# 2022 대한모발학회 제20차 Hair Forum



• 일시: 2022년 8월 20일 (토) 15:20-18:30

• 장소: 대전 유성호텔 8층 스타볼룸

대 한 모 발 학 회

# 2022 대한모발학회 제20차 Hair Forum

2022. 8. 20 (토) 오후 15:20~18:30

대전 유성호텔 8층 스타볼룸

# 일정표 15:20-15:25 개회사 회 장 김문범 일정소개 총무이사 허창훈 진행 학술이사 유박린 Session I. 자유연제 15:25-15:35 Risk and incidence of comorbid diseases, and mortality associated with lichen planopilaris: A Korean nationwide population-based study 연세원주의대 임성하 / 6

	with lichen planopilaris: A Korean nationwide population-based study
	·······연세원주의대 <b>임성하 /</b> 6
15:35-15:45	Quality of life and financial stress assessment in Korean patients with female pattern hair loss ······· 인하의대 황혜원 / 15
15:45-15:55	Irisin, myokine, stimulates the telogen-anagen transition through Wnt signaling pathway 중앙의대 이정옥 / 23
15:55-16:05	The possible role of virus infection as a trigger to induce an inflammatory response in alopecia areata 충남의대 이 영 / 31
16:05-16:15	The diagnosis of undiagnosed genetic hair disease: Beyond the exome ····································
16:15-16:25	Combination treatments of JAK 1/2 inhibitor (Baricitinib) and immunosuppression therapy in alopecia totalis ····· 중앙의대 고영규 / 58
16:25-16:40	Coffee Break

Session II. Special Lecture:	모발 연구의 기초와 시	작				
,						
16:40-17:10 <b>모발 기초 실험실</b>	연구 시작과 준비 …		서울의대	권오상	/	70
17:10-17:40 Androgenetic al	lopecia 기초 실험 연구			성영관	/	78
Session III. 2022년도 대한모발	학회 연구비 : 연구계획	<b>발표</b>				
17:40-17:50 <b>탈모발생에서 고지</b> 	방 식이와 장내 환경의		서울의대	박현선	/	94
17:50-18:00 원형 <b>탈모에서 조</b> 절	설 T 세포의 역할에 대한	한 연구	중앙의대	석 준	/ 1	00
18:00-18:10 <b>보건의료빅데이터</b> 	를 이용한 원형탈모 환		아주의대	김진철	/ 1	05
18:10-18:20 <b>코로나19 팬데믹</b>	기간 중 초발한 탈모 경	질환 분석	건국의대	유다애	/ 1	12
18:20-18:30 폐회사 기념 촬영				·· 회 장	김등	문범
18:30-20:00 저녁식사 및 간친	회					

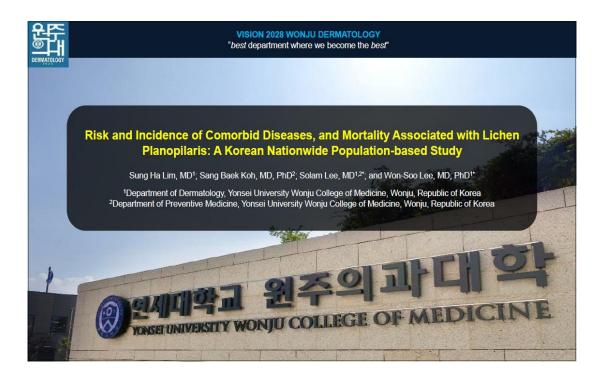
# 2022 대한모발학회 제20차 Hair Forum

# Session I. 자유연제



# Risk and incidence of comorbid diseases, and mortality associated with lichen planopilaris: A Korean nationwide population-based study

Sung Ha Lim<sup>1</sup>, Sang Baek Koh<sup>2</sup>, Solam Lee<sup>1,2\*</sup>, Won-Soo Lee<sup>1\*</sup>



<sup>&</sup>lt;sup>1</sup>Department of Dermatology, Yonsei University Wonju College of Medicine, Wonju, Korea <sup>2</sup>Department of Preventive Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea



#### Introduction

- Lichen planopilaris (LPP)
  - A primary cicatricial alopecia which is thought to be triggered by an autoimmune response targeting hair follicles.
  - LPP has been reported to be associated with various comorbid diseases, such as allergic diseases, lichen planus, thyroid diseases, systemic lupus erythematosus, and diseases related to androgen hormone
- However, the data regarding <u>comorbidity risks or incidence on LPP</u> is lacking, and <u>the prognosis of patients with LPP</u> are largely unexplored.



Donati A et al. J Am Acad Dermatol. 2011 Fechin COC et al. An Bras Dermatol. 2022

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### **Purpose**

In this background, we investigated *Risk and Incidence of comorbid diseases, and mortality* in patients with LPP and controls based on the National Health Insurance Service database and the National Death Registry of Korea.

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#### **Materials and Methods**

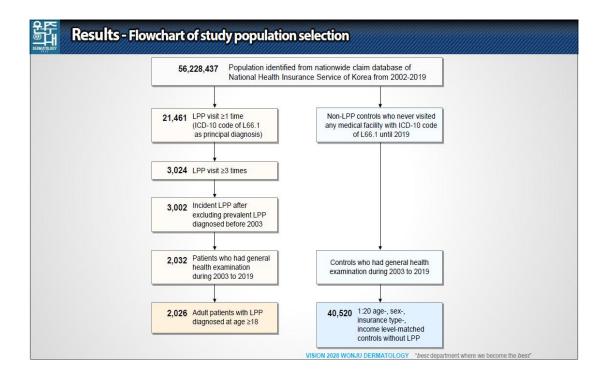
#### Data source and study population

- Patients aged ≥18 years who have ≥3 documented visits to medical facilities
- January 2003 December 2019
- ICD-10 code of L66.1 (LPP) as a principal diagnosis
- For comparison, 1:20 age, sex, insurance type, and income level matched controls who had never visited any
  medical facility with LPP during the observational period
- Connective tissue disease: RA, SLE, SSC, Sjogren's disease, Behcet's disease, AS, psoriasis, AA, CD, UC, MS

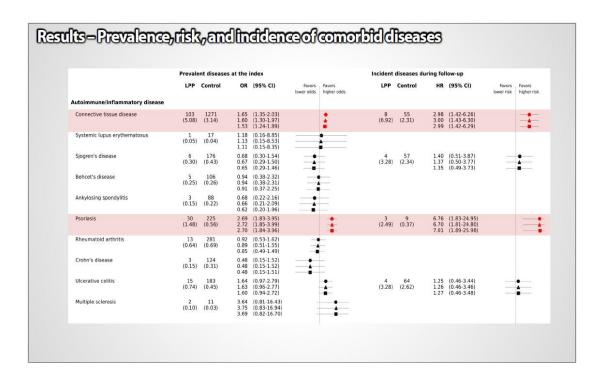
#### Statistical analyses

- Independent t-test or chi-squared test, and a multivariate logistic regression analyses were done to estimate
  odds ratio (OR) in patients with LPP compared with those in controls.
- The death rates per 10,000 person-years multivariable Cox proportional hazards regression analyses
  - Model 1: only adjusted by matching variables (age, sex, insurance type, and income levels).
  - · Model 2: additionally adjusted for current smoking status, drinking, and body mass index (BMI)
  - Model 3: further adjusted with <u>Charlson comorbidity index (CCI)</u> at the index date.

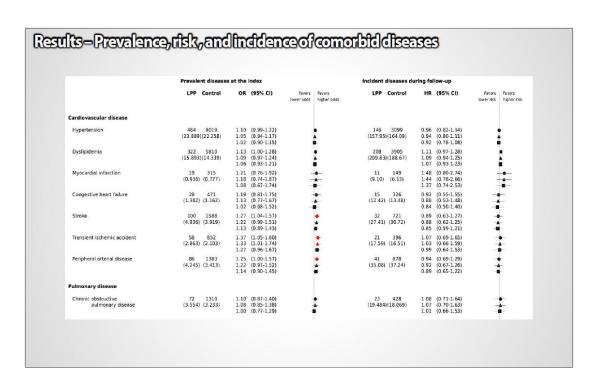
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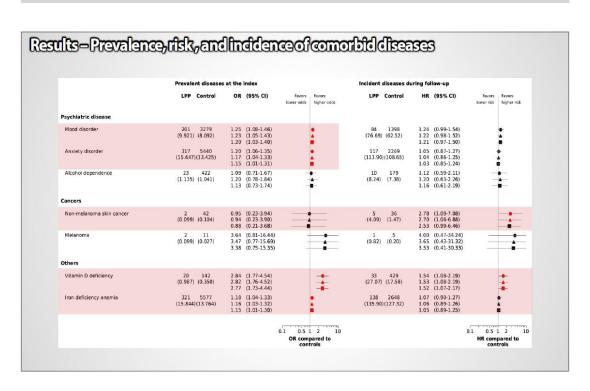


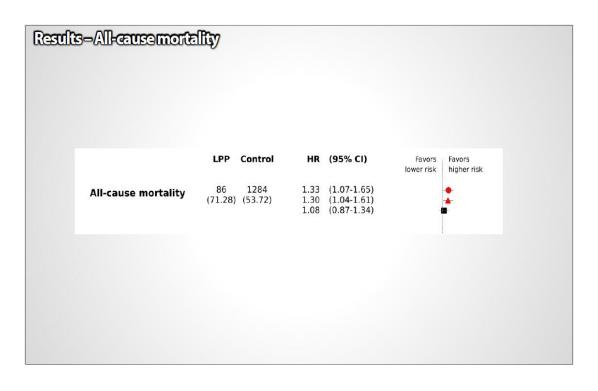
#### Results - Baseline demographics of study population Value (count [%] or mean ± SD) Characteristics Lichen planopilaris Controls p 2,026 (100%) 40.520 (100%) No. of subjects 1,178 (58.14%) 23,560 (58.14%) 1.000 Female sex, n (%) Characteristics Lichen planopilaris Controls p 47.80 ± 16.19 47.80 ± 16.20 1.000 Age at index, years Health Examination Characteristics BMI, kg/m<sup>2</sup> 23.71 ± 3.60 23.52 ± 3.49 <.05 1.000 Insurance type, n (%) 682 (33.66%) 12,685 (31.31%) Obesity\*, n (%) <.05 Standard 1,877 (92.65%) 37,540 (92.65%) 79.90 ± 10.49 79.39 ± 12.12 Waist circumference, cm Medicaid 149 (7.35%) 2,980 (7.35%) 555 (27.39%) Central obesity<sup>†</sup>, n (%) 10,104 (24.94%) <.05 Income level, n (%) Systolic BP, mmHg 120.51 ± 15.05 120.99 ± 15.49 .17 Highest 737 (36.38%) 14,740 (36,38%) Diastolic BP, mmHg 74.83 ± 10.20 75.23 ± 10.26 .09 583 (28.78%) 11,660 (28.78%) Higher Fasting glucose, mg/dL 97.59 ± 26.44 98.00 ± 25.54 .48 449 (22.16%) 8,980 (22.16%) 192.43 ± 37.98 193.10 ± 42.34 .50 Total cholesterol, mg/dL Lower 57.46 ± 20.89 57.49 ± 24.79 257 (12.69%) 5,140 (12.69%) HDL, mg/dL .96 LDL, mg/dL 112.36 ± 42.75 113.38 ± 51.66 .45 Smoking, n (%) TG, mg/dL 119.67 ± 99.87 122.63 ± 91.29 21 1,409 (70.00%) 27,663 (68.90%) Never smoker AST, U/L 24.85 ± 17.06 25.03 ± 19.71 .69 266 (13.21%) 4,770 (11,88%) Ex-smoker 24.31 ± 26.78 23.77 ± 24.97 ALT, U/L 338 (16.79%) 7,717 (19.22%) Current smoker 32.94 ± 48.75 33.90 ± 51.91 γ-GT, U/L .42 981 (48.42%) 20,849 (51.45%) <.01 Drinking, n (%) Creatinine, mg/dL 0.88 ± 0.64 0.89 ± 0.91 .65 CCI at index date 2.32 ± 2.50 2.18 ± 2.41 <.05 eGFR, ml/min/1.73m<sup>2</sup> 89.30 ± 41.41 88.67 ± 41.46 .53 VISION 2028 WONJU DERMATOLOGY "best department where we become the best"



	Prevalent diseases	at the index		Incident diseases du	ring follow-up	
Allergic disease	LPP Control	OR (95% CI)	Favors lower odds higher odds	LPP Control	HR (95% CI)	Favors Favors lower risk higher risk
Atopic dermatitis	359 3141 (17.720) (7.752)	2.56 (2.27-2.89) 2.57 (2.28-2.90) 2.57 (2.28-2.90)	1	110 1276 (110.97) (57.09)	1.94 (1.60-2.36) 1.95 (1.60-2.36) 1.93 (1.59-2.35)	:
Allergic rhinitis	978 18084 (48.272)(44.630)	1.16 (1.06-1.27) 1.15 (1.05-1.25) 1.14 (1.04-1.25)		367 6112 (655.47)(498.29)	1.32 (1.18-1.46) 1.32 (1.18-1.46) 1.32 (1.18-1.46)	
Asthma	433 7546 (21.372)(18.623)	1.19 (1.07-1.33) 1.17 (1.05-1.30) 1.15 (1.03-1.29)		132 2338 (138.64)(119.55)	1.16 (0.97-1.38) 1.14 (0.96-1.36) 1.14 (0.95-1.35)	•
Endocrine disease						
Diabetes mellitus	268 4720 (13.228)(11.649)	1.16 (1.01-1.32) 1.12 (0.98-1.28) 1.07 (0.92-1.25)		103 2023 (96.66) (94.03)	1.03 (0.85-1.26) 1.00 (0.82-1.21) 0.98 (0.80-1.19)	<b>:</b>
Hyperthyroidism	69 1395 (3.406) (3.443)	0.99 (0.77-1.26) 0.98 (0.77-1.25) 0.97 (0.76-1.24)	:	41 526 (34.96) (22.27)	1.57 (1.14-2.16) 1.57 (1.14-2.16) 1.58 (1.15-2.17)	<u></u>
Hypothyroidism	128 1748 (6.318) (4.314)	1.50 (1.24-1.80) 1.46 (1.21-1.76) 1.45 (1.20-1.74)	<b>:</b>	58 1042 (50.71) (44.71)	1.13 (0.87-1.48) 1.13 (0.86-1.47) 1.12 (0.86-1.46)	÷
Thyroiditis	59 901 (2.912) (2.224)	1.32 (1.01-1.72) 1.30 (0.99-1.70) 1.29 (0.99-1.69)	•	36 502 (30.50) (21.01)	1.45 (1.04-2.04) 1.45 (1.04-2.04) 1.46 (1.04-2.04)	<u>.</u>
Polycystic ovarian disease	8 153 (0.395) (0.378)	1.05 (0.51-2.13) 1.03 (0.50-2.09) 1.04 (0.51-2.12)	-	4 136 (3.28) (5.58)	0.59 (0.22-1.59) 0.61 (0.22-1.64) 0.62 (0.23-1.68)	









#### Discussion

- Our data identified <u>risk and incidence of comorbid diseases</u>, and <u>mortality</u> in patients with LPP compared to those without LPP.
- Autoimmune nature of LPP
  - <u>Connective tissue diseases</u> and <u>psoriasis</u> was both more prevalent and showed increased risks in LPP patients.
- Allergic diseases revealed a significant association with LPP.
  - State of a high level of estrogen level may affect shifting T-helper (Th) type 1 to Th2 immune response,
    which may support an increased prevalence of LPP in females.

    Tavakolpour S et al. Int J Womens Dermatol 2019.
    Sabahi F et al. Am J Reprod Immunol 1995.
  - Previous studies showed a high prevalence of contact allergies, suggesting routine patch testing for patients with LPP and FFA.

Prasad S et al. J Am Acad Dermatol 2020. Pastor-Nieto MA et al. Contact dermatitis 2021.

 However, the precise mechanism in associating LPP and Th1 or Th2 response is remained to be identified.

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#### Discussion

- Thyroid diseases and LPP
  - Thyroid signaling on keratinocytes and hair follicles was proposed for this association.
  - Antibodies to the unknown follicular antigen may cross-react against the thyroid, leading to thyroiditis or
    eliciting an aberrant humoral response to the thyroid, or vice versa.

Trager MH et al. J Am Acad Dermatol 2021 Atanaskova Mesinkovska N, et al. J Am Acad Dermatol 2014

- Current evidence on the relation between LPP and cardiovascular diseases is unclear
- Skin cancers and LPP
  - Chronic inflammation and damage of epidermal stem cells could be one factor, resulting development of SCCs
  - Although the underlying pathogenesis in transition into the atypical cells and progress to the cancers is remained to be fully elucidated, such risk is not negligible to date, considering the significance of the disease.

Manatis-Lornell A,et al. J Am Acad Dermatol 2020. Garrido Colmenero C et al. J Dermatol Case Rep 2013. Ratushny V et al. J Clin invest 2012.

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#### **Discussion**

- Iron deficiency anemia and vitamin D deficiency in LPP
  - The relation between hair loss and nutritional deficiencies has been reported, and the authors found a reduced amount of hair loss in the iron and L-lysine supplemented group compared to the placebo group (31% vs. 9%).
  - However, causality or definite association between iron deficiency and LPP is inconsistent

Cevasco NC et al. J Am Acad Dermatol 2007. Bolduc C et al. J Am Acad Dermatol 2016.

- Vitamin D deficiency has been evaluated in many reports, most of which have shown variable results.
- As vitamin D deficiency is associated with alopecia areata, a disease also mediated by the immunologic response, it may also have a role in scarring alopecia or LPP.

Arasu A et al. JAAD Int 2022. Tsai TY et al. J Am Acad Dermatol 2018.

- · All-cause mortality not significantly differed
  - The specific causes of death did not show significance differences (infectious, neoplasms, endocrine, neurologic, cardiovascular, and respiratory causes)
  - · An autoimmune reaction itself or associated autoinflammatory conditions could be one of the contributors.

Mitratza M et al. Rheumatology 2021.

