지 follow up만 시행함.
- Relapse rate : 17.9% (maintenance O: 7/39) / 57.1% (maintenance X: 4/7)

J Eur Acad Dermatol Venereol. 2010;24(3):264-269.

Predictive Model for Immunotherpay of AA with DPC

- Relapse : > 25% Regrowth hair loss
- 37mon까지 follow up.
- No statistical difference with or without maintenance treatment

Arch Dermatol. 2001;137(8):1063-8.

Background & Objective

Topical Immunotherapy of Severe Alopecia Areata with DPCP Experience in an Iranian

- 6-12months까지 follow up.
- Maintenance treatment: Complete Remission이나 Partial Response를 보인 22명을 환자
- Relapse rate : 59.10% (13/22)

BMC Dermatol. 2005;26;5-6.

Objective

- To evaluate the efficacy of topical DPCP maintenance therapy of alopecia areata in Korean patients

Materials and Methods

- **Patients**
  - **230 Alopecia areata patients** who had visited Wonju Severance Christian hospital for treatment with **Topical DPCP immunotherapy** were enrolled.
- **Topical DPCP immunotherapy**
  - Each of patients was sensitized with dose of **0.1% DPCP**.
  - After a week, DPCP challenge started with dose of **0.01%**, in increasing doses of **0.025%, 0.05%** depending on patient's response.

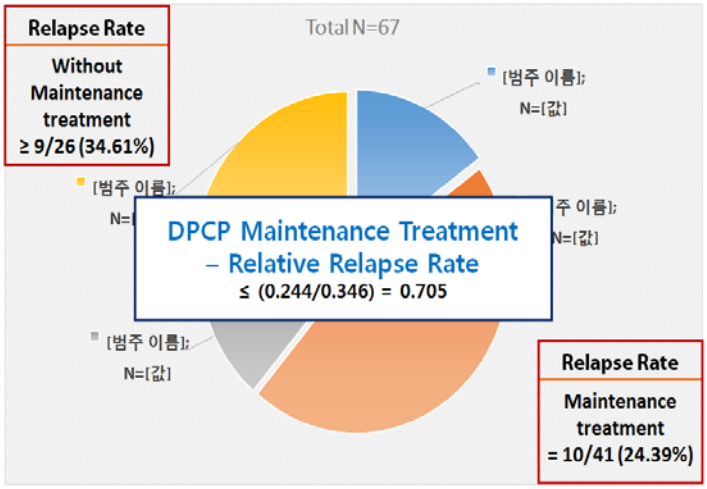
Materials and Methods

- **Change to Maintenance treatment**
  - I. Clinical response evaluation (5 stage)
    - Complete response / Cosmetically acceptable response
  - II. Low disease activity for at least 6weeks after clinical improvement

→2가지를 모두 만족하는 환자들에서
이후 치료는 Maintenance treatment로 간주

- **Maintenance treatment (N=41)**
  - 유지치료 기준에 해당하였으나 이후 지속적으로 치료하지 않고 follow up loss된 환자는 Maintenance treatment그룹에서 제외하였고, 치료 간격이 길어지더라도 지속적으로 병원에 내원하여 Disease progress가 명확하게 판단 가능한 경우로 한정하였음.
- **Relapse: ≥ 25% regrowth hair loss**
  - Maintenance treatment를 시행하지 않는 환자에서 Follow up loss되어 Relapse 여부가 명확하지 않은 경우 Relapse하지 않은 것으로 간주하여 비교하였음.

Result



Result

Table 1. Patient demographic and hair loss features at baseline.

	DPCP Maintenance w/o relapse	DPCP Maintenance w/ relapse	DPCP Maintenance (-) w/o relapse	DPCP Maintenance (-) w/ relapse
N	31	10	17	9
Age	41.9	43.3	39.18	39.22
Sex(M/F)	19/12	6/4	10/7	5/4
FHx of AA	5	3	2	2
Type (P/T/U)	26/3/2	8/1/1	13/2/2	9/1/0
Autoimmune disease Hx	3	1	1	1
ANA Abnormality	4	2	1	2
Duration before DPCP treatment (mon)	20.13	17.4	9.12	9.33