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#### Discussion

- Limitations
  - The lack of detailed characteristics of each group and its single ethnicity

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## Conclusion

- Our study demonstrates the landscape of disease association and overall mortality risk in patients with LPP.
- Among investigated, <u>psoriasis</u>, <u>allergic diseases</u>, <u>thyroid disease</u>, <u>NMSCs</u>, <u>psychiatric</u>
   <u>diseases</u>, <u>vitamin D deficiency</u>, <u>and iron deficiency anemia</u> seem to be associated with
   LPP.
- All-cause mortality risk was not significantly differed between LPP and control groups.
- Clinicians should comprehend the disease risks in patients with LPP; thus, optimization of laboratory works and treatments with close follow-ups should be needed.

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# Quality of life and financial stress assessment in Korean patients with female pattern hair loss

Hye Won Hwang, Sunmin Ryou, Jae Won Lee, Kyung-Ju Lee, Seon Bok Lee, Hyun-Tae Shin, Ji Won Byun, Jeonghyun Shin, Gwang Seong Choi

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





# Quality of life and financial stress assessment in Korean patients with female pattern hair loss

<u>Hye Won Hwang,</u> Sunmin Ryou, Jae Won Lee, Kyung-Ju Lee, Seon Bok Lee, Hyun-Tae Shin, Ji Won Byun, Jeonghyun Shin and Gwang Seong Choi

<sup>1</sup>Department of Dermatology, Inha University School of Medicine, Incheon, Republic of Korea.

\*Conflicts of interest: The authors have nothing to disclose



# Introduction

- Alopecia is a dermatologic condition that affects the pilosebaceous unit in both men and women.
- The most common cause of <u>hair loss in women is female pattern hair loss(FPHL)</u> experienced by up to 40% of women.
- Although alopecia is a benign disorder, it results psychosocial aspects of the female patients' quality of life(QoL) and in an increase of frequent clinic visiting.
- Nevertheless, there are few epidemiological studies on their <u>relationship with QoL of FPHL patients in Korea.</u>
  - Patients with alopecia areata demonstrate poor QoL scores.

Br J Dermatol. 2016 Sep;175(3):561-71.

- The severity of male and female pattern hair loss in Korean was not associated with QoL.
   Korean J Dermatol 2015;53(9):700-707.
- Female alopecia have and severe impact on psychosocial aspect.
   Int J Womens Dermatol. 2018 Mar; 4(1): 18–22.

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# **Objectives**

The purpose of this study was to investigate <u>relationship</u> between quality of life and financial stress in FPHL patients among Korean female patients.

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# Materials and Methods

#### **Participants**

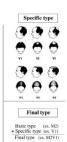
- · A single-center: Inha university hospital, department of dermatology
- Total of <u>167 Korean female pattern hair loss patients</u> for 2020.06 2022.06 who visited for management of pattern hair loss
- Age: 15 74 years old, all female patients

#### Methods

- · Investigation of quality of life
  - Interviewed questionnaire: the Hair Specific Skindex-29
- The severity of hair loss: "BASP classification"
  - · Evaluated by dermatologists
  - Mild: L, M0, M1, C1, V1, and F1
  - Moderate: M2, C2, V2, and F2
  - Severe: M3, C3, U1, U2, U3, V3, and F3
- · The questionnaires for financial stress include
  - · Overall and medical expenses for alopecia
  - The number of clinic visiting

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# **Materials and Methods**

#### Statistical analyses

- SPSS statistics version 24.0 (SPSS Inc, Chicaco, III) software was used for statistical analysis
- <u>Pearson correlation test</u>: to know the correlation between the severity of FPHL and QoL and total medical expenditure
- <u>Linear regression analysis</u> was performed to find factors that affect the quality of life based on the result of Pearson correlation test.
- For statistical tests, the level of significance was set at <u>p < 0.05</u>.

#### **Ethics statement**

 This study was approved by the in (IRB number: INHAUH 2020-06-011) and was conducted in accordance with the declaration of Helsinki principles.

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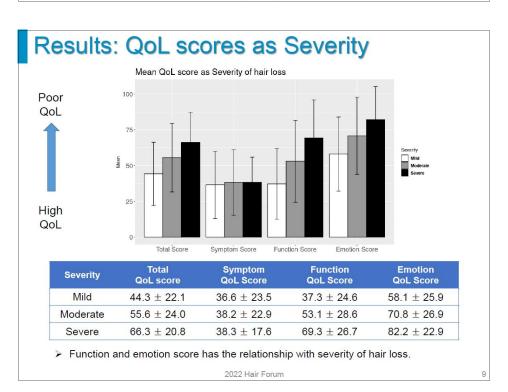
# General characteristics of FPHL patients

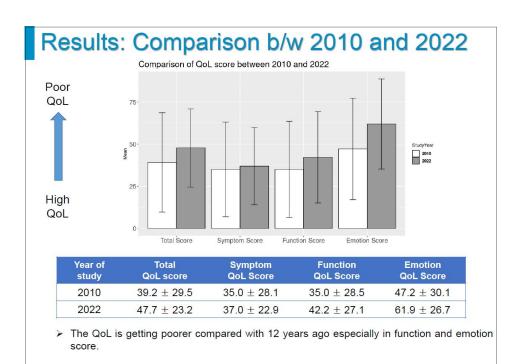
Characteristics Value		Characteristics	Value	
Total number of patients	167	Marital status		
Age	$37.5 \pm 13.4$	Married	91 (54.49%)	
< 20	8 (4.79%)	Single	74 (44.31%)	
20 ~ 25	29 (17.37%)	Non-response	2 (1.20%)	
26 ~ 35	45 (26.95%)	<b>Duration of hair loss</b>		
36 ~ 50	57 (34.13%)	≤ 1 year	20 (11.98%)	
51 ~ 65	23 (13.77%)	1 ~ 5 years	68 (40.72%)	
≥ 66	5 (2.99%)	≥ 5 years	79 (47.31%)	
Family history of hair los	s	Severity of hair loss		
Yes	90 (53.89%)	Mild	127 (76.05%)	
No	76 (45.51%)	Moderate	28 (16.77%)	
Non-response	1 (0.60%)	Severe	12 (7.19%)	

# Questionnaires – Hair specific skindex-29

변호	질 문	변호	질 문					
1	두피가 아프다. (Sx)	16	물에 닿는 것이 번거롭다(목욕, 세수). (Fx)					
2	나의 탈모상태는 숙면에 영향을 준다. (Fx)	17	나의 탈모 상태 때문에 다른 사람에게 호강을 표시하기 어렵다. (Fx)					
3	나는 나의 탈모 상태가 혹시 심각한 것이 아닐지 걱정한다. (Em)	18	나의 두피는 자극에 민감하다. (Sx)					
4	나의 탈모 상태는 일이나 취미생활을 힘들게 한다. (Fx)	19	나의 탈모 상태는 대인관계에 영향을 미친다. (Fx)					
5	나의 탈모 상태는 나의 사회생활에 나쁜 영향을 미친다. (Fx)	20	나는 탈모 상태 때문에 난처하다. (Em)					
6	나의 탈모상태는 나를 우울하게 한다. (Em)	21	나의 탈모 상태는 내가 사랑하는 사람들에게도 걱정거리이다. (Fx)					
	두피가 화끈거리거나 따갑다. (Sx)	22	나는 탈모 상태로 좌절감을 느낀다. (Em)					
8	나는 탈모 상태 때문에 집에 있으려고 하는 편이다. (Fx)	23	나의 두피는 예민하다. (Sx)					
9	나는 탈모 상태 때문에 횽이 남지 않을까 걱정한다. (Em)	24	탈모 상태 때문에 다른 사람과 함께 있고 싶지 않다. (Fx)					
10	두피가 가렵다. (Sx)	25	나는 탈모 상태 때문에 수치심을 느낀다. (Em)					
	나의 탈모 상태는 내가 좋아하는 사람들과 친밀하게 지내는 데에 영향을 미친다.(Fx)	26	두피에서 피가 난다. (Sx)					
12	나는 탈모 상태 때문에 부끄럽다. (Em)	27	나의 탈모 상태 때문에 짜증이 난다. (Em)					
13	나는 탈모 상태가 점점 더 나빠질까 걱정된다. (Em)	28	나의 탈모 상태는 나의 성생활에 방해가 된다. (Fx)					
14	나는 탈모 상태 때문에 일을 혼자서 하려는 경향이 있다. (Fx)	29	탈모 상태 때문에 피곤하다. (Fx)					
15	나는 탈모 상태 때문에 화난다.(Em)							
<ul> <li>Symptom (Sx): 7 questions</li> <li>Function (Fx): 12 questions</li> <li>Emotion (Em): 10 questions</li> </ul>								
	2022 Ha	air Foru	7					

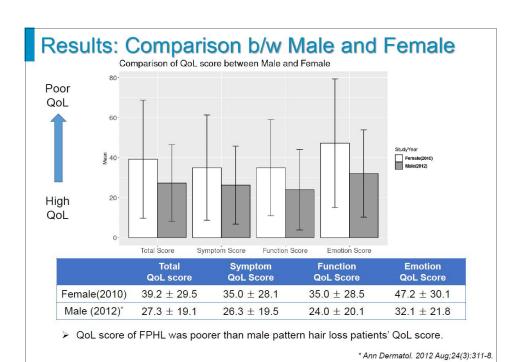
#### Results: Skindex-29 scores QoL Score Poor QoL 100 80 90 9 40 50 High QoL Moderate **BASP** severity Total Score Mild Moderate Severe QoL score QoL Score QoL Score QoL Score 47.75 55.61 66.25 44.27 Mean Standard 23.17 22.08 23.99 20.83 Deviation > The total score of QoL is getting poorer as severity of hair loss worse. 2022 Hair Forum





2022 Hair Forum

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2022 Hair Forum

#### Results: Comparison b/w Male and Female Comparison of QoL score between Male and Female Poor QoL High QoL Total Score Emotion QoL Score Symptom QoL Score **Total Function QoL Score** QoL score Female(2022) $47.7 \pm 23.2$ $37.0 \pm 22.9$ $42.2 \pm 27.1$ $61.9 \pm 26.7$ $26.3 \pm 19.5$ Male (2012)\* $27.3 \pm 19.1$ $24.0 \pm 20.1$ $32.1 \pm 21.8$

QoL score of FPHL was poorer than male pattern hair loss patients' QoL score.

2022 Hair Forum

# Discussion

- > This is the study of quality of life for Korean female pattern hair loss.
  - In previous study including 90 patients of FPHL, the severity of male and female pattern hair loss was not associated with QoL and the severity of FPHL was not associated with QoL.

김동영, 권오상, Korean J Dermatol 2015;53(9):700-707.

\* Ann Dermatol. 2012 Aug;24(3):311-8.

- · However, this study results the severity of FPHL is related with QoL.
- · The difference of the two studies
  - Our study includes: under 20 year-old patient and severe degree of female patients.
- > Total QoL, function and emotion score have been worse than 10 years ago.
  - FPHL affects patients' QoL much more than 10 years ago.

2022 Hair Forum

# **Limitation & Conclusion**

- Selection bias
  - > Single centered
  - > Visitor of department of dermatology
- Small number of patients in more than 66-year-old group. (5, 2.99%)
- > The is preliminary study. We are going to collect more participants for the study.
- > Seventeen patients had other diseases:
  - ➤ 10 patients of seborrheic dermatitis, and 3 patients of atopic dermatitis, 3 patients of seborrheic dermatitis and PCOS, and 1 patient of vitiligo.
  - > All were mild severity of hair loss
- > The Korean female patient's psychological stress for hair loss could result poor quality of life and motivate the patient to visit clinics more according to the severity of hair loss.

2022 Hair Forum

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# Irisin, myokine, stimulates the telogen-anagen transition through Wnt/β-catenin signaling pathway

Jung Ok Lee, Yu Jin Kim, Jung Min Lee, Beom Joon Kim

Department of Dermatology, College of Medicine, Chung-Ang University, Seoul, Korea

August 20, 2022

Irisin, myokine, stimulates the telogenanagen transition through Wnt/β-catenin signaling pathway

Department of Dermatology, College of Medicine, Chung-Ang University, Seoul 06974, Korea

Lee Jung Ok, Kim Yu Jin, Lee Jung Min, Kim Beom Joon

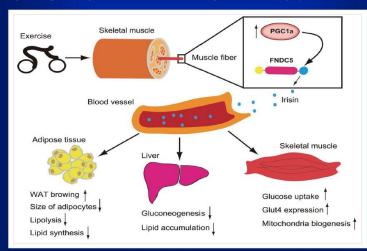


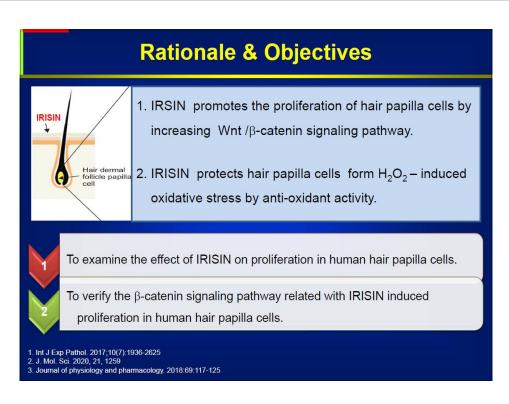
## **Contents**

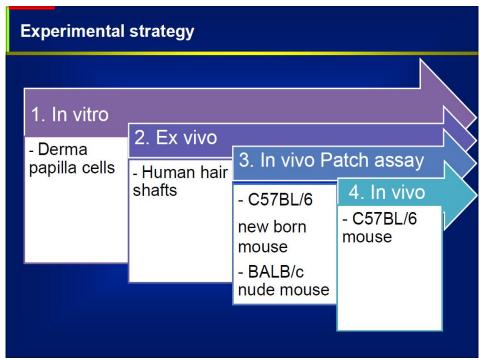
- **I.** Introduction
- II. Rationale & Objective
- **III.** Method
- **IV.** Results
- V. Conclusion

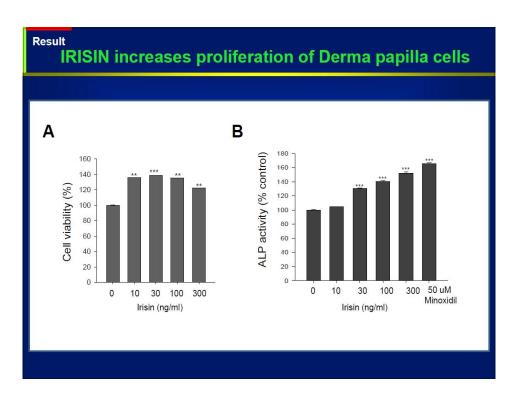
# Introduction What is IRISIN? Adipo-myokine

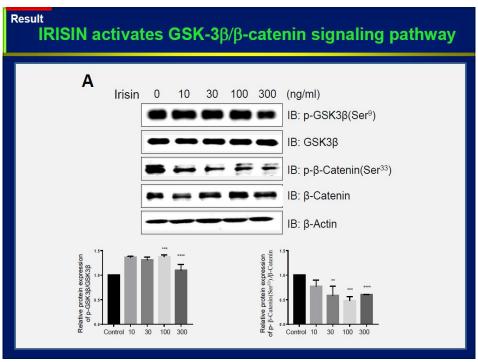
- ➤ Known as FNDC5 (Fibronectin type Ⅲ domain-containing protein 5)
- Play a regulatory role in an immune system activity ( IL-6 or TNF-α)

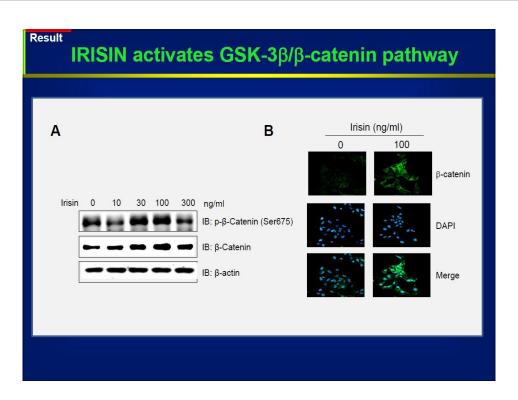


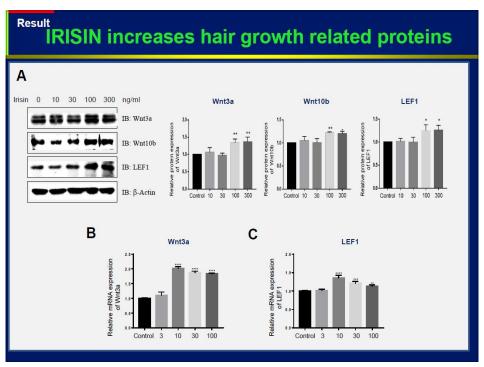


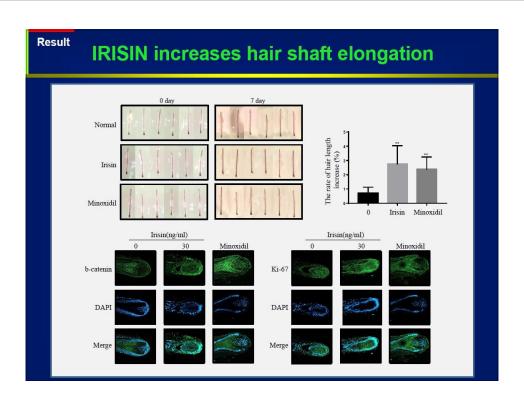




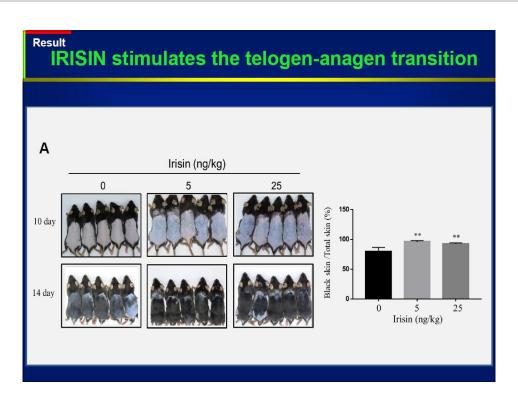


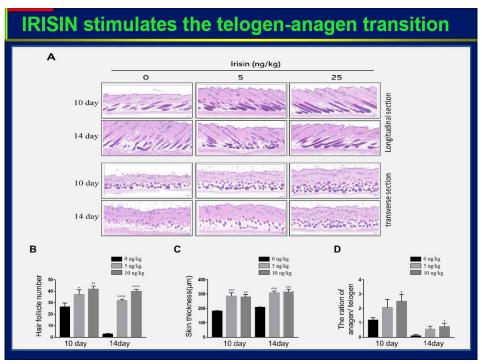


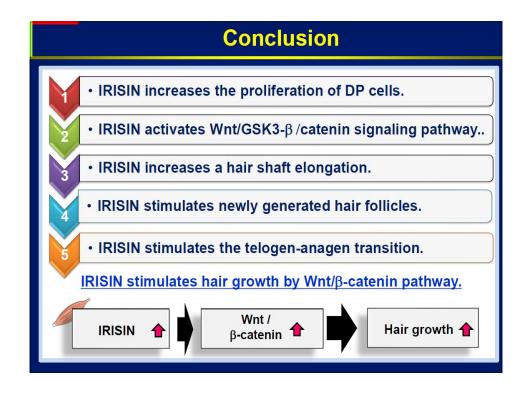








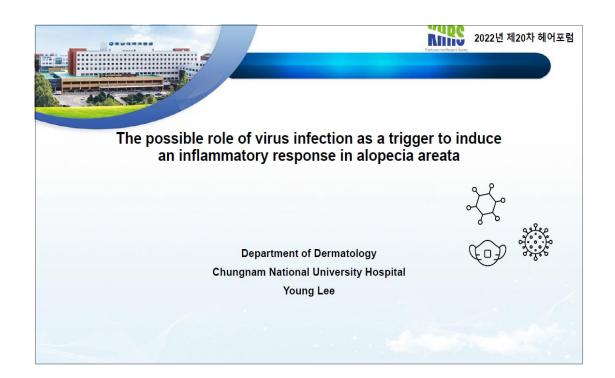


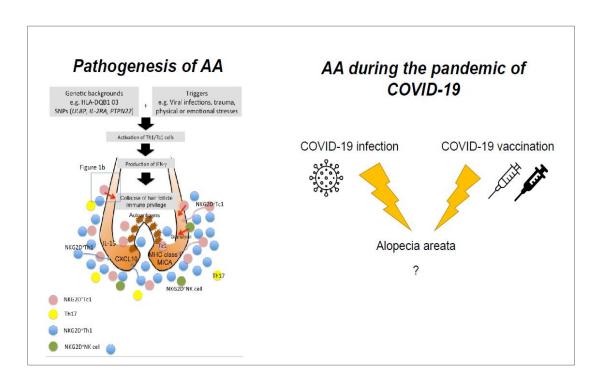


# The possible role of virus infection as a trigger to induce an inflammatory response in alopecia areata

### Young Lee

Department of Dermatology, Chungnam National University Hospital, Daejeon, Korea





# Human coronaviruses and their cellular receptors

Coronavirinae Genera	Strains	Discovery	Cellular receptor
Alpha-corovavirus	HCoV-229E	1966	Human Aminopeptidase N (CD13)
	HCoV-NL63	2004	ACE2
Beta-coronavirus	HCoV-OC43	1967	9-O-Acetylated sialic acid
	HCoV-HKU1	2005	9-O-Acetylated sialic acid
	SARS-CoV	2003	ACE2
	MERS-CoV	2012	DPP4 (CD26)
	SARS-CoV-2	2020	ACE2

DPP4, Dipeptidyl peptidase-4; ACE2, Angiotensin-converting enzyme 2

Lim YX. et al., Diseases. 2016 Jul 25;4(3). Hoffmann M Cell. 2020 Apr 16;181(2):271-280.e8.

# Alopecia in patients with COVID-19: A systematic review and meta-analysis

Characteristics	AA	AE	AGA	PA	TE	Unclassified
Number of patients (n = 1826)	143 (7.8%)	2 (0.1%)	561 (30.7%)	2 (0.1%)	362 (19.8%)	756 (41.4%)
Mean age (y), number of patients with reported age, age range	36.1 (n = 10) Fange: 7-64	29.5 (n = 2) Range: 24-35	61.1 (n = 484) Range: 18-100	43.0 (n = 2) Range: 37-49	48.0 (n = 352) Range: 15-88	51.5 (n = 206) Range: NR
Sex	4 M 6 F 133 NR	0 M, 2 F	504 M, 57 F	2 M, 0 F	68 M, 284 F 10 NR	29 M, 161 F 566 NR
Country of patient	Italy	Brazil	Brazil	Brazil	Brazil	Brazil
	Netherlands	Iraq	Iran	United States	China	China
	Turkey		Peru		Iraq	Iran
	United States		Spain		Italy	Japan
			Switzerland		Pakistan	Mexico

AA, Alopecia areata; AE, arragen effluvium; AGA, andregenic alopecia; F, female; M, male; NR, not reported; P1, pressure-induced alopecia; Ti

Alopecia areata (AA) Androgenic alopecia (AGA) Telogen effluvium (TE)

#### Systematic reviews/meta-analysis

# Association between alopecia areata and COVID-19: A systematic review

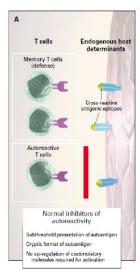
Rachel E. Christensen, BS,  $^{\rm a}$  and Mohammad Jafferany, MD  $^{\rm b}$  New Brunswick, New Jersey and Mount Pleasant, Michigan

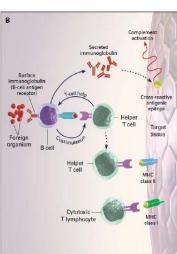
#### **CAPSULE SUMMARY**

- This study synthesizes various independent reports of patient experience with alopecia areata following infection with SARS-CoV-2.
- Assessing the existing literature of alopecia areata following infection with SARS-CoV-2 may assist dermatologists in identifying patients at risk for alopecia areata and educating these patients on seeking dermatologic care should hair loss occur.

JAAD Int. (2022)

## Molecular mimicry and autoimmunity





Molecular mimicry is the prevailing hypothesis as to how viral antigens initiate and maintain autoimmune responses which lead to specific tissue damage.

Foreign organism  $\rightarrow$  antigen presentation

- → T cell stimulation
- → Immune response to molecular mimicry (host)

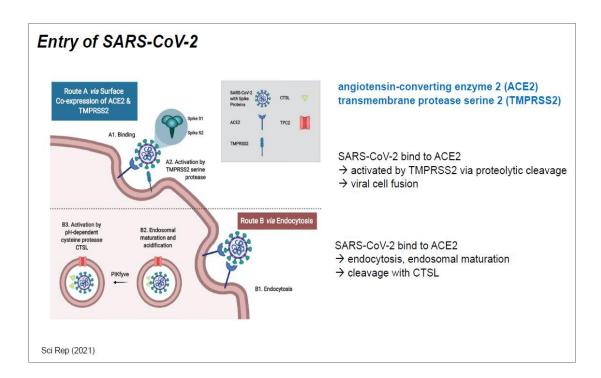
B cell  $\Rightarrow$  antibody production  $\Rightarrow$  activation of complement pathway  $\Rightarrow$  tissue damage

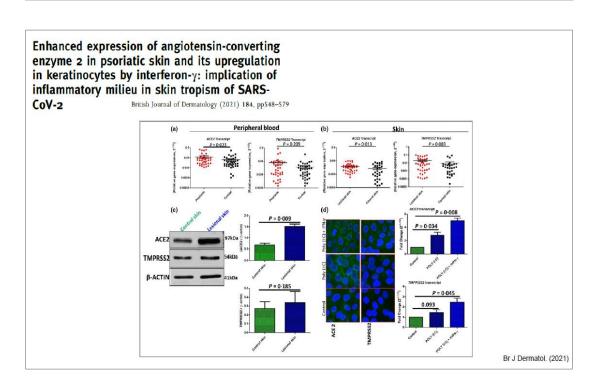
N Engl J Med (1999)

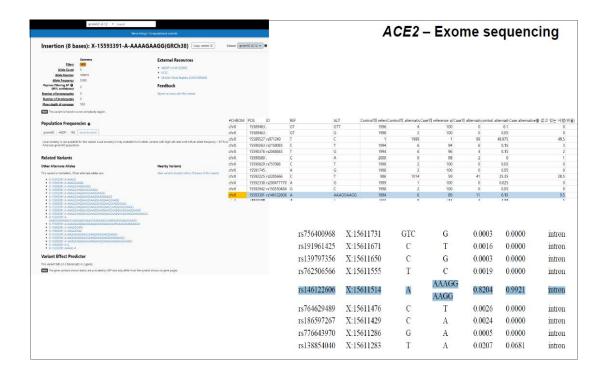
#### Reaction of Human Monoclonal Antibodies to SARS-CoV-2 Proteins With Tissue Antigens: Implications for Autoimmune Diseases

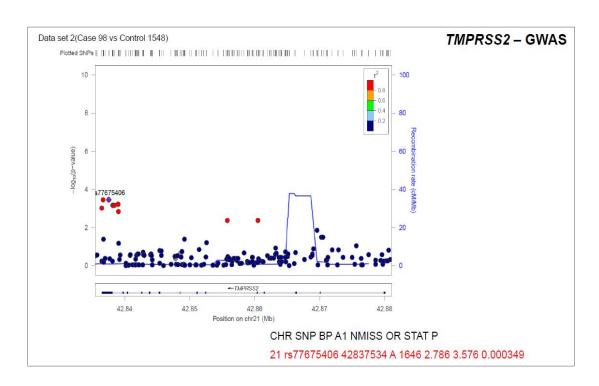
TABLE 1 | % Reactivity of SARS-CoV-2 Spike, Nucleoprotein, Envelope and Membrane Protein Antibodies with the Same Proteins and Different Cross-Reactive

Antigens	Spike protein OD	% reactivity	Nucleoprotein OD	% reactivity	Envelope protein OD	% reactivity	Membrane protein OD	% reactivity
SARS-CoV-2	3.40	100 ++++	3.76	100 ++++	3.68	100 ++++	3.78	100 ++++
Actin	0.74	17.6 +	1.1	27.1 ++	0.78	18.0 +	0.95	22.2 +
Mitochondrial antigen	1.52	41.8 +++	1.94	50.1 +++	2.03	53.4 +++	2.58	67.0 ++++
(M2)								
ENA.	0.85	21.0 +	0.44	9.0 +	0.53	11.0 +	0.21	22-
NA	1.34	36.2 ++	0.97	23.6 +	0.13	0.0 -	0.46	8.8 +
Histone	0.65	14.8 +	0.92	22.2 +	0.27	3.7 -	0.78	17.6 +
S100B	0.46	9.0 +	0.87	20.8 +	0.23	2.5 -	0.44	8.2 +
MBP	0.53	11.1 +	0.55	12.0 +	0.41	7.6 +	0.32	4.9 -
NEP	1.98	56 ++++	0.42	8.5 +	0.27	3.7 -	2.0	51.1 +++
Synapsin	0.81	19.8 +	0.95	23.0 +	0.17	0.08 -	0.28	3.8 -
Beta-amyloid P	0.83	20.4 +	0.82	19.4 +	0.18	1.1 -	0.36	6.0 +
Tau protein	0.41	7.4 +	0.23	3.3 -	0.18	1.1 -	0.28	3.8 -
Collagen	0.45	8.6 +	0.65	14.8 +	0.18	1.1 -	0.85	19.2 +
Alpha-myosin	0.72	17.0 +	0.89	21.3 +	0.36	6.2 +	0.94	21.2 +
Tropomyosin	0.21	1.2 -	0.25	3.8 -	0.25	3.1 -	0.58	12.1 +
TPO	0.98	25.1 ++	0.95	23.0 +	0.26	3.3 -	0.96	22.5 +
Liver microsome	1.00	25.7 ++	1.00	24.4 +	0.17	0.08 -	0.30	4.4
PDH peptide	0.91	22.9 +	0.94	22.7 +	0.22	2.2 -	0.64	13.7 +
GAD-65	1.35	36.5 ++	1.08	26.5 ++	0.15	0.03 -	0.43	7.9 +
Insulin	0.25	2.5 -	0.16	0.4 -	0.15	0.03 -	0.97	22.8 +
Insuin-R	0.72	17.0 +	1.77	45.5 +++	0.21	1.9 -	0.52	10.4 +
Phospholpid	0.93	23.5 +	0.83	19.7 +	0.37	6.5 +	0.95	22.2 +
tTG-6	0.58	12.7 +	0.44	9.0 +	0.17	0.08 -	0.20	1.6 -
tTG-3	0.42	23.2 +	0.92	22.2 +	0.18	1.1 -	0.23	2.4 -
tTG-2	0.79	19.2 +	0.72	16.7 +	0.24	2.8 -	0.25	3.0 -
Int epi cells	0.49	9.9 +	0.46	9.6 +	2.13	56.0 ++++	0.95	22.2 +
Beta-catenin	0.95	24.1 +	0.56	12.3 +	0.24	2.8 -	0.15	0.3 -
Claudin	0.33	4.9 -	0.26	4.1 -	0.15	0.03 -	0.17	0.8 -
Occ + zon	0.72	17.0 +	1.32	33.0 ++	0.61	13.2 +	1.12	26.9 ++
27 other tissues*	0.34	5.2 -	0.36	6.8 -	0.30	4.5	0.32	4.9









Journal of Genetics (2020)99:53 https://doi.org/10.1007/s12041-020-01217-7 RESEARCH NOTE

Assessment of risk conferred by coding and regulatory variations of TMPRSS2 and CD26 in susceptibility to SARS-CoV-2 infection in human

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\*\*Popartnent of Biochemistry: School of Basic and Applied Sciences, Central University of Punjab, Bathinda 151 001, India
\*\*For correspondence: E-mail: subyasschi1012\*\*Gonund \*\*----

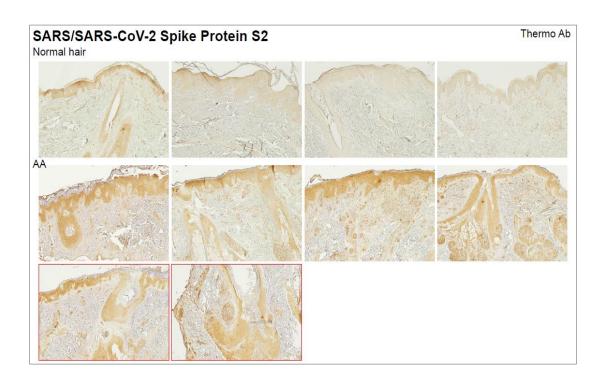
Received 13 April 2020; revised 10 May 2020; accepted 11 May 2020

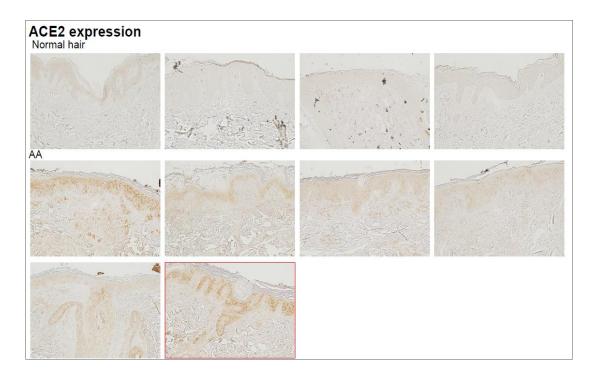
Abstract. At present, more than 200 countries and servicries are directly affected by the connavirus disease. 19 (COVID-19) pandemis, Incidence and case finally rate are significantly higher among elderly individuals (age 5-60 years), by pe 2-darbotes and hypertension patients. Cellular receptor ACE2, sering protease IMMFSS2 and ecoropcibles CD26 (also known as DPF4) are the three merhenes board proteins potentially implicated is ASRS-COV.20 infections. We hypothesised that connect variants from TAPSS2 and CD29 may play critical nois in infection assceptibility of predisposed populations for group of individuals. Coding (unseems) and regulatory variants from TAPSS2 and CD29 were studied acrose 5 global populations. From instense and two regulatory SMN+ were identified to have differential allicis frequency. Significant linkage discipation (LD) signature was observed in different populations. Modelled protein-protein intention (PPI) profited dation guideduit intentions between these two receptors and SARS-CoV-2 pales proteins (1S domain). However, two missiones SNN-pales patients (1S domain). However, two missiones SNPs, pales 2250760 (TAPSS2) and rs112999 (CD26), were not found to be involved physically in the salt intention for these participations and the direction of the contraction of the contractio on. Four regulatory suriants (is11267469, rs11916678, ps7765406 and rs713400) from TAPPRSS were found to one of TAPPRSS2 and publishighted yelevant ACC. rs13015288 a °UTUR virtual from CDV-flavor significant role in one of key regulatory agrees that could be involved in SARS-CoV-2 internalization. Overceptossion CDM through attention at rs13015288-C alkele was found critical and could explain the higher SARS-CoV-2 infected fatality rate in

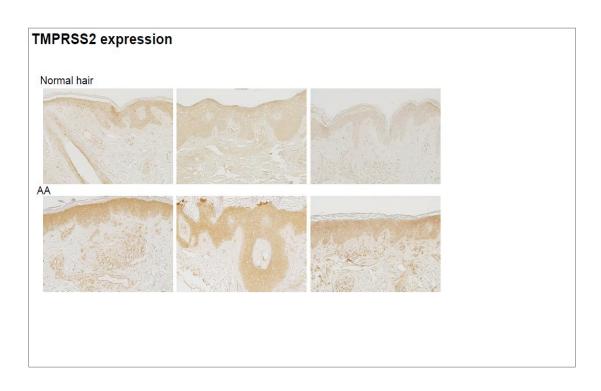
Keywords. coronavirus disease-19; severe acute respiratory syndrome coronavirus-2; dipeptidyl peptidase-4; transm serine 2; spike protein; type-2 diabetes.