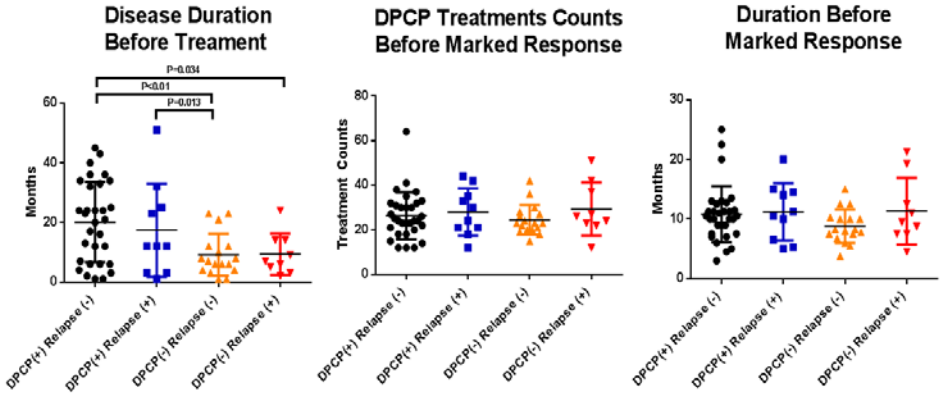
Result

Table 2. Characteristics associated with DPCP immunotherapy

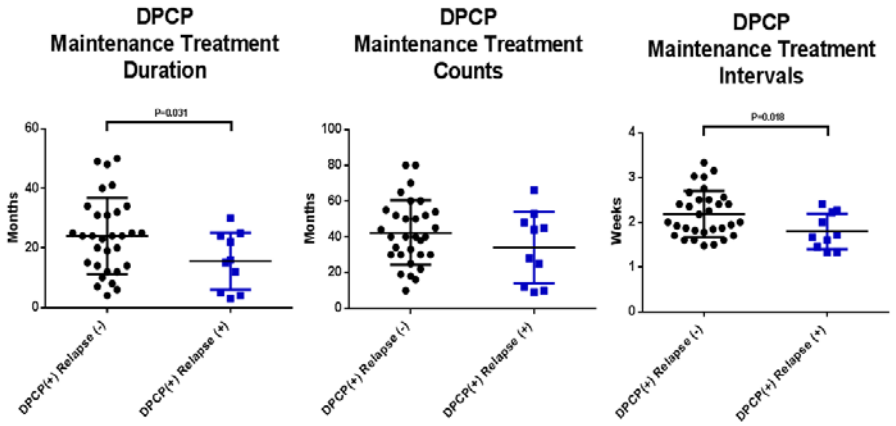
	DPCP Maintenance w/o relapse	DPCP Maintenance w/ relapse	DPCP Maintenance (-) w/o relapse	DPCP Maintenance (-) w/ relapse
DPCP treatments counts before marked response	26.32	28	24.53	29.33
Duration before marked response (mon) (after DPCP treatment initiation)	10.81	11.2	8.79	11.30
Last DPCP Conc. (0.01/0.025/0.05)	11/15/5	3/5/2	7/7/3	4/5/0
Maintenance treatment duration (mon)	24.03	15.6*		
Maintenance treatment counts	42.32	34		
Maintenance treatment interval (week)	2.18	1.80*		

*; P<0.05

Result



Result



Result

Table 3. Correlation between Variables

		P-value	Pearson correlation coefficient
Relapse	**Maintenance treatment interval**	p=0.037	r=0.327
Duration Before Marked Response	**Maintenance Treatment Interval**	p=0.043	r=0.317
Maintenance treatment counts	**Maintenance treatment Interval**	p=0.011	r=0.394
Autoimmune disease history	ANA Abnormality	p=0.005	r=0.336
Family History of AA	**Disease Duration Before Treatment**	p=0.005	r=-.342
DPCP Maintenance treatment	**Disease Duration Before Treatment**	p=0.001	r=0.399

Result

Table 4. DPCP Re-treatment after relapse

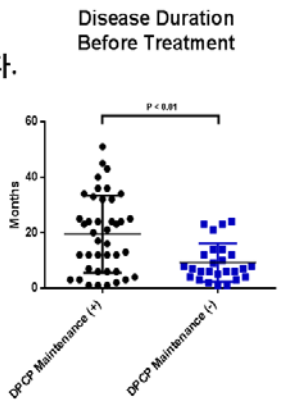
- Total N = 16
  - Follow up loss = 3

	DPCP Maintenance w/ relapse	DPCP Maintenance (-) w/ relapse
N	10 → 8	9 → 8
Age	43.3 → 41.25	39.22 → 39.25
Sex(M/F)	6/4 → 4/4	5/4 → 5/3
FHx of AA	3 → 2	2 → 2
Type (P/T/U)	8/1/1 → 6/1/1	9/1/0 → 8/1/0
Autoimmune disease Hx	1 → 1	1 → 1
ANA abnormality	2 → 2	2 → 2
DPCP treatments counts before marked response	28 → **14.38**	29.33 → **13.63**
Duration before marked response (mon) (after DPCP treatment initiation)	11.2 → **5.13**	11.30 → **4.37**

Discussion & Conclusion

- DPCP maintenance는 재발률을 낮춘다.
- DPCP 유지 치료 간격이 길어지면 재발률이 높아진다.
- 재발하더라도 재치료시 예전보다 치료 반응이 더 좋다.
- 유지치료의 농도는 치료 결과와 상관이 없다.

- **Disease Duration Before Treatment**
  - 유지 치료를 한 군과 하지 않은 **군내에서는 차이가 없음.**
  - **유지 치료를 한 군이 상대적으로 오랜 유병 기간**을 보임.
    - 오랜 유병기간 = QOL↓
      → 치료에 좋은 반응을 보였을 때,
      이를 유지하려는 노력이 환자 Compliance에 반영?
  - **AA 가족력이 있는 환자들에서 질병의 치료 전 기간이 짧음.**
    - 질환에 대한 인식 수준↑ → 조기 치료 시작



Discussion & Conclusion

- **Maintenance treatment Interval**
  - **DPCP(+) Relapse (-) > DPCP (+) Relapse (+)**
    장기간 유지치료를 한 환자들이 포함되어 평균 유지 치료 기간 및 간격이 통계적으로 차이를 보이는 것으로 생각됨.
  - **유지치료로 전환하는데 기간이 길어지면 유지치료 간격이 길어짐**
  - **유지치료 횟수가 많아지면 유지치료 간격이 길어짐**
    → 치료 기간 및 횟수가 증가하면서 환자 Compliance ↓
  - **유지치료 간격이 길어지면 재발률이 높아짐**
    → 증상이 호전되어도 일정한 간격을 유지하는 것이 중요
    → 치료 간격을 늘릴 때에는 세심한 주의가 필요

Discussion & Conclusion

- **Further evaluation**
  - For maintenance treatment, maintain last DPCP concentration or not?
  - Optimal treatment interval?
  - How long for maintenance treatment?
- **Limitation**
  - Long term prognosis
  - Selection bias
  - Insufficient data (Follow up loss patients & AU/AT Type)

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Long-term prognosis of alopecia totalis and alopecia universalis: a 10-year or more longitudinal follow-up study

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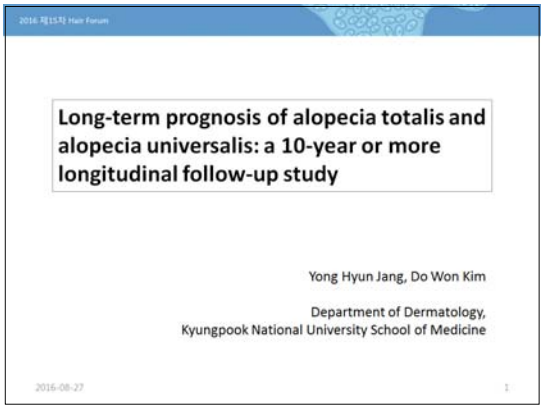
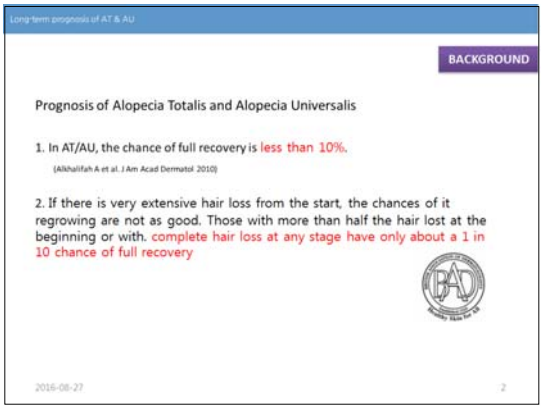
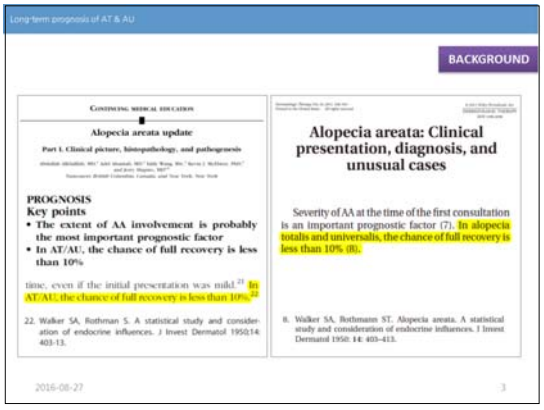
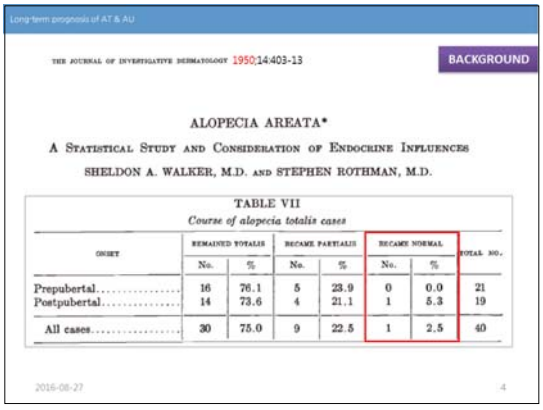




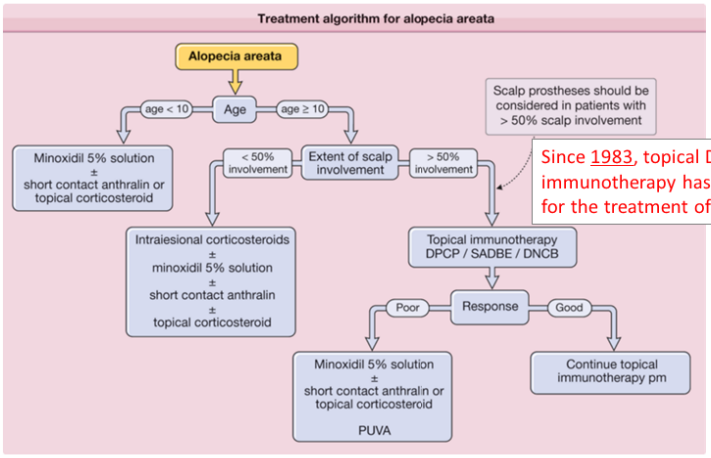




Long-term prognosis of AT & AU

BACKGROUND

Treatment guideline (National Alopecia Areata Foundation)



Since 1983, topical DPCP immunotherapy has been introduced for the treatment of AA.

From Fitzpetrick's 8th ed. 2012
Figure 88-13 Treatment algorithm for alopecia areata. (Copyright ⓒ by Jerry Shapiro, Vera Price and Harvey Lui)

Long-term prognosis of AT & AU

Efficacy of DPCP immunotherapy

1. At present, topical DPCP immunotherapy is considered the most effective for AA, with success rates ranging from 4% to 85%.

2. In our analysis, the average response rate to DPCP treatment was 55.65 ± 1.00% (95% confidence interval, 53.70–57.61). *(unpublished data)*

	Mean	Standard error	Lower limit	Upper limit	Prelative weight	Std Residual
Tosti *et al.* 1986	63.640	4.880	54.075	73.205	2.63	2.05
Hatzis K *et al.* 1988	29.220	5.480	18.479	39.961	2.09	-4.52
Hull *et al.* 1988	35.710	5.990	23.970	47.450	1.75	-3.04
Ashworth *et al.* 1989	22.350	2.860	16.745	27.955	7.67	-11.43
Monk *et al.* 1989	61.110	4.280	52.721	69.499	3.42	1.75
Hull *et al.* 1991	48.910	5.460	38.209	59.611	2.10	-0.90
Shapiro *et al.* 1993	58.930	2.510	54.010	63.850	9.95	2.17
Gordon *et al.* 1996	35.110	4.430	26.427	43.793	3.20	-4.28
Schuttelaar *et al.* 1996	39.200	6.870	25.735	52.665	1.33	-2.13
Pericin *et al.* 1998	49.190	4.470	40.429	57.951	3.14	-1.04
Sharma *et al.* 1998	65.000	7.250	50.790	79.210	1.19	1.56
Cotellessa *et al.* 2001	58.650	6.040	46.812	70.488	1.72	0.82
Wiseman *et al.* 2001	63.510	2.050	59.492	67.528	14.92	5.16
Aghaei *et al.* 2005	49.820	5.620	38.805	60.835	1.99	-0.71
Singh *et al.* 2007	75.000	3.400	68.336	81.664	5.42	6.43
Sotiriadis *et al.* 2007	59.740	3.960	51.979	67.501	4.00	1.54
Akhiani *et al.* 2008	52.190	6.630	39.195	65.185	1.43	-0.24
Avgerinou *et al.* 2008	59.260	4.910	49.637	68.883	2.60	1.14
El-Zawahry *et al.* 2010	61.730	2.540	56.752	66.708	9.72	3.31
Ohlmeier *et al.* 2012	53.440	3.290	46.992	59.888	5.79	-0.10
Salsberg *et al.* 2012	37.900	4.800	28.492	47.308	2.72	-3.32
El Khoury *et al.* 2013	48.150	6.130	36.135	60.165	1.67	-0.92
Luk *et al.* 2013	37.410	6.420	24.827	49.993	1.52	-2.56
Chiang *et al.* 2015	57.650	3.400	50.986	64.314	5.42	1.18
Durdu *et al.* 2015	51.230	9.730	32.160	70.300	0.66	-0.26
Pan *et al.* 2015	51.310	5.690	40.158	62.462	1.94	-0.43
	53.751	0.792	52.199	55.303		

BACKGROUND

Natural history of extensive alopecia areata

- The natural evolution of AT is unpredictable, but recurrences of alopecia areata (not necessarily alopecia totalis) are expected.
- In a study involving 736 patients, the relapse rate was 90% over 5 years. (Muller SA et al, Arch Dermatol. 1963)

Few studies have been reported long-term follow-up data!