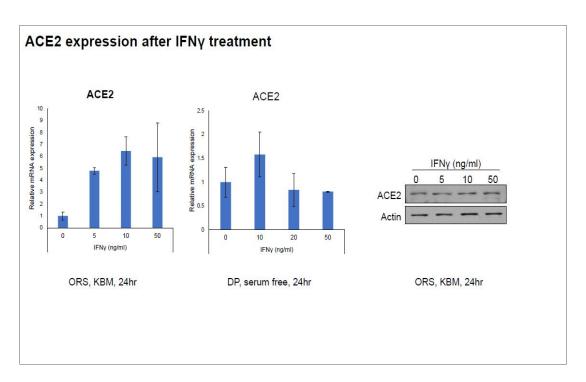
Four of these variants (rs112657409, rs11910678, rs77675406 and rs713400) are independent of the nonsynonymous SNP rs12329760 and have significant eQTL effects on MX1 and TMPRSS2 in different tissues

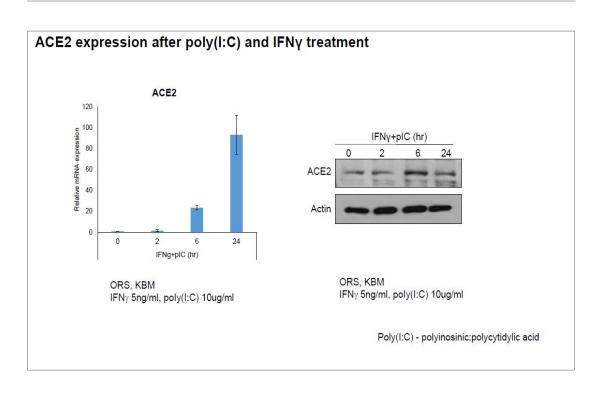
Four regulatory SNPs from TMPRSS2 (rs112657409, rs11910678, rs77675406 and rs713400) and one from CD26 (rs13015258) have significant role in regulation of expression of key regulatory genes (TMPRSS2, CD26 and MX1) that could be involved in SARS-CoV-2 infection.











### 1. 환자 임상경과 확인



Then, what??



GWAS 390명 (variant, SNP유무 확인)

- COVID-19 Vaccination 유무
- COVID-19 감염 여부
- Vaccination, 코로나 감염 이후 원형탈모의 변화 (악화정도)

## 2. in vitro study (1) molecular mimicry Spike Protein (5) Membrane protein (M) Envelope protein (E) Nucleocapsid (N) Spike protein expression in AA patients

IHC staining of membrane protein, envelope

protein, necleocapsid in AA scalp

(2) inflammation induction after COVID-19



induces virus—cell membrane fusion  $\rightarrow$  increases the infectivity of SARS-CoV-2



Inflammation pathway induction in ORS cells - NF-kB, inflammasome etc.

Spike (S) protein potently induces inflammatory cytokines and chemokines including IL-6, IL-1 $\beta$ , TNF $\alpha$ , CXCL1, CXCL2, and CCL2

elife. 2021

### The diagnosis of undiagnosed genetic hair disease: Beyond the exome

Hyun-Tae Shin

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

The diagnosis of undiagnosed genetic hair disease: beyond the exome

Inha University Hyun-Tae Shin

### Content

- Introduction
- Case 1: r/o keratosis follicularis spinulosa decalvans due to structure variation of ChrX
- Case 2: r/o hypotrichosis due to compound heterozygous mutations of HR
- Discussion

# Introduction Next generation sequencing (NGS): high throughput sequencing technology Preprocessing & Sequencing Alignment & variants call Reference sequence Cryule 1 Cycle 2 Cycle 3 Roy Signal Roy Signa

Meyerson, M., Gabriel, S., & Getz, G. (2010). Nature Publishing Group, 11(10), 685-696.

### Introduction

Whole exome sequencing (WES) vs whole genome sequencing (WGS)

	전장유전체 염기서열분석 (WGS)	전체 엑솜 염기서열분석 (WES)
탐색범위	전체 유전체 범위    신규 변이 탐색 가능	<ul> <li>엑솜 영역에 한정 (전체 유전체의 2%)*</li> <li>신규 변이 탐색 가능</li> </ul>
탐색항목	~400만개의 변이*     높은 해상도의 복제수변이     구조변이	~2만개의 변이*     낮은 해상도의 복제수변이     제한된 영역의 구조변이
비용	• 높음 (170만원 이하/소비자가)	보통 (70만원 이하/소비자가)
데이터량	• 많음 (120Gb from 30x)**	• 보통 (8Gb from 100x)**
5*	exon	intron 3* xon exon 결분석 (WGS)
5*	exon e 전체 엑솜 염기서일	xon exon 결분석 (WES)

Service	Price (만원)
WGS_30X	₩120-150
WGS_60X	₩200-300
WGS_100X	₩300-450
mRNA-Seq	₩50-60
WES(200X)	₩55-100
WES(100X)	₩42-60
Single Cell Gene Expression	₩700-800
Spatial transcriptome	₩850 ~

2021.10 기준, 세금제외

### Introduction

### Diagnostic rate of WES for congenital diseases

Regardless of DNA sequencing approach, it is estimated that the diagnostic rate using exome or genome sequencing is plateauing between 35% and 50% (Taylor et al. 2015; Wortmann et al. 2015; Clark et al. 2018; Powis et al. 2018). There is a need for other ap-

Cold Spring Harb Mol Case Stud. 2018 Dec; 4(6): a003392.

patients remain undiagnosed for years and many even die without an accurate diagnosis. In recent years, gene panels, microarrays, and exome sequencing have helped to identify the molecular cause of such rare and undiagnosed diseases. These technologies have allowed diagnoses for a sizable proportion (25–35%) of undiagnosed patients, often with actionable findings. However, a large proportion of these patients remain undiagnosed. In this review, we focus

Genome Med. 2022 Feb 28;14(1):23.

### Introduction

### Diagnostic rate of WES for congenital diseases

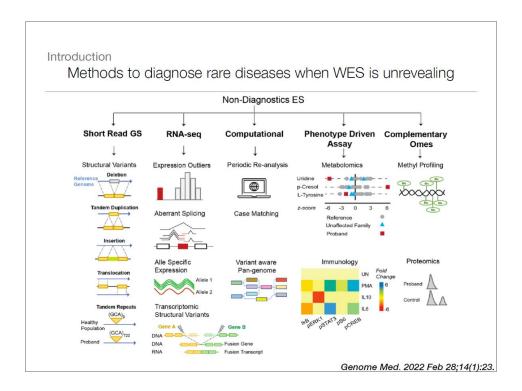
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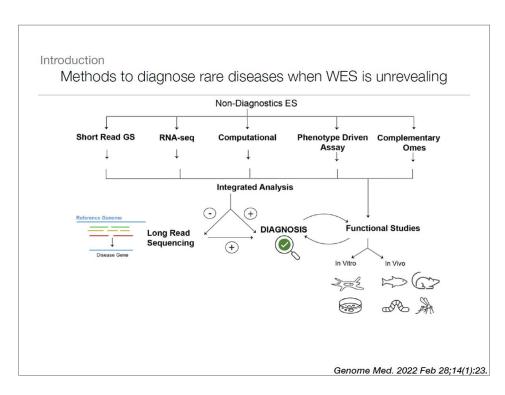
Cold Spring Harb Mol Case Stud. 2018 Dec; 4(6): a003392.

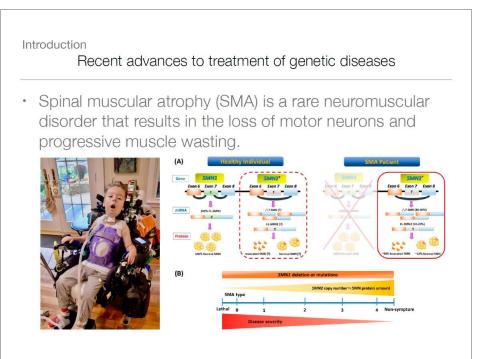
patients remain undiagnosed for years and many even die without an accurate diagnosis. In recent years, gene panels, microarrays, and exome sequencing have helped to identify the molecular cause of such rare and undiagnosed diseases. These technologies have allowed diagnoses for a sizable proportion (25–35%) of undiagnosed patients, often with actionable findings. However, a large proportion of these patients remain undiagnosed. In this review, we focus

Genome Med. 2022 Feb 28;14(1):23.

=> A large proportion of genetic disease patients remain undiagnosed.

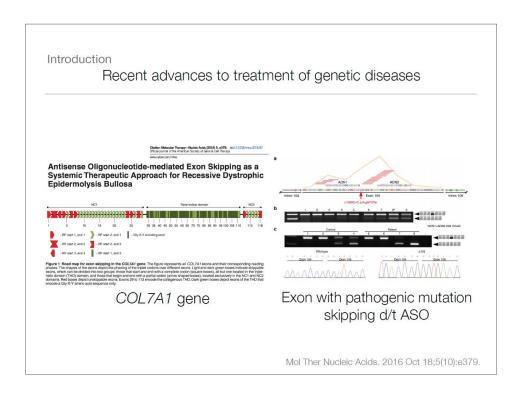


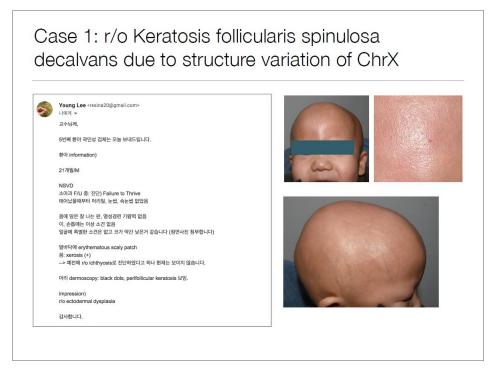


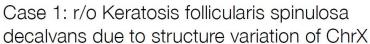


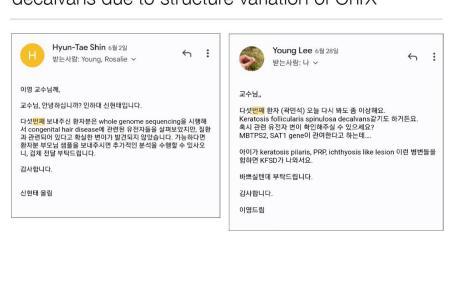
### Introduction Recent advances to treatment of genetic diseases FDA approved SMA therapy SMN2-Targeted Therapy SMN1-Targeted Therapy Α В С D SMN2 ---pre-mRNA---X ed (2016) ASO: antisense oligonucleotide 전세계서 가장 비싼 약 '졸겐스마' 마침내美 승인 한화 약 23억원 Brain Sci. 2021 Feb 5;11(2):194.



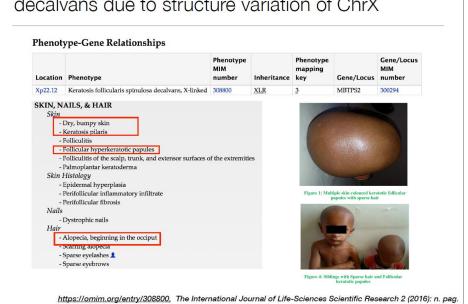










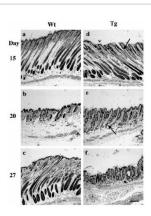


### Case 1: r/o Keratosis follicularis spinulosa decalvans due to structure variation of ChrX

Relation of Skin Polyamines to the Hairless Phenotype in Transgenic Mice Overexpressing Spermidine/Spermine N¹-Acetvltransferase

Marko Pietilä, Jyrki J. Parkkinen, Leena Alhonen, and Juhani Jänne

Pietila et al. found that overexpression of the SAT enzyme in a mouse model resulted in putrescine accumulation and a phenotype with skin and hair abnormalities reminiscent of human KFSD.



Dermal changes around the time of first catagen.

J Invest Dermatol. 2001 May;116(5):801-5.

### Case 1: r/o Keratosis follicularis spinulosa decalvans due to structure variation of ChrX

Hum Genet (2002) 111:235-241 DOI 10.1007/s00439-002-0791-6

### ORIGINAL INVESTIGATION

Giorgio Gimelli · Sabrina Giglio · Orsetta Zuffardi · Leena Alhonen · Suvikki Suppola · Roberto Cusano Cristiana Lo Nigro · Rosanna Gatti · Roberto Ravazzolo · Marco Seri

Gene dosage of the spermidine/spermine  $N^1$ -acetyltransferase (SSA7) gene with putrescine accumulation in a patient with a Xp21.1p22.12 duplication and keratosis follicularis spinulosa decalvans (KFSD)

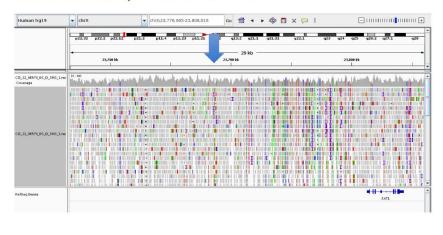
By analysis of polyamine metabolism in the cells of their patient, Gimelli et al. found that the levels of metabolites such as putrescine, spermidine, and spermine were consistent with overexpression of the SAT1 gene.

=> They proposed that overexpression of SAT1 and the consequent putrescine accumulation are involved in the KFSD phenotype.

Hum. Genet. 111: 235-241, 2002.

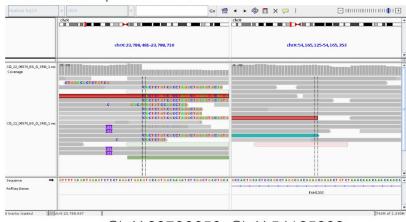
### Case 1: r/o Keratosis follicularis spinulosa decalvans due to structure variation of ChrX

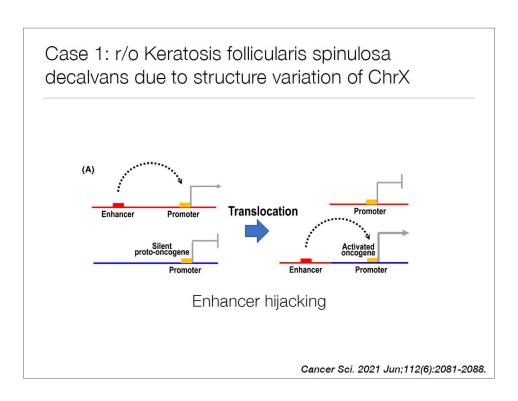
- No mutation in KFSD associated genes in Xp22.2-p21.2
- Inversion on upstream 12k of SAT1

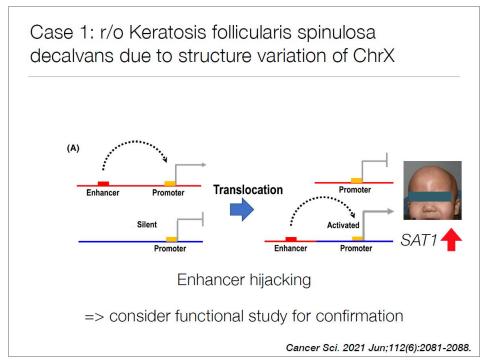


### Case 1: r/o Keratosis follicularis spinulosa decalvans due to structure variation of ChrX

- No mutation in KFSD associated genes in Xp22.2-p21.2
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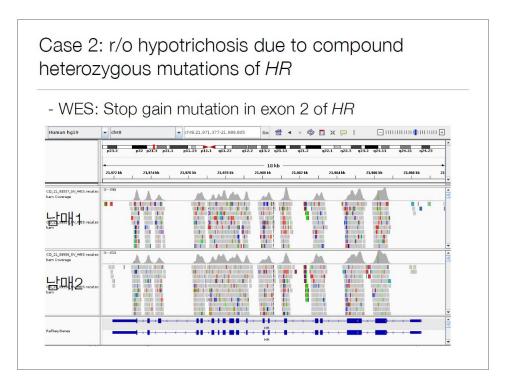


Case 2: r/o hypotrichosis due to compound heterozygous mutations of *HR* 





병력: 30대 남매 동반증상, 가족력 없음



### Case 2: r/o hypotrichosis due to compound heterozygous mutations of *HR*

### Androgenetic alopecia in heterozygous carriers of a mutation in the human hairless gene

Eli Sprecher, MD, PhD, <sup>a,b</sup> Adel Shalata, MD, <sup>a,c</sup> Kamal Dabhah, MD, <sup>d</sup> Boris Futerman, <sup>c</sup>
Shai Lin, MD, <sup>c</sup> Raymonde Szargel, MSc, <sup>a</sup> Reuven Bergman, MD, <sup>b</sup>
Rachel Friedman-Birnbaum, MD, <sup>b</sup> and Nadine Cohen, PhD<sup>a</sup> *Haifa and Deir El Assad, Israel* 

Sprecher et al. assessed the pattern of androgenetic alopecia in 31 healthy male second-degree relatives of patients affected with APL belonging to a large consanguineous kindred.

Sprecher et al. concluded that the presence of a deleterious mutation in one allele of the 'hairless' gene does not affect the pattern of androgenetic hair loss.

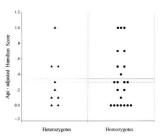
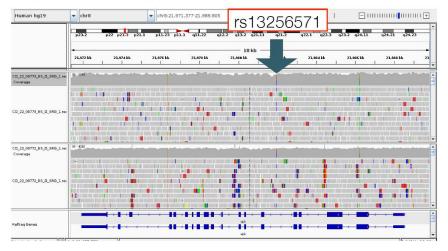


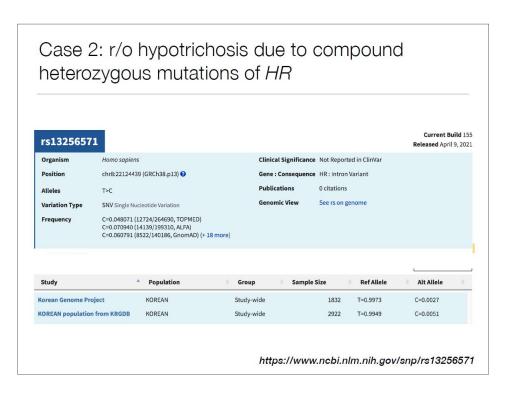
Fig. 3. Scatter plot of age-adjusted Hamilton score in healthy homoorypotes and heterozygous carriers of the 349-kdelC muration. Hamilton scores were corrected for age as indicated in "Material and Methods" (solid line: mean score in homozygotes; dotted line: mean score in homozygot

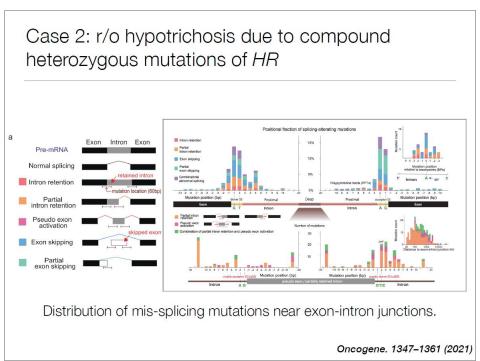
J. Am. Acad. Derm. 42: 978-982, 2000.