- F/U or Recurrence assessment: commonly 1- or 2-year F/U after Tx
- Duration of study : 3 -24 months

OBJECTIVE

The purpose of this study is to better assess the long-term evolution of AT and AU and the effects of known prognostic factor.

SUBJECTS & METHODS

Patient population

- Enrolled patients: 73 with AT or AU
- Sex ratio: 38 male and 35 female subjects.
- The age range of the patients at initial visit: 2 to 68 years (mean 33.9 years), including 65 adults (≥15 years old) and 8 children (<15 years old)
- Follow-up duration: 12-23 years (mean 15.5 years)
  *All presented as new consultations between 1994 and 2005

Evaluation tools

- All study patients were contacted by phone by a training residents.
- The database included 189 patients, although 113 phone numbers were no longer in existence. Three patients refused phone-interview.
- Patients were asked about their current hair status and treatments.

RESULTS I

Long-term prognosis of 73 patients with alopecia totalis (AT) or alopecia universalis (AU)

	No hair regrowth	Partial hair regrowth				Complete hair regrowth
		<10%	10-49%	50-89%	≥90%	
AT (n=24)	5 (20.8%)		7 (29.1%)	3 (12.5%)	4 (16.7%)	5 (20.8%)
AU (n=49)	31 (63.3%)	2 (4.1%)	5 (10.2%)	2 (4.1%)	1 (2.0%)	8 (16.3%)
Total (n=73)	36 (49.3%)	2 (2.7%)	12 (16.4%)	5 (6.8%)	5 (6.8%)	13 (17.8%)

RESULTS II

Long-term prognosis according to the duration of AT or AU at time of first visit

	No hair regrowth	Partial hair regrowth				Complete hair regrowth
		<10%	10-49%	50-90%	>90%	
<3 months (n=16)	6 (37.5%)		2 (12.5%)	2 (12.5%)	2 (12.5%)	4 (25%)
3-11 months (n=18)	9 (50%)	1 (5.56%)	3 (16.7%)	2 (11.1%)	1 (5.56%)	2 (11.1%)
12-24 months (n=10)	4 (40%)		2 (20%)			4 (40%)
2-5 years (n=12)	7 (58.3%)		1 (8.3%)	1 (8.3%)	1 (8.3%)	2 (16.7%)
>5 years (n=17)	10 (58.8%)	1 (5.8%)	4 (23.5%)		1 (5.8%)	1 (5.8%)
Total (n=73)	36 (49.3%)	2 (2.7%)	12 (16.4%)	5 (6.8%)	5 (6.8%)	13 (17.8%)

RESULTS III

Long-term prognosis according to the age of onset

	No hair regrowth	Partial hair regrowth				Complete hair regrowth
		<10%	10-49%	50-90%	>90%	
<10 years (n=11)	5 (45.4%)	1 (9.1%)	3 (27.2%)	1 (9.1%)	1 (9.1%)	
10-19 years (n=12)	7 (58.3%)		1 (8.3%)		1 (8.3%)	3 (25%)
20-29 years (n=12)	7 (58.3%)		2 (16.7%)	2 (16.7%)		1 (8.3%)
30-39 years (n=15)	9 (60%)		3 (20%)			3 (20%)
40-49 years (n=11)	5 (45.4%)	1 (9.1%)	1 (9.1%)		1 (9.1%)	3 (27.2%)
50-59 years (n=9)	3 (33.3%)		1 (11.1%)	2 (22.2%)	2 (22.2%)	1 (11.1%)
≥60 years (n=3)			1 (33.3%)			2 (66.7%)
Total (n=73)	36 (49.3%)	2 (2.7%)	12 (16.4%)	5 (6.8%)	5 (6.8%)	13 (17.8%)

RESULTS IV

Sex distribution of the patients with AT and AU

	No hair regrowth	Partial hair regrowth				Complete hair regrowth
		<10%	10-49%	50-90%	>90%	
Male (n=38)	14 (36.8%)	1 (2.6%)	7 (18.4%)	2 (5.3%)	5 (13.2%)	9 (23.6%)
Female (n=35)	22 (62.9%)	1 (2.9%)	5 (14.3%)	3 (8.6%)		4 (11.4%)
Total (n=73)	36 (49.3%)	2 (2.7%)	12 (16.4%)	5 (6.8%)	5 (6.8%)	13 (17.8%)

RESULTS V

Long-term prognosis according to family history

	No hair regrowth	Partial hair regrowth				Complete hair regrowth
		<10%	10-49%	50-90%	>90%	
Yes (n=6)	5 (83.3%)		1 (16.7%)			
No (n=67)	31 (46.3%)	2 (3.0%)	11 (16.4%)	5 (7.5%)	5 (7.5%)	13 (19.4%)
Total (n=73)	36 (49.3%)	2 (2.7%)	12 (16.4%)	5 (6.8%)	5 (6.8%)	13 (17.8%)

RESULTS VI

Long-term prognosis according to main therapeutic modalities

	No hair regrowth	Partial hair regrowth				Complete hair regrowth
		<10%	10-49%	50-90%	>90%	
DPCP (n=18)	11 (61.1%)		1 (5.6%)	2 (11.1%)	1 (5.6%)	3 (16.7%)
Systemic immunesuppressants (n=19)	12 (63.2%)	1 (5.3%)	3 (15.8%)		1 (5.3%)	2 (10.5%)
Topicals (n=11)	2 (18.2%)		4 (36.4%)	1 (9.1%)	1 (9.1%)	3 (27.3%)
Combined and/or Intercurrent (n=23)	11 (47.8%)	1 (4.3%)	4 (17.4%)	2 (8.7%)	2 (8.7%)	3 (13.0%)
Others (n=2)						2 (100%)
Total (n=73)	36 (49.3%)	2 (2.7%)	12 (16.4%)	5 (6.8%)	5 (6.8%)	13 (17.8%)

RESULTS VII

Long-term prognosis according to the period from onset of alopecia

	No hair regrowth	Partial hair regrowth				Complete hair regrowth
		<10%	10-49%	50-90%	>90%	
10-14 years (n=35)	15 (42.9%)	2 (5.7%)	4 (11.4%)	3 (8.6%)	3 (8.6%)	8 (22.9%)
15-19 years (n=34)	17 (50.0%)		8 (23.5%)	2 (5.9%)	2 (5.9%)	5 (14.7%)
≥20 years (n=4)	4 (100%)					
Total (n=73)	36 (49.3%)	2 (2.7%)	12 (16.4%)	5 (6.8%)	5 (6.8%)	13 (17.8%)

RESULTS VIII

Current treatment status in patients with no/partial hair regrowth

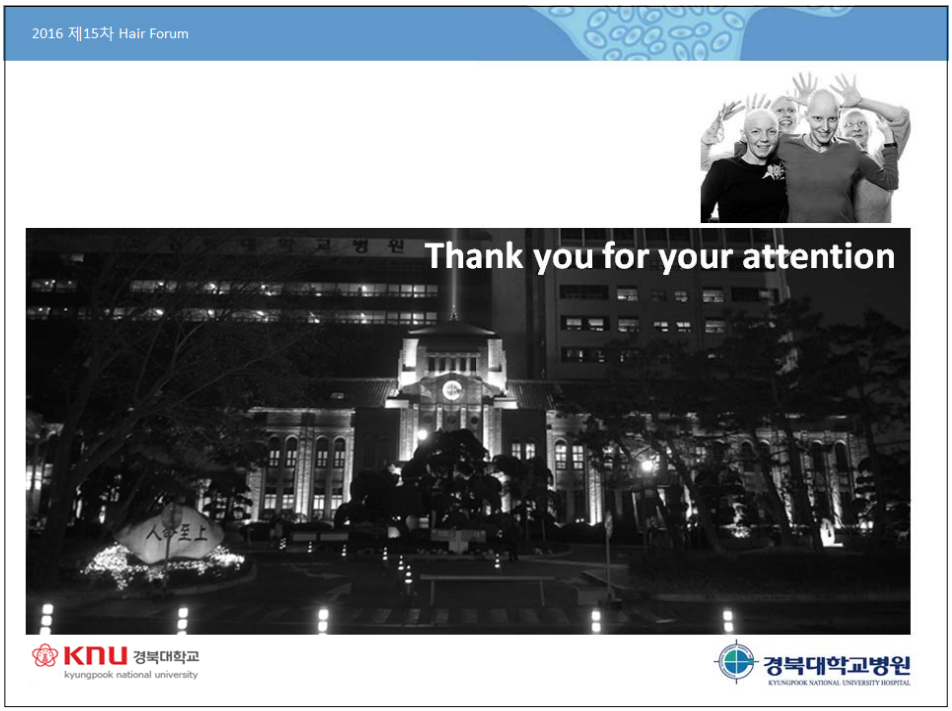
Current treatments	No hair regrowth	Partial hair regrowth			
		<10%	10-49%	50-90%	>90%
Yes (n=11)	3 (27.3%)	1 (9.1%)	6 (54.5%)	1 (9.1%)	
No (n=49)	33 (67.3%)	1 (2.0%)	6 (12.2%)	4 (8.2%)	5 (10.2%)
Total (n=60)	36 (49.3%)	2 (2.7%)	12 (16.4%)	5 (6.8%)	5 (6.8%)

SUMMARY

Long-term prognosis of AT & AU

I. Thirteen patients (17.8%) out of 73 with AT or AU had complete hair regrowth.
- AT 5/24 (20.8%)
- AU 8/49 (16.3%)

II. Eighteen patients (24.6%) out of 73 with AT or AU showed hair regrowth greater than or equal to 90%.
- AT 9/24 (37.5%)
- AU 9/49 (18.3%)


2016 제15차 Hair Forum
Thank you for your attention
KNU 경북대학교
kyungpook national university
경북대학교병원
KYUNGPOOK NATIONAL UNIVERSITY HOSPITAL

2016

대한모발학회

제15차 Hair Forum

제 2 부 : 주제 발표

The Korean Hair Research Society

■ **CURRICULUM VITAE** ■

이 장 영

메디포스트㈜ 사업개발본부장, 전무

학력:

2001-2003	연세대학교 경영대학원 경영학 전공(석사)
1990-1995	한국과학기술원 (KAIST) 생물과학과 전공(석사, 박사)
1986-1990	연세대학교 생명공학과 (학사)

경력:

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2007-2012	태평양제약 메디컬뷰티 사업본부장, 상무 (2011-2012), 개발마케팅 본부장, 이사 (2008-2011), 개발팀장 (2007-2008)
1997-2007	아모레퍼시픽 기술전략팀장 (2000-2007), 책임연구원 (1997-2000)
1995-1996	PACIFIC NORTHWEST LABORATORY 포스트닥 연구원