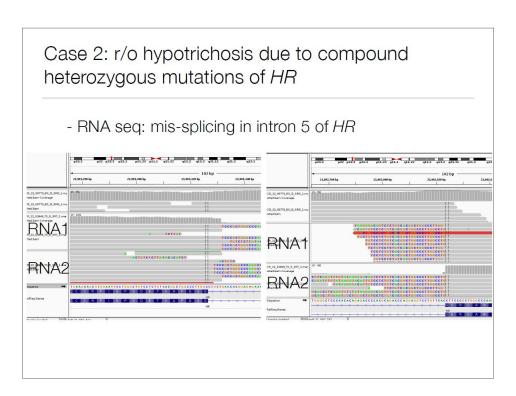
### Case 2: r/o hypotrichosis due to compound heterozygous mutations of *HR*

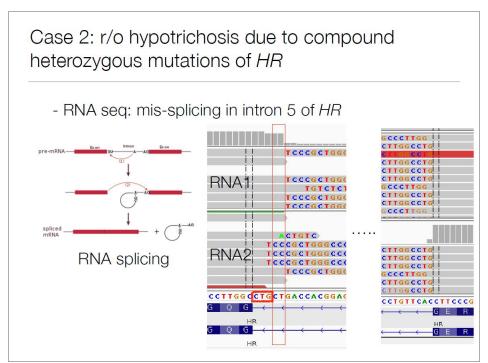
- WES: SNP in intron 5 of HR

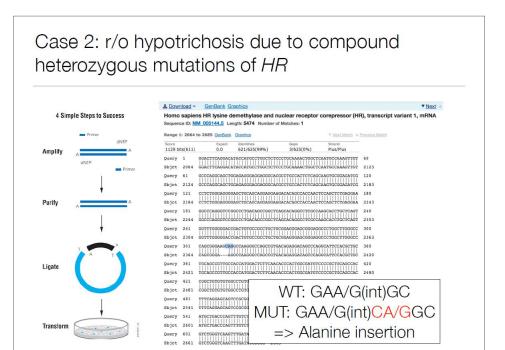


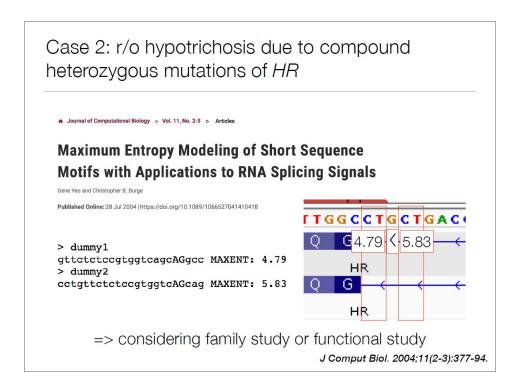












### Discussion

- Whole exome sequencing에서 음성인 경우, whole genome sequencing, RNA sequencing 등이 진단에 도움됨
- 진단을 위해서는 임상적인 정보가 중요함 (+ 주치의의 진단 의 지)
- 추가 functional study를 통한 ASO등의 치료 적용 시도 고려해 볼 수 있음

### Combination treatments of JAK 1/2 inhibitor (Baricitinib) and low dose immunosuppression therapy in alopecia totalis

Young Gue Koh<sup>1</sup>, Jae Wan Park<sup>1</sup>, Sun Hye Shin<sup>1</sup>, Ka Ram Kim<sup>1</sup>, Joon Seok<sup>1</sup>, Sun Young Choi<sup>1</sup>, Beom Joon Kim<sup>1</sup>, Kwang Ho Yoo<sup>2</sup>

<sup>1</sup>Department of Dermatology, Chung-Ang University College of Medicine, Seoul, Korea <sup>2</sup>Department of Dermatology, Chung-Ang University Gwangmyeong Hospital, Chung-Ang University College of Medicine, Gwangmyeong, Korea



### Combination treatments of JAK 1/2 inhibitor(Baricitinib) and low dose immunosuppression therapy in alopecia totalis

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<sup>2</sup>Department of Dermatology, Chung-Ang University Gwangmyeong Hospital,

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Republic of Korea



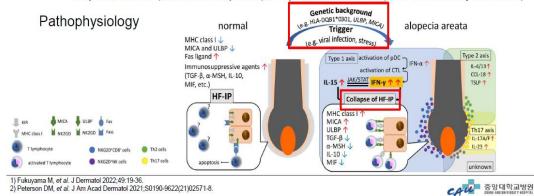
### **▶** Introduction

Alopecia areata (AA)

Nonscarring autoimmune hairloss disorder

Different terminology depending on the area of invasion

- Alopecia totalis (AT, total scalp loss), Alopecia universalis (AU, whole body hair loss)



### **▶** Introduction

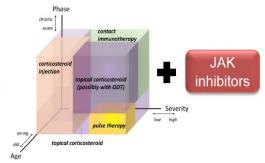
Treatment of alopecia areata

Classified to age, phase, and severity

- Topical treatment
  - Topical steroid ± intralesional injection
  - Contact immunotherapy

Systemic treatment

- Systemic steroid ± cyclosporine



Baricitinib (JAK1/2 inhibitor, Olumiant®)

Approved for the treatment of AA in June 2022

Not recommended for use with other potent immunosuppressants

- Other JAK inhibitors, biologic immunomodulators, and cyclosporine



3) Rubin R. JAMA 2022;328:235.



### ► Case report

Patient: M/26

Chief complaint : Hair loss
 Onset : 15 years ago

Present illness

Multiple bald patches on the whole scalp, SALT 70 (Figure. 1)

Wax and wane (+): recently aggravated

Pretreatment (+): partial response to intralesional triamcinolone injection, methotrexate, diphenylcyclopropenone topical immunotherapy, and tofacitinib(JAK1/3 inhibitor, *Xeljanz*®)

- Past medical history: Atopic dermatitis, allergic rhinitis, asthma (20 YA)
- Family history : Not contribute



### Case report Laboratory findings CBC, TFT, ANA, lupus anticoagulant WNL Histopathologic findings Nonscarring alopecia with increased telogen/catagen, C/w Alopecia areata **Diagnosis** Alopecia totalis Treatment and prognosis Stopped d/t Methylpredenisolone Oriental herb medicine cardiovascular risk (IV pulse#1+ oral tapering) AA occured Cyclosporine MTX, ILI, DPCP 50→25mg/day Tofacitinib Baricitinib 4mg/day July Age (years) CAW 중앙대학교병원

### ▶ Clinical findings

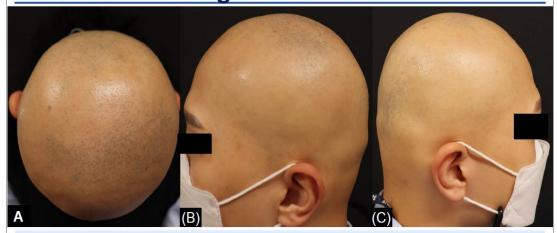


Figure 1 (A, B, C). Multiple bald patches on the scalp before treatment



### ► Clinical findings

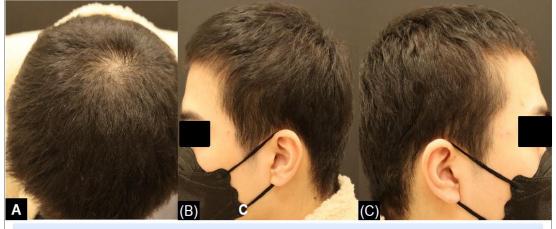


Figure 2 (A, B, C). Almost recovered after 4 months with treatment of baricitinib and steroid pulse with subsequent tapering



### Clinical findings

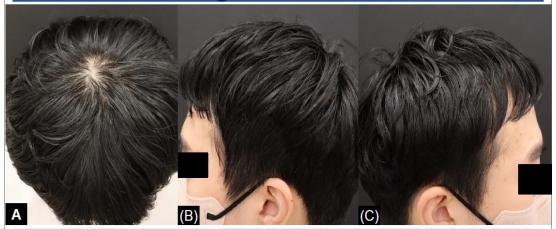
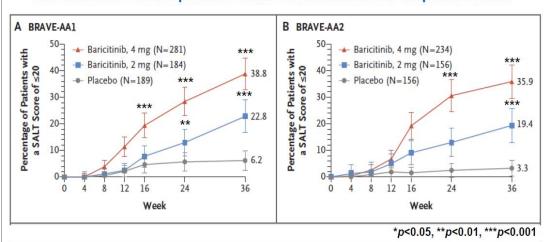


Figure 3 (A, B, C). Hair growing maintained for 3 months after steroid replacement with cyclosporine

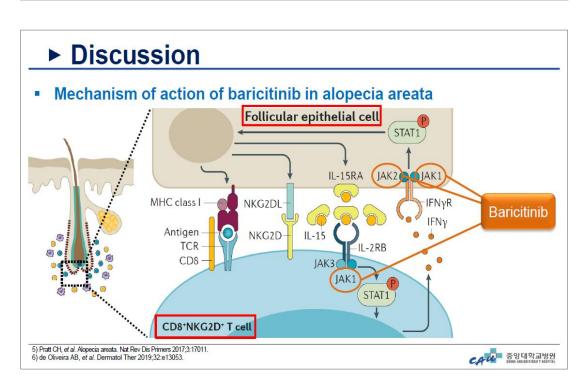


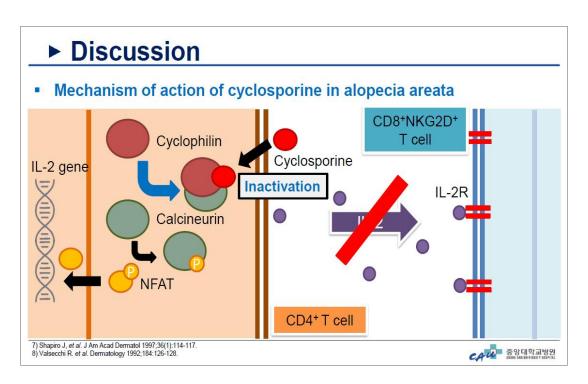
### **▶** Discussion

### Clinical data of two phase 3 trials of baricitinib for alopecia areata



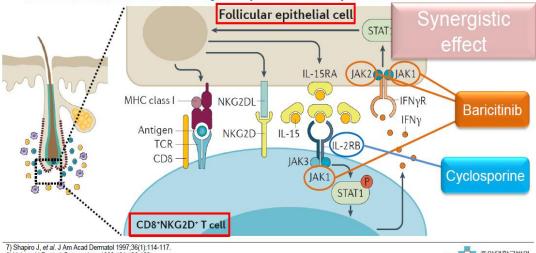
4) King B, et al. N Engl J Med 2022;386:1687-1699.





### **▶** Discussion

Mechanism of action of cyclosporine in alopecia areata



7) Shapiro J, et al. J Am Acad Dermatol 1997;36(1):114-117. 8) Valsecchi R. et al. Dermatology 1992;184:126-128.



### Discussion

### Concurrent use of JAK inhibitor and cyclosporine

### Alopecia Is Approved

JAMA. 2022 Jul 19;328(3):235. doi: 10.1001/jama.2022.11869.

First Systemic Treatment for Severe Randomized Phase 2b Trial of Tofacitinib (CP-690,550) in De Novo Kidney Transplant Patients: Efficacy, Renal Function and Safety at 1 Year American Journal of Transplantation 2012; 12: 2446–2456 Wiley Periodicals Inc.

The most common adverse effects associated with baricitinib included upper respiratory tract infections, headache, acne, hyperlipidemia, nasopharyngitis, and herpes zoster. Baricitinib isn't recommended for use with other JAK inhibitors, biologic immunomodulators, cyclosporine, or other potent immunosuppressants.

The overall findings of this Phase 2b study suggest that tofacitinib, when combined with MPA at conventional doses, is effective in preventing allograft rejection and has a beneficial effect on renal allograft function and parenchymal preservation. However, this result was achieved at the expense of hematological toxicity and over-immunosuppression as demonstrated by increased incidences of serious infection, opportunistic viral infection and PTLD. MPA: Mycophenolic acid

No clinical data of concurrent use in AA

9) Rodriguez-Garcia JL, et al. Rheumatology (Oxford) 2021;60:399-407 10) Vincenti F, et al. Am J Transplant 2012;12:2446-2456.



### **▶** Discussion

### Therapeutic doses and side effects of cyclosporine

Cyclosporine With and Without Systemic Corticosteroids in Treatment of Alopecia Areata: A Systematic Review Dermatol Ther (Heidelb)

Authors CsA dose 2.5 mg/kg/day Yeo et al. Açıkgöz et al. 2.5-6 mg/kg/day Lcc D ct al. 2.5-5 mg/kg/day Ferrando and 5 mg/kg/day Lee JR et al. 100-200 mg/day Grimalt (~ 150 mg/day) Kim et al. 200 mg/day Jang et al. 50-400 (~ 180.9) mg/day Shaheedi-Dadras 2.5 mg/kg/day 5-7.5 mg/kg/day Constantopoulos et al. et al. Shapiro et al. 5 mg/kg/day Gupta et al. 6 mg/kg/day Lai et al. 4 mg/kg/day Teshima et al. 2.5 mg/kg/day Yeo et al. 2.5 mg/kg/day Gadzhigoroeva 3.5 mg/kg/day

the treatment, as lower doses of cyclosporine contribute to a decreased risk of developing severe side effects, such as nephrotoxicity or immune suppression [7]. Lee et al. concluded

Journal of the American Academy of Dermatology Volume 63, Issue 6, December 2010, Pages 949-972

The use of cyclosporine in dermatology:

For the most part, these side effects are dose dependent, related to the duration of therapy,

Our case: Up to 50mg/day (<1mg/kg/day) + pulse & tapering steroid + baricitinib

Is it really dangerous?

11) Nowaczyk J, et al. Dermatol Ther (Heidelb) 2020;1:387-399. 12) Ryan C, et al. J Am Acad Dermatol 2010;63:949-974.



### **▶** Discussion

### Baricitinib and pulse steroids combined treatment in COVID-19



POS1242

BARICITINIB AND PULSE STEROIDS COMBINED TREATMENT IN SEVERE COVID-19 PNEUMONIA: PRELIMINARY DATA FROM A RHEUMATOLOGIC EXPERIENCE IN INTENSIVE CARE UNIT

BPS approach was based on <u>baricitinib 4 mg daily for 10-14 days plus 6-methyl-prednisolone pulses (250-500 mg) for three consecutive days followed by rapid tapering.</u>

SoC included dexameth-

asone 6 to 8 mg daily plus remdesivir (+/- antibiotics and hydroxychloroquine);

Conclusion: Our real-life experience, in an ICU setting, showed that baricitinib and pulse steroids combination was associated with a lower mortality rate paralleled by a prompt reduction of inflammatory biomarkers. These results shed new light on the possible usefulness of baricitinib for the treatment of rapidly progressive ILD in patients with systemic autoimmunity and hyper-inflammation.

13) Ferro F, et al. Annals of the Rheumatic Diseases 2022;81:955



### **▶** Discussion

### Combination treatments of baricitinib and immunosuppression

Inhibits T cell-mediated inflammation through different mechanisms

- Baricitinib inhibits JAK-STAT pathway and subsequent cytokine production
- Cyclosporine inhibits CD8+ T cell by suppressing the expression of IL-2

Concurrent use of JAK inhibitor and cyclosporine is not recommended

- Caution for serious infections and malignancy (ex. Lymphoma)
- However, in our case, no serious adverse events occurred
  - ➤ Young and healthy patient with low dose of immunosuppressants

### In conclusion

### Combination treatment of baricitinib and immunosuppression therapy

Effective for refractory alopecia areata, but needed to assure the safety



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- 3. Rubin R. First Systemic Treatment for Severe Alopecia Is Approved. JAMA. 2022;328:235.
- King B, Ohyama M, Kwon O, et al. Two Phase 3 Trials of Baricitinib for Alopecia Areata. N Engl J Med. 2022;386:1687-1699.
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- 8. Valsecchi R, Imberti G, Martino D, et al. Alopecia areata and interleukin-2 receptor. Dermatology. 1992;184:126-128.



### **▶** Reference

- 9. Rodriguez-Garcia JL, Sanchez-Nievas G, Arevalo-Serrano J, et al. Baricitinib improves respiratory function in patients treated with corticosteroids for SARS-CoV-2 pneumonia: an observational cohort study. Rheumatology (Oxford). 2021;60:399-407.
- Vincenti F, Tedesco Silva H, Busque S, et al. Randomized phase 2b trial of tofacitinib (CP-690,550) in de novo kidney transplant patients: efficacy, renal function and safety at 1 year. Am J Transplant. 2012;12:2446-2456.
- Nowaczyk J, Makowska K, Rakowska A, et al. Cyclosporine With and Without Systemic Corticosteroids in Treatment of Alopecia Areata: A Systematic Review. Dermatol Ther (Heidelb). 2020;1:387-399.
- Ryan C, Amor KT, Menter A. The use of cyclosporine in dermatology: part II. J Am Acad Dermatol. 2010;63:949-974.
- 13. Ferro F, Elefante E, Italiano N, *et al.* pos1242 Baricitinib and pulse steroids combined treatment in severe covid-19 pneumonia: preliminary data from a rheumatologic experience in intensive care unit Annals of the Rheumatic Diseases. 2022;81:955.



2022 대한모발학회 제20차 Hair Forum

### Session II. Special Lecture : 모발 연구의 기초와 시작



### ■ CURRICULUM VITAE ■

### 권오상

서울대학교 의과대학 피부과학교실 교수

### 학력:

2002.8-2005.2 서울대학교 대학원 피부과학 박사 1997.3-1999.2 서울대학교 대학원 피부과학 석사 1988.3-1994.2 서울대학교 의과대학 의학사



### 경력:

2015.3-현재 서울의대 피부과학교실 교수 2007.7-2009.7 미국 University of Pennsylvania 피부과 / visiting scholar 2003.4-2003.4 미국 Oregon Health Science University 피부과 / visiting fellow 2002.3-2003.4 서울대학교병원 피부과 전임의 1995.3-1999.2 서울대학교병원 피부과 전공의

### 학회활동:

2022.6-현재 대한모발학회 부회장

### 관심분야:

모발생물학, 줄기세포생물학, 재생의학

### 모발 기초 연구 시작하기

서울의대 피부과학교실

권 오 상



### 모발 기초 연구 시작하기

서울의대 피부과학교실 권오상

### Why we perform basic research?

### JID Editorial Board e-mail Circulation

### ☆ 2021 Impact Factors Announced

보낸 사람 JID Editor 〈jideditor@sidnet.org〉 (06.29 03:48) 받는 사람 Elizabeth Blalock 〈blalock@sidnet.org〉

### Dear Fellow Editors:

Today the results of the 2021 Impact Factor (IF) calculation by Clarivate were published. The JID's impact factor went down from last year's high of 8.51, to 7.59. This is still higher than the 2019 IF of 7.14. In the ranking of 93 dermatology journals the JID is now in position five, outperformed only by the four clinical dermatology journals JAAD (IF 15.487I), JAMA Dermatology (IF 11.816), BJD (IF 11.113) and JEADV (IF 9.228). (The list of the ten highest ranked journals as well as the development of the JID IF over the past 20 years are below).