Alopecia project using MSC conditioned media

Jay Lee

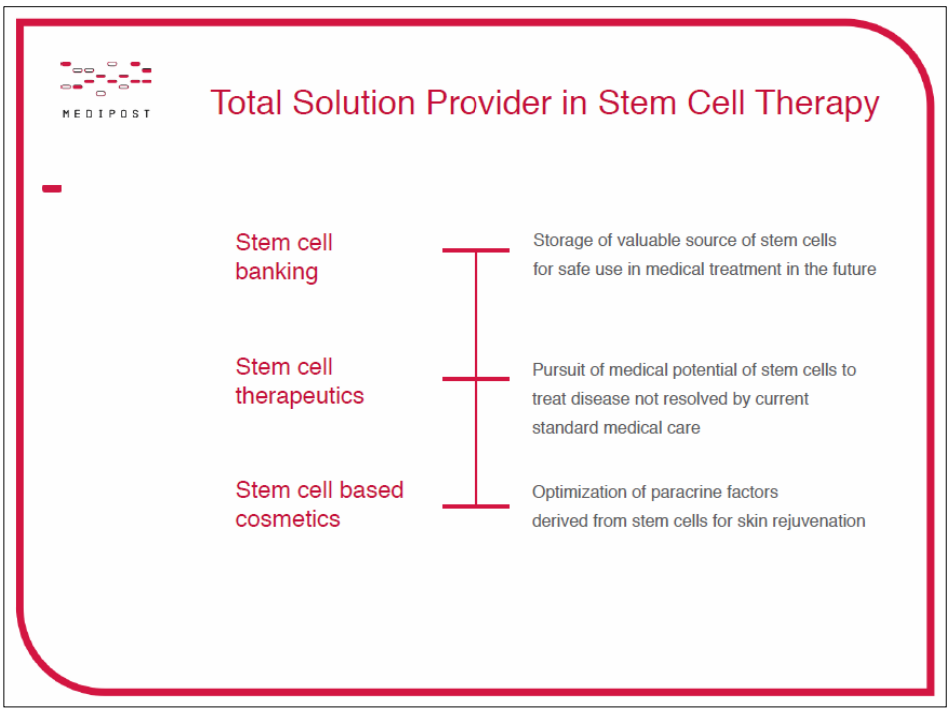
MEDIPOST

Mesenchymal stem cell (MSC) belongs to an adult stem cells and is often found in some tissues in human body including umbilical cord blood and bone marrow. MSC is the most popular modality in development of stem cell therapeutics at the moment. All six stem cell drugs approved in the world are based on the MSC. As opposed to other modality in stem cell therapeutics, it is free from ethical issues and has some unique properties useful in the therapeutic application including immune neutrality and homing effect to the injury site.

Paracrine effect is known to play a key role in therapeutic efficacy in MSC. Upon being administered in the body, MSC adapts itself to the new environment in the diseased areas and starts to secret various trophic factors including cytokines and growth factors involving in anti-inflammation, anti-apoptosis, mitogenesis and activation of endogenous stem cells. The therapeutic effects of the trophic factors secreted by the MSC are collectively referred as paracrine effect or paracrine action of MSC. MSC conditioned media (MSC CM) is a collection of such therapeutic trophic factors secreted by the cells.

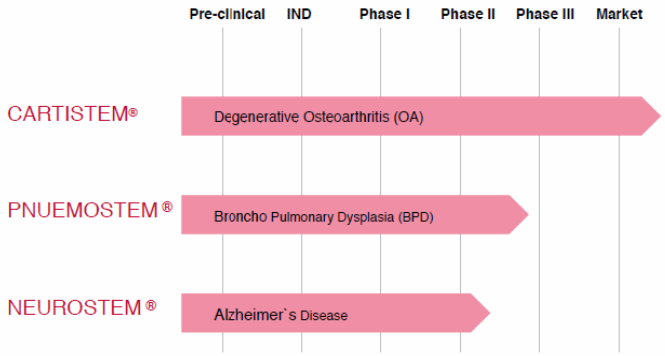
Alopecia project at MEDIPOST is based on the MSC CM to take advantage of the paracrine effect of MSC for the treatment of one of the most widespread disease in men and women, hair loss. The project is being conducted in collaboration with AMOREPACIFIC and CHUNG ANG University and is financially supported by Ministry of trade, industry and energy in Korea.


MEDIPOST
Alopecia Program


MEDIPOST
Total Solution Provider in Stem Cell Therapy
Stem cell banking
Storage of valuable source of stem cells for safe use in medical treatment in the future
Stem cell therapeutics
Pursuit of medical potential of stem cells to treat disease not resolved by current standard medical care
Stem cell based cosmetics
Optimization of paracrine factors derived from stem cells for skin rejuvenation

Stem cell therapeutics (1) : Products

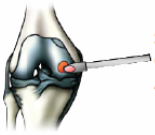
The world leader in allogeneic stem cell drugs



Stem cell therapeutics (2) : Cartistem

API (Active Pharmaceutical Ingredient): hUCB-MSCs

Excipient: sodium hyaluronate (lyophilized)



Surgical Application: Open Arthrotomy or Arthroscopic Surgery

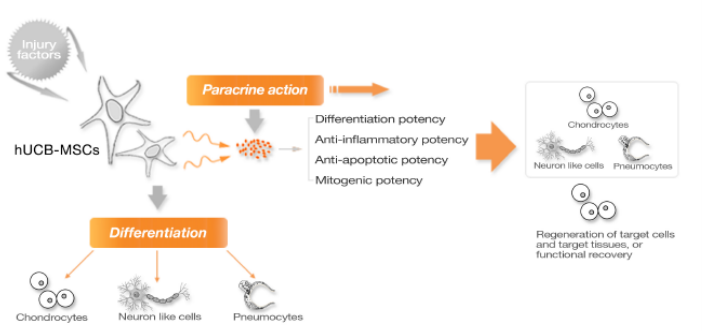
- Co-developed in partnership with SAMSUNG MEDICAL CENTER Dept. of Orthopedics
- Market-Approval: Biologics License Application (BLA) received in 2012, Korea.
- Label: "Treatment of repetitive and/or traumatic cartilage degeneration including Degenerative Osteoarthritis (OA) without age limit".
- 3,391 patients (with 3,784 doses) have been treated with 322 hospitals/clinics currently offering CARTISTEM® in Korea (May 2016).
- 600 patient Post Market Surveillance (PMS) is complete.

Stem cell therapeutics (3) - Showcase

News Article (English)

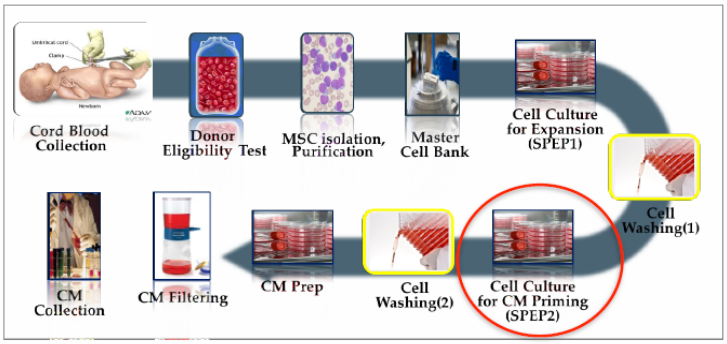
Paracrine actions

- Much of therapeutic efficacy of adult stem cells (MSC) are explained by paracrine action (trophic factors secreted by stem cells).
- Cells automatically adapt itself by changing the secretome upon exposure to disease environment.