Together with Elsevier I will analyze the reasons for both the drop of the IF of our Journal and the rise of the IF of the clinical dermatology journals. I will share and discuss with you the results of this analysis at our Editorial Board meeting at the ESDR congress in Amsterdam. Together we will devise strategies to increase the ranking of our Journal in the future.

Best regards,

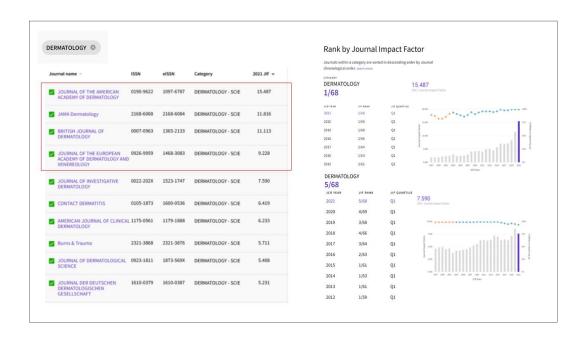
Erwin

### E-mail circulation for JDS Section editors

### 2021 Impact Factor 1기의 학교 JDS Nilipsta vjds@med niligata-u.ac.p> 2022년 6월 29월 오전 9:39 반는사랑: JDS Nilipsta vjds@med niligata-u.ac.p> Dear JDS Section Editors, Thank you for your continued contributions to the Journal of Dermatological Science. The 2021 Impact Factor has been released. JDS IF number is 5.408 and it has risen 0.845 from the 2020 IF number 4.563. The rank for JDS in dermatological journals has risen five spots from 14<sup>th</sup> in 2020 to 9<sup>th</sup>. I greatly appreciate your ongoing support and excellent contributions to the journal. I look forward to continuing to work with you in this upcoming year. Sincerely.

2021 Rank	Full Journal Title	Total Cites	Impact Factor	2020 Rank	Total Cites	Impact Factor	IF Change From 2020 to 2021
1	JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY	41,522	15.487	1	40,257	11.527	3.960
2	JAMA Denuitology	9,228	11,816	2	8,448	19.292	1.534
3	BRITISH JOURNAL OF DERMATOLOGY	35,240	11.113	3	36,064	9.302	1811
4	JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY	20,754	9.228	7	19,427	6.166	3.062
5	JOURNAL OF INVESTIGATIVE DERMATOLOGY	38,659	7.590	-4	37,630	8.551	-0.961
6	CONTACT DERMATITIS	7,694	6.419	6	7,973	6.600	-0.181
7	AMERICAN JOURNAL OF CLINICAL DERMATOLOGY	4,907	6.233	5	4.264	7.403	4.170
8	Burns & Trauma	1.222	5.711	10	937	5.099	0.612
,	JOURNAL OF DERMATOLOGICAL SCIENCE	7,172	5.408	14	6,869	4.563	0.845
10	JOURNAL DER DEUTSCHEN DERMATOLOGISCHEN GESELLSCHAFT	3,770	5.231	8	3,597	5.584	4353
11	DERMATOLOGY	6,911	5.197	9	6,824	5.366	-0.169
12	Advances in Wound Care	4,318	4.947	12	3,381	4,730	0.217
13	MYCOSES	6,227	4.931	16	5,252	4.377	0.554
14	Decoutitis	2,284	4.867	- 11	1,762	4.845	0.022
15	EXPERIMENTAL DERMATOLOGY	10.091	4.511	19	9,059	3.960	0.551
16	CLINICAL AND EXPERIMENTAL DERMATOLOGY	6,461	4.481	25	6.342	3,470	1.011
17	Pigment Cell & Melsmona Research	5,837	4.159	13	5,765	4.693	-0.534
18	ACTA DERMATO- VENEREOLOGICA	8,242	3.875	15	8,418	4.437	-0.562
19	Demutologic Therapy	6,862	3.858	36	4,699	2.851	1.007
20	Dematology and Therapy	1.631	3.661	30	1.279	3.264	0.397

Riichiro Abe
Editor-in-Chief
Journal of Dermatological Science





# Writing Tradition in Western Civilization

- Writing, the key for both communication and learning
- "Interesting and unpublished" is "not-existent"



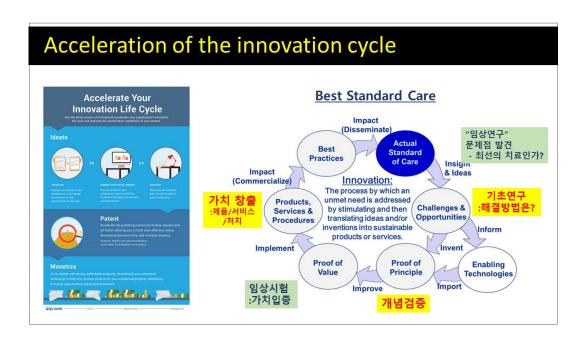
# Where we start?

- Strength & Competitive advantage
- Circle of competence

# Specification of Hair research fields

# Past works & publications

- Big data & metanalysis
- Clinical Research
- Clinical trials
- Genetic association studies
- Collaborative research
- Descriptive research
- Mechanistic research



# What is basic research?

# Field Specialization of Basic Research



Basic research includes theoretical research and early-stage investigations in the laboratory or field.

- A tolerance for uncertainty and ambiguity is essential.
- The basic researcher is driven by curiosity and a desire to explore unknown territory.

# **Typical Job Functions**

- Basic research is where it all starts: <u>new ideas, fundamental theories, unanswered questions</u>
- $\bullet \quad \text{It requires the ability to identify interesting problems and to come up with original ideas.}\\$
- <u>Basic research projects usually involve teams</u>. Teams may involve researchers in many locations around the world.
   Chemists may work with materials scientists, biologists, geologists, physicists, or medical doctors.
- They may also enlist the help of computer scientists, engineers, and instrument design specialists to help them develop the new capabilities they need.

# Typical activities involved in basic research include:



- 1) Identifying research topics
  - Conducting literature searches and reading scientific publications
- 2) Applying for funding & Establishing Research environment
- 3) Team building with best available members
- 4) Collecting and analyzing laboratory and field data
- 5) Developing synthesis procedures & Constructing models and theories
- 6) Performing computational laboratory studies
- 7) Publishing articles in scientific journals
- 8) Making presentations at conferences

# Typical activities involved in basic research include:

### **Funding**

for basic research commonly comes from **government grants or nonprofit organizations**.

(Private industry is less likely to fund this type of research, because there is often no clear path to a marketable product.)

### **Career Paths**

- Basic research almost always requires a Ph.D. for entry (training required)
- · They may supervise research teams consisting of undergraduate and graduate students, postdocs, or technical staff members.
- Some experienced researchers move into program management or administration, where they spend much of their time
  preparing budgets and schedules and obtaining funding, in addition to overseeing research programs and other researchers.

# Take-home message

# Writing Tradition in Western Civilization

"Interesting and unpublished" is "not-existent"

# Starting points

- Strength, Competitive advantage / Circle of competence
- Clinical, experimental/translational, both

# Establishment of own basic hair research lab (Team sports)

- 1) Training required (like acquisition of driving license and road training)
- 2) Concept development & identifying research topic
- 3) Funding / Grant (seed money: 임상시험, 용역연구)
- 4) Recruit of best available members & Supervise/coordinate the process
- 5) Publication & Presentation

# ■ CURRICULUM VITAE ■

# 성영관

경북대학교 의과대학 면역학교실 교수

# 학력:

1988-1992경북대학교 자연과학대학 유전공학과 (이학사)1993-1996영국 임페리얼 칼리지 생물학과 (이학박사)

# 경력:

1996-1996	캠브리지대학교 포스트닥
1997-2001	존스홉킨스 의과대학 포스트닥
2002-2004	경북대학교 생체분자공학 실용화 연구소 연구초빙교수
2004-2006	경북대학교병원 의학연구소 기금교수
2006-현재	경북대학교 의과대학 면역학교실 조교수/부교수/교수

# 학회 활동:

2012-현재	Korean Hair Research Society
2012-현재	Tissue Engineering and Regenerative Medicine International Society
2006-현재	Korean Society for Molecular and Cellular Biology
2006-현재	Korean Society for Biochemistry and Molecular Biology

# 관심 분야:

탈모 및 모낭성장기전연구, 발모제 스크리닝, 세포기반 모낭재생

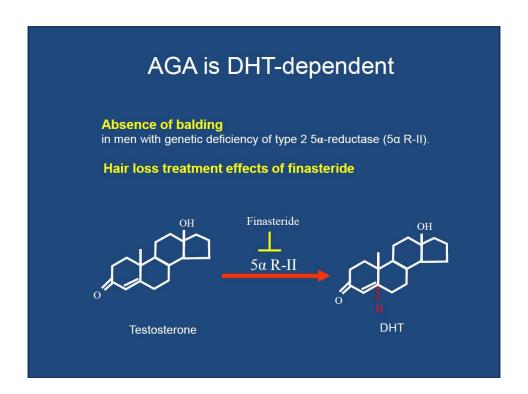
# AGA 기초 실험 연구 준비와 연구 기법

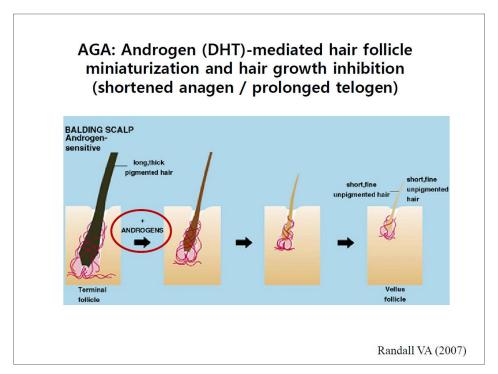
경북의대

성 영 관

# AGA 기초 실험 연구 준비와 연구 기법

경북의대 성영관





# AGA 기초 실험 연구 Key: androgen(DHT)-inducible pathogenic mediators 발굴/검증 Target (모유두) 분리 및 모유두세포 배양 AR 발현 확인 (필요시 AR 과발현) 후 T/ DHT 처리 RNA level 분석 : - microarray, RNA sequencing - RT-PCR (qPCR) 검증 Protein level 분석: - MS / Proteome profiler array - ELISA / Western blot / Immunostaining 검증 조직배양 (HF organ culture) Hair shaft 길이 측정 Immunostaining (Ki67 / TUNEL) 동물실험 Hair cycle 분석 (shortened anagen / prolonged telogen)

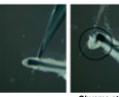
# 모유두 분리 및 배양



non-balding balding

IRB 신청 / 승인 (2~3 개월)

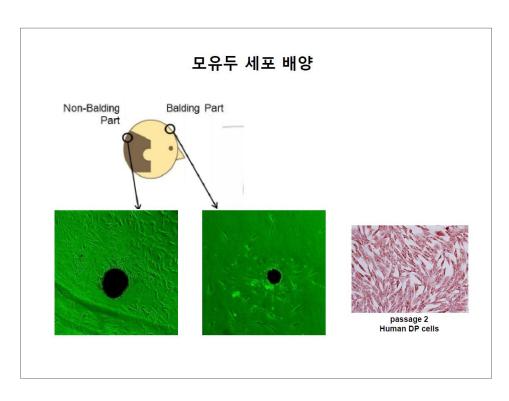
# Surgical micro-dissection: gold standard for obtaining DP

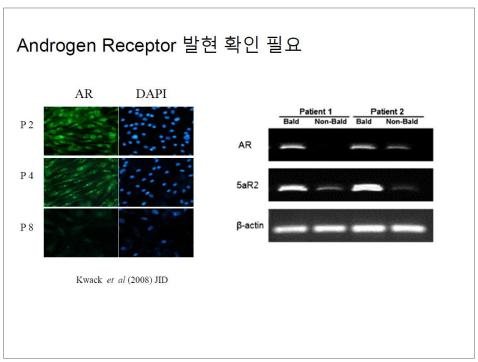


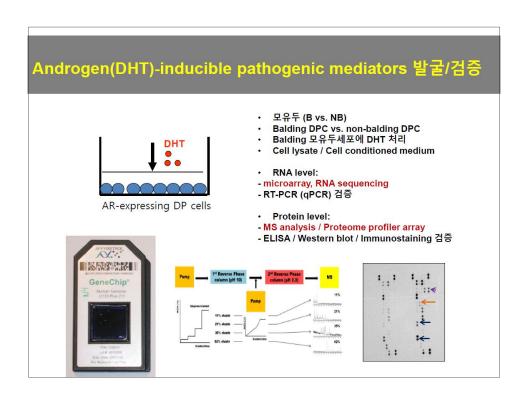


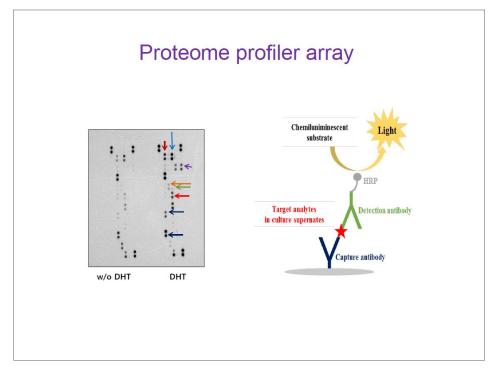


Ohyama et al. (2009) EXD 19: 89-99



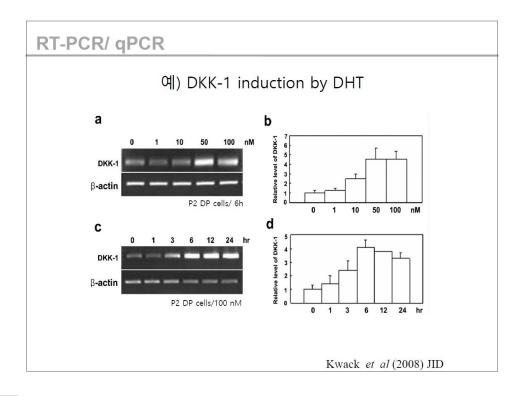


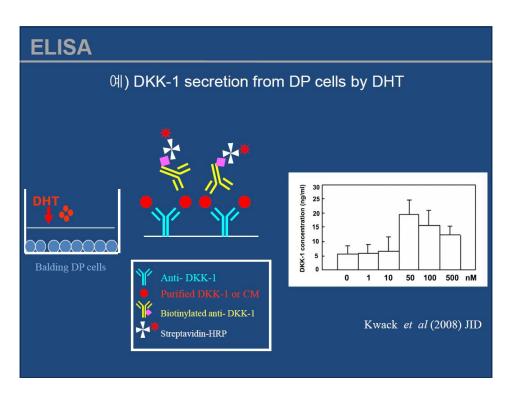


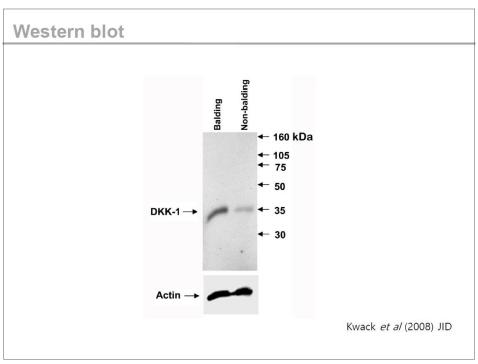


# Androgen(DHT)-inducible pathogenic mediators 발굴/검증

- · RNA level:
- RT-PCR (qPCR) 검증
- · Protein level:
- ELISA / Western blot / Immunostaining 검증

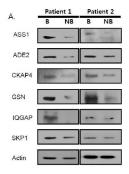


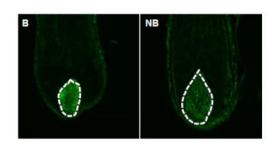




# Western blot / immunostaining

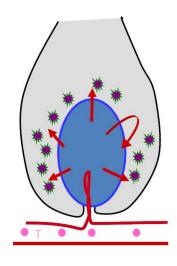
**128 up-regulated and 12 down-regulated proteins among 690 distinct proteins** were identified in balding DP cells compared to non-balding DP cells



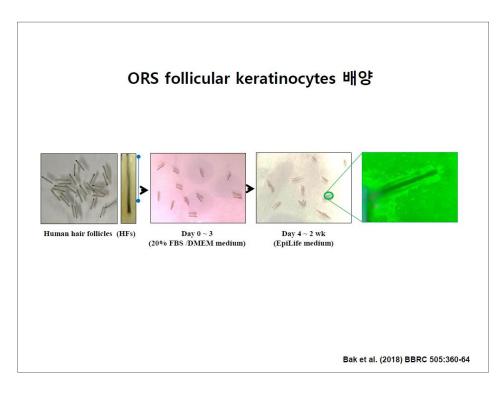


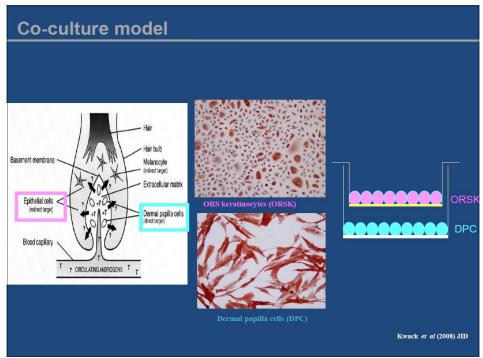
Moon et al (2013) J proteomics

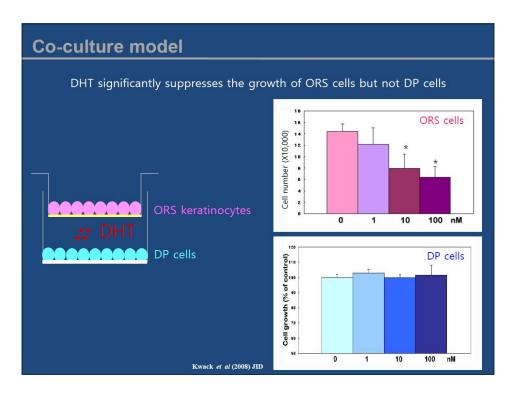
# AGA 관련 단백질 기능 연구

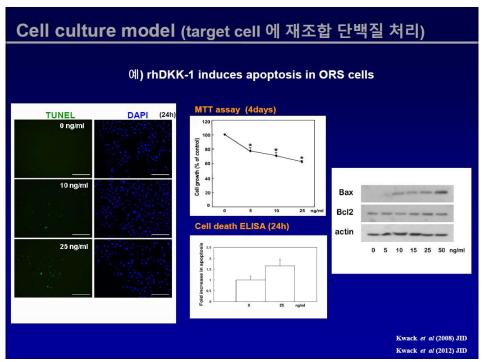


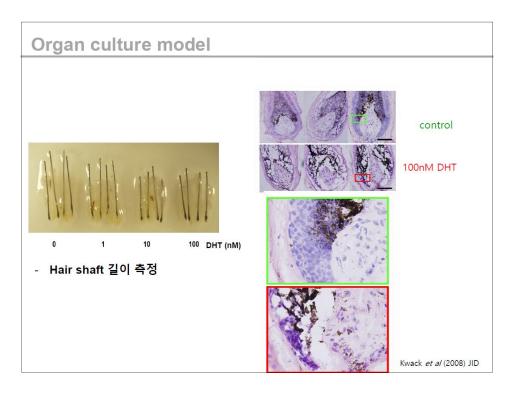
- Cell culture model (including co-culture)
- Hair follicle organ culture model
- mouse model

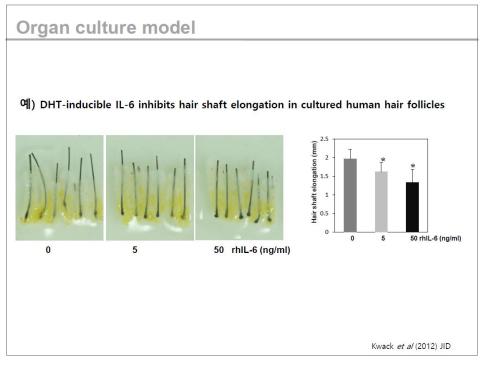


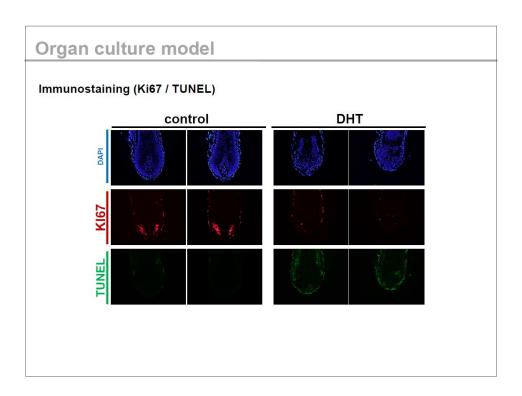


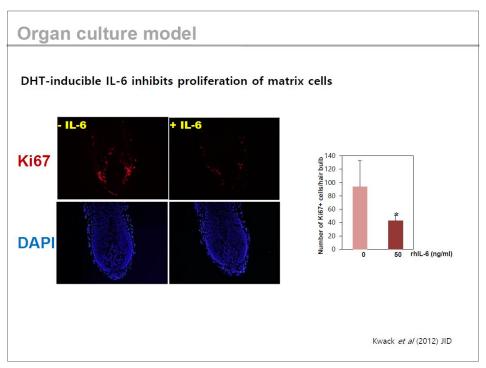




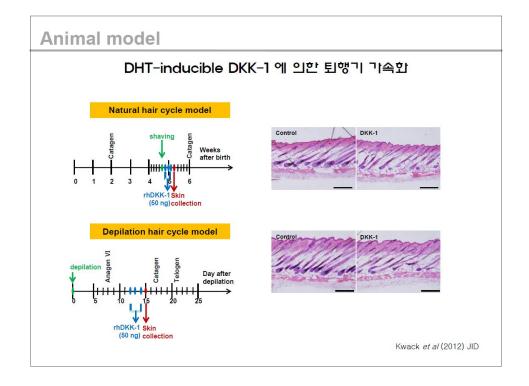


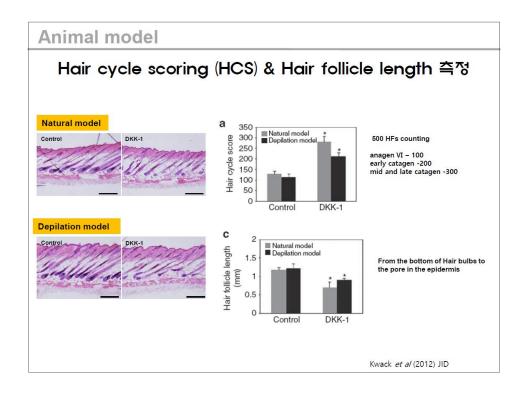






# \*\*Stump-tailed macaque spontaneous baldness model - Human balding scalp grafted nude mouse model - Transgenic mouse model (K5-hAR Tg) - C57BL/6 Mouse model - Hair cycle 분석 \*AGA (shortened anagen / prolonged telogen) \*\*C57BL/6 Natural hair cycle \*\*G57BL/6 Natural hair cycle \*\*G6\*\*\* \*\*Depilation-induced hair cycle \*\*day after depilation \*\*Depilation is a single managen vi anagen vi anage





2022 대한모발학회 제20차 Hair Forum

# Session III. 2022년도 대한모발학회 연구비 : 연구계획 발표



# Investigation on the role of high fat diet and gut environment in the development of alopecia

**Hyunsun Park** 

Department of Dermatology, SMG-SNU BoramaeMedical Center

# Investigation on the role of high fat diet and gut environment in the development of alopecia

Department of Dermatology

SMG-SNU Boramae Medical Center

Hyunsun Park

# When the patients hear their diagnosis,...

- OK, then what should I *eat*?
- Or what should I not eat?
- Isn't it associated with my internal organ problem?



**Article** 

# Sleep Loss Can Cause Death through Accumulation of Reactive Oxygen Species in the Gut

Vaccaro et al., 2020, Cell 181, 1307–1328 June 11, 2020 @ 2020 Elsevier Inc. https://doi.org/10.1016/j.cell.2020.04.049

# 한국인 과학자 부부, 자폐아 출산 원인 밝혔다

허준렬·글로리아 최 교수 부부, 네이처誌에 논문 2편 발표 임신 중 모체의 장내세균이 태아의 뇌세포에 영향

이영완 과학전문기자

입력 2017.09.14 03:00







허준렬(왼쪽), 글로리아 최.

재미(在美) 한국인 과학자 부부가 여성의 장내세균 이 자폐아 출산에 직접적인 영향을 미친다는 사실을 처음으로 밝혀냈다. 이와 함께 자폐 증세를 유발하는 뇌 영역도 새로 찾아냈다.

아직 동물실험 단계이지만 자폐증을 근본적으로 치료할 수 있는 길을 열었다는 평가를 받고 있다.

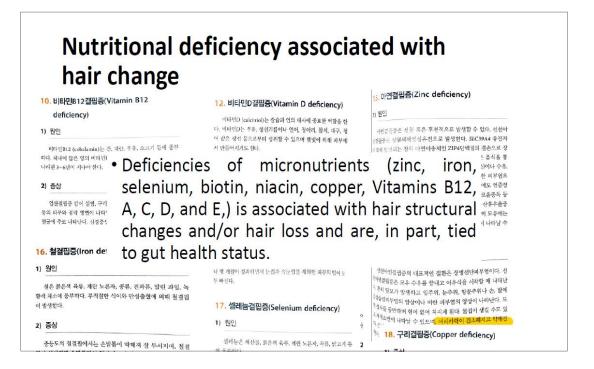
# The history of Brain-Gut-Skin theory

Over 90 years have passed

since dermatologists John H. Stokes and Donald M. Pillsbury first proposed

a gastrointestinal mechanism for the overlap between depression, anxiety and skin conditions such as acne.

The effect on the skin of emotional and nervous states: theoretical and practical consideration of a gastrointestinal mechanism. Arch Dermatol Syphilol 1930, 22:962-93.



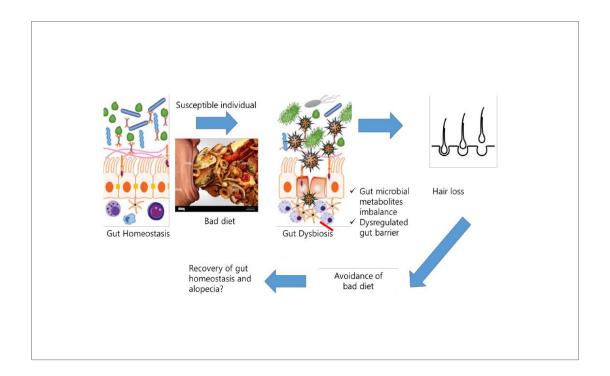
ACG Case Rep J. 2017; 4: e107. PMCID: PMC5599691 Published online 2017 Sep 13. doi: 10.14309/crj.2017.107 PMID: 28932754 Hair Growth in Two Alopecia Patients after Fecal Microbiota Transplant Dionne Rebello, MD, MD, Elaina Wang, BS, 1 Eugene Yen, MD, 3 Peter A. Lio, MD, 4 and Colleen R. Kelly, MD, Case 2 \* Author information \* Article notes \* Copyright and License information A 20-year-old man with severe ileocolic Crohn's disease was treated with FMT after requiring 5 recurrent <sup>1</sup>Alpert Medical School, Brown University, Providence, RI courses of antibiotics for CDI. He remained CDI-free after the procedure. He had been diagnosed with <sup>2</sup>Division of Gastroenterology, Rhode Island Hospital, Providence, RI alopecia universalis approximately 2 years prior to FMT, which had been treated with intralesional <sup>3</sup>University of Chicago Pritzker School of Medicine, Chicago, IL corticosteroid injections, topical steroids, squaric acid, and laser treatments with no measurable <sup>4</sup>Northwestern University Feinberg School of Medicine, Chicago, IL improvement. After FMT, the patient had significant improvement in his hair loss. Only 2 additional <sup>M</sup>Corresponding author. intralesional corticosteroid injections with the same strength were done after FMT without any further Correspondence: Dionne Rebello, Department of Internal Medicine, R. treatment. Prior to FMT, he was persistently noted to have stage \$4b alopecia (95-99% hair loss) despite Providence, RI 02903 (dionne.rebello@lifespan.org). intralesional injections, but he improved at least 2 grades to stage \$2 (25-49% hair loss) after FMT (Figure 2). Notably, while the steroid injections had only been administered to his scalp, after FMT he has had regrowth of hair in other areas of his body as well. A 38-year-old man with alopecia universalis diagnosed 10 years pre and abdominal pain. On physical examination, he had diffuse abdon evaluation revealed leukocytosis. Abdominal computed tomography terminal ileum. Stool C. difficile polymerase chain reaction was pos metronidazole. He was treated with oral vancomycin for 2 further ej difficile-positive stools. After FMT for recurrent CDI, he experience follow-up 8 weeks later, he reported new hair growth on his head, fa had previously been refractory to steroid injections, and he was on r

time. Three years later, he continues to have patchy hair growth on I

shaves regularly.

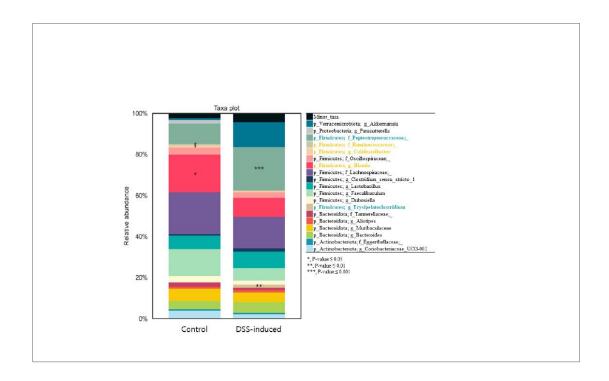
# 탈모에서 장내 환경의 역할과 미충족 수요

- 원형탈모 환자나 동물 모델에서 탈모가 없는 개체 대비 장내 미생물의 변화가 관찰됨
- 장질환과 원형탈모가 같이 있는 환자에서 대변이식 이후 원형탈모가 회복되었다는 일부 증례보고가 있음
- 휴지기 탈모와 철분 결핍이 연관되어 있음
- 다양한 영양소의 결핍의 표현형으로 탈모가 있음
- 이처럼 다양한 형태의 탈모와 식이, 혹은 이와 연관된 장내환경의 변화가 연관되어 있을 것으로 추정되나 아직 이에 대해서는 아직 알려진 바가 없으며 연구가 부족함



# 동물 연구

- 마우스에서 고지방 사료로 정상 사료대비 탈모 병변 유발 재현 확인
- 면역프로파일, 장내 환경 차이 (장염 여부, 장내미생물, 장내대사체, 장점막 투과도) 비교 분석
- 탈모가 유발된 마우스 개체에서 정상 사료로 전환 시 탈모 병변이 완화되는지 분석



# The investigation of role of regulatory T cell in alopecia areata

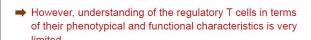
중앙의대

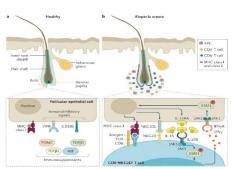
석 준



# Alopecia areata (AA)

- AA is a T-cell mediated autoimmune disease phenotypically characterized by hair loss
- Well-demarcated patches of non-scarring, inflammatory hair loss that can progress to include all scalp or body hairs
- 1.7-2.1% of the general population at some point during their lifetimes
- IL-15 and its receptors on CD8+T cells show increased expression around hair follicles in AA
- IL-15/IL-15R signal increase the expression of NKG2D on infiltrated CD8 T cells, resulting in NKG2D-dependent killing of hair follicles







Xing L et al., Nat Med, 2014. 20(9): 1043-9 Pratt CH et al., Nat Rev Dis Primers, 2017. 3: 17011

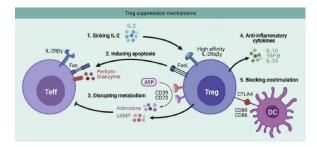
# Regulatory T cell (T<sub>reg</sub> cell)

 $T_{eff}$ : Effector T cell

 $\succ$  T<sub>reg</sub> can suppress T<sub>eff</sub>-mediated inflammation by multiple direct and indirect mechanisms.

# ► Basic mechanisms used by T<sub>reg</sub> cells

- 1) Starving T cells of IL-2
- 2) Promoting T-cell apoptosis
- 3) Modulating T-cell metabolism to reduce effector function
- 4) Secreting anti-inflammatory cytokines
- 5) Inhibiting immunostimulatory signals on antigen presenting cells (APCs)



Victoire G, et al. J Invest Dermatol. 2022;142

# $T_{\text{reg}}$ cell in skin

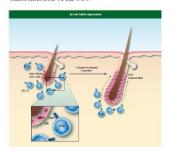
HFSC : Hair follicle stem cell

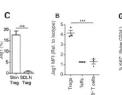
### $\succ$ Skin $T_{reg}$ cell function

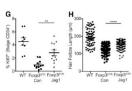
The orchestration of stem cell-mediated <u>hair follicle regeneration</u>, <u>augmentation of wound healing</u>, and <u>promoting adaptive immune tolerance to skin commensal microbes</u>.

### $\succ T_{\rm reg}$ cell and hair follicle regeneration

- $1. \quad \text{Subpopulation of $T_{reg}$ cells in telogen skin localize in close proximity to HFSCs in the bulge region of the hair follicle.}$
- 2. More abundant in telogen skin relative to anagen skin.
- 3. T<sub>reg</sub> cell expression of the Notch ligand Jagged-1 (Jag1) was required to promote HF cycling by enhancing the activation and





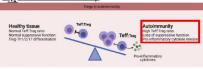


Ali N, et al. Immunology, 2017; 152

Ali N, et al. Cell, 2017; 169

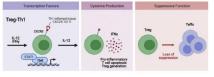
# Regulatory T cell ( $T_{\text{reg}}$ cell) in autoimmunity

➤ T<sub>reg</sub> cell in autoimmunity



- $\triangleright$  In healthy tissues, the ratio of  $T_{effs}$  to  $T_{reg}$  cells is sufficiently low, and  $T_{reg}$  cells retain their suppressive function.
- ➤ In autoimmune disease, inflamed tissues have high T<sub>effs</sub>-to-T<sub>reg</sub> cells ratios, and T<sub>reg</sub> cells isolated from the tissue have reduced suppressive capacity in vitro.

# $\rightarrow \underline{T_{reg} - Th1 cell}$

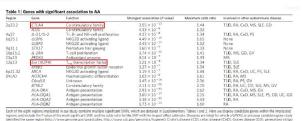


- $\succ$  Human and mouse  $T_{reg}$  cells can differentiate into Th1-like cells after excessive activation or exposure to type-1 inflammation.
- These T<sub>reg</sub>-Th1 cells can be induced to produce IFN-γ and lose their suppressive function.

Victoire G, et al. J Invest Dermatol. 2022;142

# AA and Treg cell

➤ Genes with significant association to AA



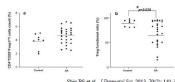
Petukhova I. et al. Nature 2010-466(7302)

Gene sequencing confirmed that the single-base polymorphism of the FOXP3 gene, which plays an important role in the development and maintenance of T<sub>reg</sub> cells, increased compared to healthy controls, indicating that it can reduce mRNA expression of FOXP3 and affect the development of AA.

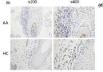
Conteduca G, et al. Clin Exp Med. 2014;14(1)

# AA and Treg cell

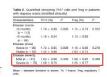
 $\succ$  T<sub>reg</sub> cells function rather than number has a key role in determining susceptibility to AA.