MSC CM manufacturing with priming

- Paracrine action being the major MOA for therapeutic efficacy of MSC, the logic goes that conditioned media of MSC (collection of trophic factors) can be used as active ingredients instead of MSC itself.
- However, if conditioned media are to be used for specific indication, MSC should first be exposed to environment artificially mimicking disease area in the body (Priming) for optimized efficacy.



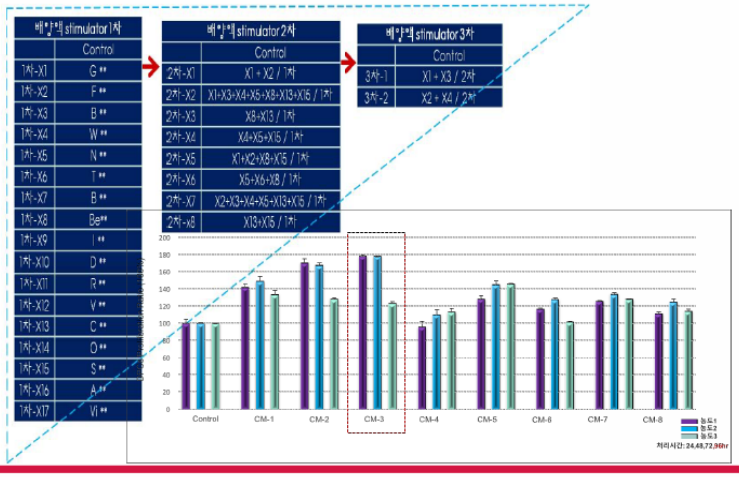
Optimum priming factors for alopecia (1)

- Literature survey to find specific molecule(s) overly expressed in alopecia patients in order to artificially design alopecia state in vitro for priming for MSC.

접근 기전	주요 탈모방지 및 발모 전략		비 고; 미세환경 모사 방안
모발주기 조절	▪ 휴지기 → 성장기 유도	➢ 혈행촉진 (Vasodilation)	✓ Minoxidil etc
		➢ Nutrition Therapy	✓ Vitamines, Minerals etc
	▪ 성장기 → 퇴행기 (휴지기) 방지	➢ Androgen Receptor Blocker	✓ Cyproterone acetate, Flutamide etc
		➢ 5α-Reductase Inhibition	✓ Finasteride, Dutasteride
		➢ Estrogen therapy	✓ Flavonoids
		➢ TGF-beta Signaling	✓ DHT, TGF-beta analog
		➢ STAT / MAPK pathway	✓ Interleukins , JAK inhibitor and LPS
모낭줄기세포조절	▪ HF Epithelial Stem Cell	➢ Wnt pathway	✓ Chemicals, Synthetic signal peptide
	▪ HF Mesenchymal Stem Cell	➢ Hedgehog pathway	✓ Stemoxide
	▪ HF Stem Cell Niche	➢ BMP pathway	✓ Cell Adhesion Molecules
	▪ Follicular Morphogenesis	➢ Immune Privilege	✓ Corticosteroids, NSAIDs

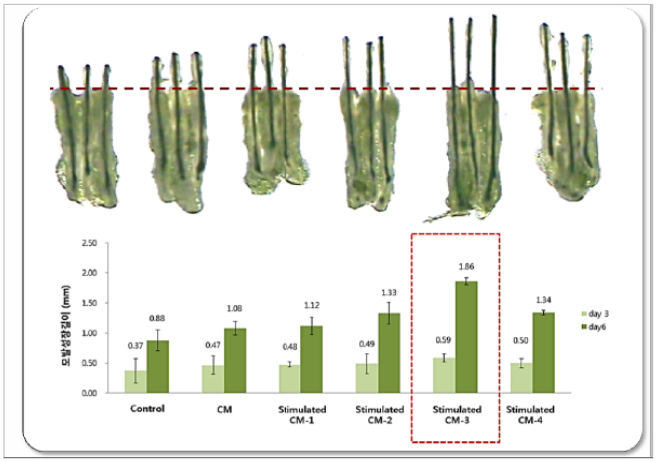
Optimum priming factors for alopecia (2)

- 17 molecules selected by the literature survey results in 147 combination for experiment.
- CM-3 was found to be most effective in priming the cells for alopecia.



Proof of concept (1) : ex vivo experiment

- MSC-CM primed by CM-3 results in 51% increase compared with control in hair length in ex vivo experiment with human hair follicles.



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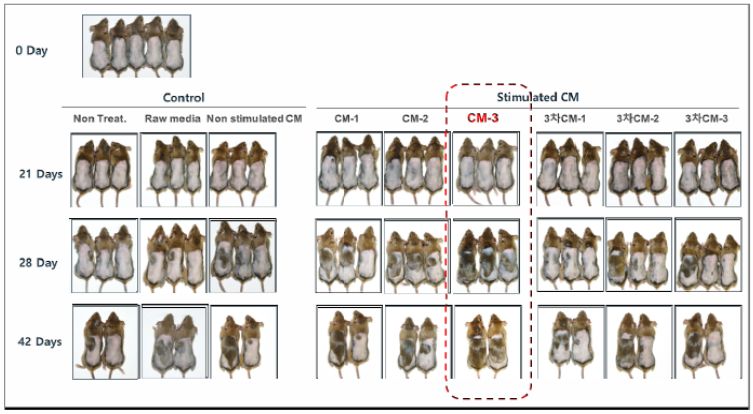
Proof of concept (2) : in vivo animal model

- Primed MSC-CM by CM-3 (Primed CM) results in notable superiority in hair growth in animal mouse model compared with control.



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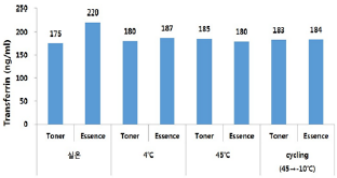
Pilot formulation for POC clinical trial

- Pilot formulation was developed with 5% MSC-CM for POC clinical trial.
- Stability of MSC-CM was tested under various conditions (ongoing).

시제품 제작

시제품 품평회 진행

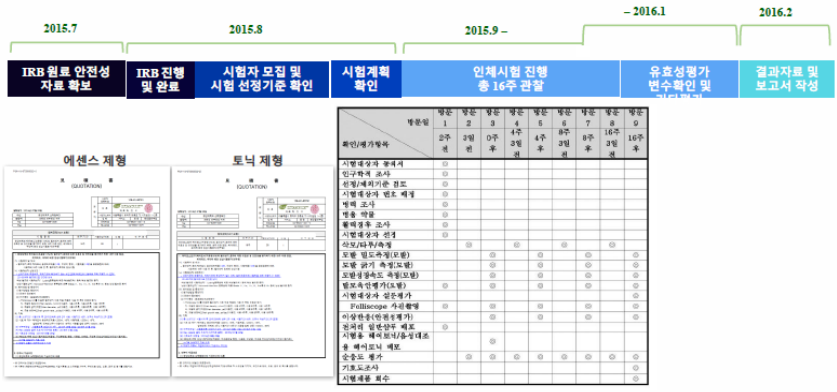
시제품 지표물질 안정도 시험 진행



* 제형을 5배 희석하여 측정한 값

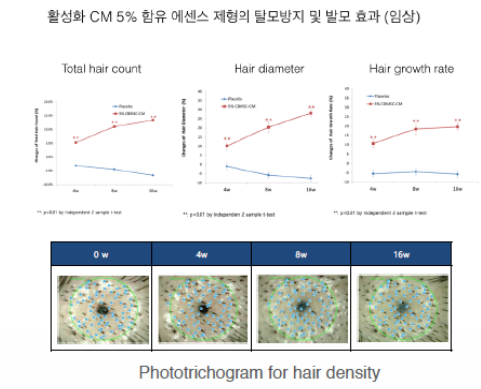
POC clinical trial (1): Synopsis

- A POC clinical trial was designed in total 16 weeks use twice daily by topical administration.
- Total 30 subjects (alopecia patients) were tested in a placebo controlled double blind trial.



POC clinical trial (2): Top-line results I

- Cosmetic formulation containing 5% MSC-CM showed statistically significant superiority in total hair count, hair diameter and hair growth rate compared with placebo control (treated with vehicle formulation only) after 16 weeks of use.



Phototrichogram for hair density

POC clinical trial (3): Top-line results II

Photo for investigator assessment
(no statistical significance between the groups)

Subject self assessment (no statistical significance between the groups)

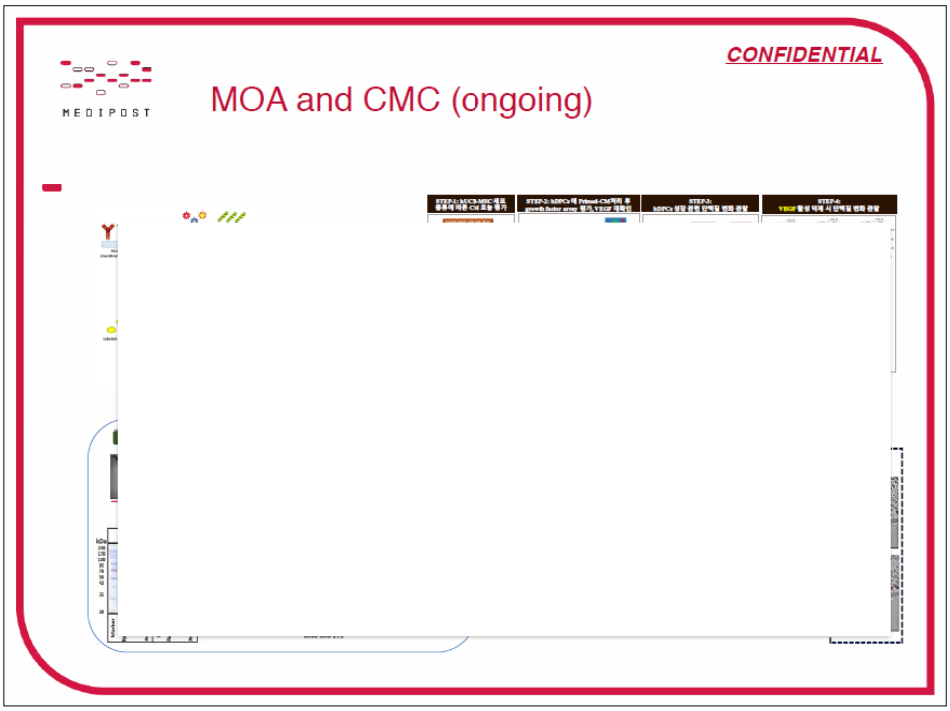
	4 week	8 week	16 week
Placebo Group	21.43%	57.14 %	57.14 %
Test Group MSC-CM 5% solution	18.75%	43.75 %	31.25 %

Efficacy comparison

- Despite shorter length of treatment period (16w vs. 24, 48 w), the MSC-CM's efficacy against alopecia is at least comparable to those published for pharmaceutical available in the market for alopecia.

Comparison with profile of competitor drugs approved for alopecia

Active Ingredient	Number of patient	Gender	Time of evaluation	Method of assessment	Protocol	Total Hair Count (change from the baseline in number/cm^2)	Total Hair Count (% change from the baseline)	p-value between groups	Investigation Area
hUCBMSC-CM	30	Female	16w	phototrichogram	MSC-CM 5% solution, 2x/day, topical	13.3	14.2%	<0.001	Vertex
Minoxidil	280	Female	24w	phototrichogram	Minoxidil1%, 2x/day, topical	15.2	8.0%	<0.001	Vertex
Minoxidil	393	Male	48w	phototrichogram	Minoxidil2%, 2x/day, topical	12.7	8.8%	<0.001	Vertex
Dutasteride	416	Male	24w	phototrichogram	Arm 1: dutasteride 0.1mg, 1X/d, oral	15.4	8.7%	<0.001	Vertex
					Arm 2: dutasteride 0.5mg,1X/d, oral	18.6	10.2%	<0.001	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