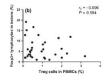


 $\succ$  Compared to the control group, the frequency of  $T_{reg}$  cells around the AA hair follicle was significantly reduced, which showed that it was related to the disease severity.









Han YM, et al. J Dermatol. 2015;42(10)

# AA and Treg cell

When the frequency of T<sub>reg</sub> cells was increased through II.-2 injection in patients with AA, there was a case in which it was confirmed that hair was successfully regenerated in 80% of patients.

Case Report / Case Serie

Effects of Low-Dose Recombinant Interleukin 2 to Promote T-Regulatory Cells in Alopecia Areata

meline Castela, MD; Florence Le Duff, MD; Catherine Butori, MD; Michel Ticchioni, MD, PhD;

kaul Hofman, MD, PhD; Philippe Rahardoran, MD, PhD; Jaan, Philippe Lacour, MD; Thierry Passeron, MD, PhD





After treatment
Castela E, et al. JAMA Dermatol. 2014;150(7)

> The results of this large prospective randomized placebo controlled trial did not further support the efficacy of low-dose IL-2 in treating.

Low-Dose IL-2 for Treating Moderate to Severe Alopecia Areata: A 52-Week Multicenter Prospective Placebo-Controlled Study Assessing its Impact on T Regulatory Cell and NK Cell Populations

Journal of Investigative Dermatology (2021) 141, 933-936; doi:10.1016/j.jid.2020.08.015

> In mice with AA, expanded Tregs also failed to decrease the number of pathogenic CD8 T cells and resume hair growth.

Selective Expansion of Tregs Using the IL-2 Cytokine Antibody Complex Does Not Reverse Established Alopecia Areata in C3H/HeJ Mice

Lee E, et al. Front Immmol. 2022;13

# Objective : The investigation of role of $T_{\text{reg}}$ cell in alopecia areata

Question) How Tregs contribute to the AA microenvironment and pathogenesis?

 $\underline{\text{Hypothesis}}: \underline{\text{In alopeica areata, T}_{\underline{\text{reg}}} \text{ cell dysfunction will occur and will not play a proper role.}}$ 

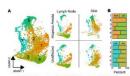
### **Phenotypical and Functional Changes**

- Investigating the distinct phenotypes and functions of  $\rm T_{\rm reg}$  cells in AA patients and AA mouse model
  - $\blacksquare$  Immunophenotyping analysis: proportion of  $\mathsf{T}_{\mathsf{reg}}$  cells and disease severity, activation marker, plasticity
  - Functional characteristics analysis: proliferative capacity, cytokine production, co-culture assay to check suppressive function

Multi-color Flow Cytometry Analysis

# **Molecular and Cellular Mechanisms**

- Examination of changes in gene expression profiles in  $\rm T_{\rm reg}$  cells
  - Identify key genes that regulate the phenotypical and functional changes in T<sub>reg</sub> cells using RNA sequencing



Nicholas, et al. *JCI insight*. 2020;5(13)

Single cell RNA sequencing

# Analysis of the patients with alopecia areata using healthcare bigdata

# Jin Cheol Kim

Department of Dermatology, Ajou University School of Medicine, Suwon, Korea

2022 Hair Forum

# Analysis of the Patients with Alopecia Areata Using Healthcare Bigdata

2022. 8. 20.

Jin Cheol Kim

Department of Dermatology, Ajou University School of Medicine, Suwon, Korea

# **Korean National Health Insurance Claims Database**

- HIRA (Health Insurance Review & Assessment) Service
  - 맞춤형연구 DB
  - 표본연구 DB
  - 결합DB
  - 의료영상DB
- NHIS (National Health Insurance Sharing) Service
  - 표본연구 DB
  - 국민건강정보 DB
  - 맞춤형연구 DB
- 전국민 건강보험 데이터를 기반으로 수요도 높은 데이터를 표본 추출
- 정책 및 학술용으로 규격화 한 DB

# NHIS-NSC (표본코호트 DB)

- 기준
  - 2006년 1년간 건강보험가입자 및 의료급여수급권자 자격을 유지한 전국민
- 대상자
  - 100만명
- 연도
  - 2002-2019년 (18개년)
- 표본추출
  - 전국민 모집단의 2% 성/연령/가입자구분/보험료분위/지역별 층화
- 내용
  - 사회/경제적 현황 (자격 및 보험료, 장애 및 사망), 의료 이용 현황 (진료 및 건강검진),
     요양기관 현황, 노인장기요양 현황



International Journal of Epidemiology, 2017, e15(1–8)
doi: 10.1093/ije/dyv319
Advance Access Publication Data: 28 January 2016
Cohort Profile



Cohort Profile

# Cohort Profile: The National Health Insurance Service-National Sample Cohort (NHIS-NSC), South Korea

Juneyoung Lee, <sup>1</sup> Ji Sung Lee, <sup>2</sup> Sook-Hee Park, <sup>3</sup> Soon Ae Shin <sup>3</sup> and KeeWhan Kim<sup>4</sup>\*

<sup>1</sup>Department of Biostatistics, College of Medicine, Korea University, Seoul, Korea, <sup>2</sup>Clinical Research Center, Asian Medical Center, Seoul, Korea, <sup>3</sup>Big Data Steering Department, National Health Insurance Service, Seoul, Korea and <sup>4</sup>Department of Applied Statistics, Korea University Sejong Campus, Sejong City, Korea

Int J Epidemiol. 2017

> PLoS One. 2021 May 7;16(5):e0250216. doi: 10.1371/journal.pone.0250216. eCollection 2021.

Alopecia areata is not a risk factor for heart diseases: A 10-year retrospective cohort study

Heera Lee 1, You Chan Kim 1, Jee Woong Choi 1

PLoS One. 2021

> Australas J Dermatol. 2021 Feb;62(1):e121-e123. doi: 10.1111/ajd.13428. Epub 2020 Aug 13.

Impact of alopecia areata on subsequent pregnancy rate: A retrospective cohort study

Jin Cheol Kim <sup>1</sup>, Jee Woong Choi <sup>1</sup>

Australas J Dermatol. 2021

J Am Acad Dermatol. 2020 Feb;82(2):484-486. doi: 10.1016/j.jaad.2019.06.1304. Epub 2019 Jul 3.

Impact of alopecia areata on psychiatric disorders: A retrospective cohort study

Jin Cheol Kim <sup>1</sup>, Eun-So Lee <sup>1</sup>, Jee Woong Choi <sup>2</sup>

J Am Acad Dermatol, 2021

> J Dermatol. 2019 Sep;46(9):e331-e332. doi: 10.1111/1346-8138.14863. Epub 2019 Mar 25.

Increasing prevalence of alopecia areata in South Korea

Byung Woo Soh <sup>1</sup>, So Min Kim <sup>1</sup>, You Chan Kim <sup>1</sup>, Gwang Seong Choi <sup>2</sup>, Jee Woong Choi <sup>1</sup>

J Dermatol. 2019

> Sleep. 2018 Sep 1;41(9). doi: 10.1093/sleep/zsy111.

The risk of alopecia areata and other related autoimmune diseases in patients with sleep disorders: a Korean population-based retrospective cohort study

Hyun-Min Seo <sup>1</sup>, Tae Lim Kim <sup>1</sup>, Joung Soo Kim <sup>1</sup>

Sleep. 2018

# Microbiome Study Using Healthcare Big Data



# ACG CASE REPORTS JOURNAL



CASE REPORT | COLON

# Hair Growth in Two Alopecia Patients after Fecal Microbiota Transplant

Dionne Rebello, MD', Elaina Wang, BS', Eugene Yen, MD³, Peter A. Lio, MD⁴, and Colleen R. Kelly, MD, FACG $^{\rm tr}$ 

Alpert Medical School, Brown University, Providence, RI
\*Division of Gastroenterology, Rhode Island Hospital, Providence, RI
\*University of Chicogo Pritzker School of Medicine, Chicago, IL
\*Northwestern University Feinberg School of Medicine, Chicago, IL

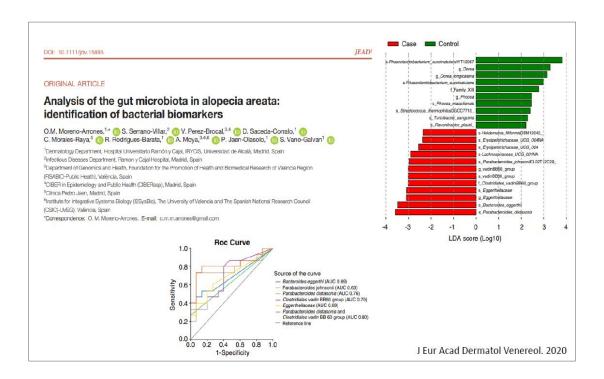


Figure 1. Hair regrowth on a 38-year-old patient's (A) face and (B) scalp 8 weeks after FMT.



Figure 2. Hair regrowth on a 20-year-old patient's scalp after FMT. (A) The patient's scalp when he first started loaing his hair at age 16. The patient's scalp (B) a few months and (C) 15 years after FMT.

ACG Case Rep J. 2017



#### Published: 12 October 2016

## The gut microbiota and gastrointestinal surgery

<u>Kristina Guyton</u> & <u>John C. Alverdy</u> □

Nature Reviews Gastroenterology & Hepatology 14, 43-54 (2017) Cite this article

- The physiological stress of surgical injury on the gastrointestinal tract can result in a profound shift in gut microbiota abundance, function and spatial location.
- · Major intestinal reconstruction alters the intestinal microbiota.
- The effects of surgical injury can, in some cases, result in an in vivo transformation of intestinal bacteria to a more virulent phenotype.

Nat Rev Gastroenterol Hepatol. 2017



ORIGINAL RESEARCH published: 16 September 2021 doi: 10.3389/fmicb.2021.724980



#### Appendectomy Is Associated With Alteration of Human Gut Bacterial and Fungal Communities

Shuntian Cai<sup>1,2</sup>t, Yanyun Fan<sup>1,2</sup>t, Bangzhou Zhang<sup>1,2</sup>t, Jinzhou Lin<sup>1</sup>, Xiaoning Yang<sup>1</sup>, Yunpeng Liu<sup>1</sup>, Jingjing Liu<sup>1,2</sup>, Jianlin Ren<sup>1,2</sup>\* and Hongzhi Xu<sup>1,2</sup>\*

Department of Gastroenterology, Zhongshan Hospital Affiliated to Xiamen University, Xiamen, China, School of Medicine, Institute for Microbial Ecology, Xiamen University, Xiamen, China

Front Microbiol. 2021

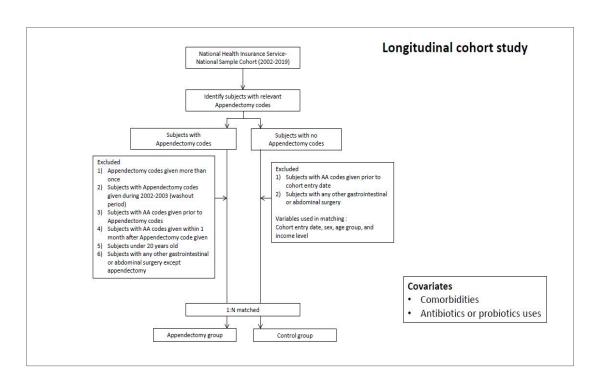
# Objective

To Investigate Association between
Post-Appendectomy status and Risk of Alopecia Areata
Using NHIS-NSC (2002-2019)



#### Relation between Appendectomy and Dermatologic diseases

Chi-square test	With appendectomy	Without appendectomy	P-value
Alopecia areata	2.75 %	2.14 %	<0.001
Vitiligo	0.88 %	0.76 %	0.029
Urticaria	2.50 %	1.97 %	<0.001
Malignancies	6.48 %	7.25 %	<0.001
Psoriasis	2.04 %	1.97 %	0.373

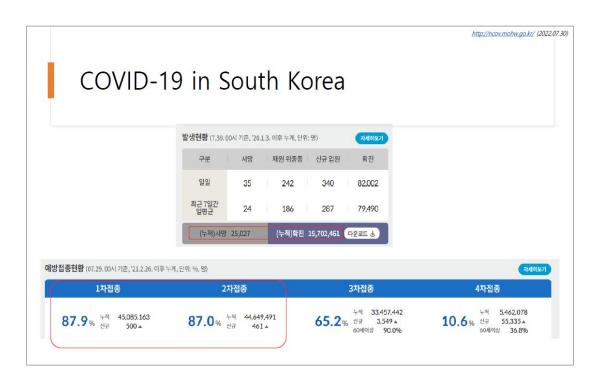


# New onset of hair loss disorders during the COVID-19 pandemic

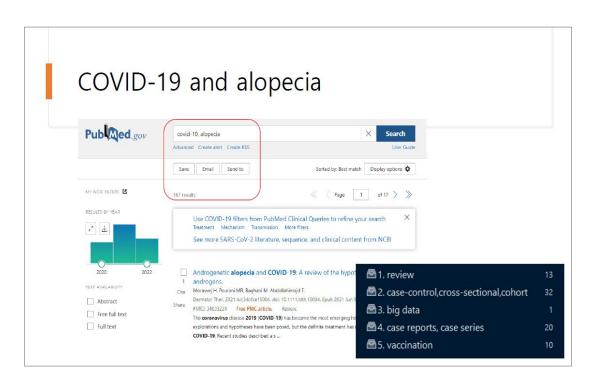
Da-Ae Yu

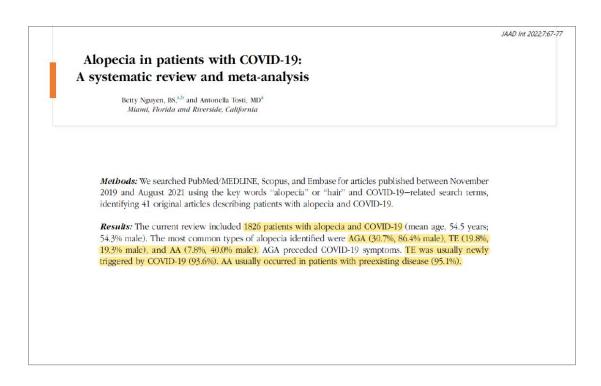
Konkuk University Medical Center











JAAD Int 2022;7:57-61 J Med Virol. 2022;94:1391–1401.

# Time to diagnosis of alopecia after COVID-19

Table I. Reports of new-onset alopecia areata after infection with SARS-CoV-2

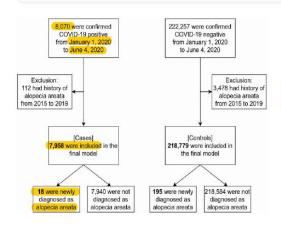
Case report	Age, y	Sex	Time to diagnosis after COVID-19	Clinical presentation
Rossi et al <sup>6</sup>	29	Female	4 wk	Patchy hair loss on vertex and parietal regions progressing to the involvement of the total scalp
Hayran et al7	13	Male	4 wk	Single 1-cm alopecic patch on scalp
Capalbo et al <sup>8</sup>	38	Male	4 wk	Variously distributed, sharply demarcated alopecic patches of the beard
Flvenson <sup>9</sup>	56	Female	8 wk	Loss of >99% of all body hair
Sgubbi et al <sup>10</sup>	54	Female	8 wk	Rapid onset of multiple patches of alopecia on the tempero- parietal area of scalp
Temiz and Kutlu <sup>11</sup>	43	Male	6 wk	Not reported
Temiz and Kutlu <sup>11</sup>	39	Female	8 wk	Not reported

these patients was 44 years and 67.5% were females. The most common trichoscopic findings were decreased hair density, the presence of empty follicles, or short regrowing hair. The mean duration from COVID-19 symptom onset to the appearance of acute TE was 74 days, which is earlier than classic acute TE. Most patients recovered from hair loss, while a few patients had persistent hair fall. Our results highlight the need to consider the possibility of post-COVID-19 acute TE in patients presenting with hair fall, with a history

# Hair loss after COVID-19 Heir folicie damage Cyteline storm Te Mirrantivi Cytelines CoviD-19 Advisimmure diseas -Disease susceptbility -medication etc.

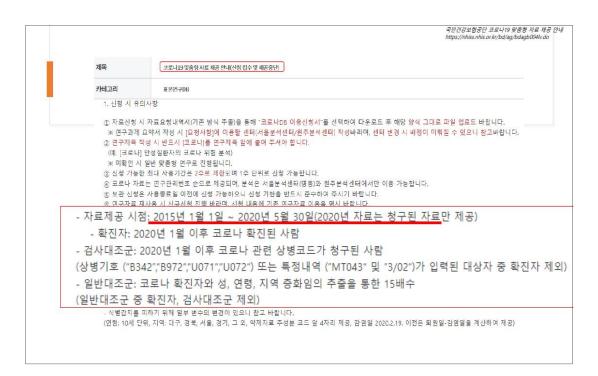
Front Med (Lausanne). 2021 Oct 13;8:758069.

#### Lack of Evidence of COVID-19 Being a Risk Factor of Alopecia Areata: Results of a National Cohort Study in South Korea



Results: A total of 226,737 individuals (7,958 [3.5%] cases and 218,779 [96.5%] controls) were included in the final analysis. The ratio of newly diagnosed AA was 187,958 (0.2%) in cases and 195/218,779 (0.1%) in controls. IRRs of COVID-19 patients having newly diagnosed AA compared to controls were 0.78 (95% CI: 0.48–1.27) when age and sex were adjusted for and 0.60 (95% CI: 0.35–1.03) when all demographic variables were adjusted for.

→ Diagnosis of COVID-19 was not significantly associated with the development of AA.

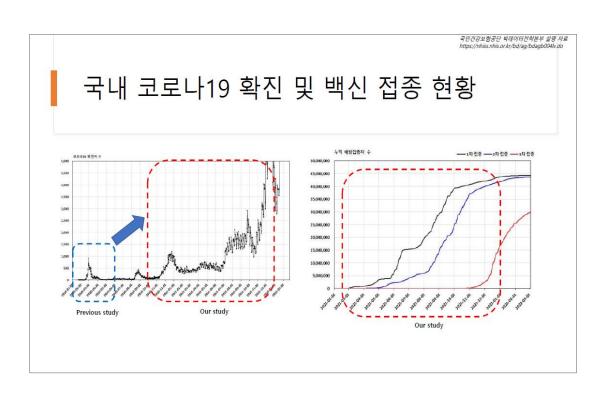


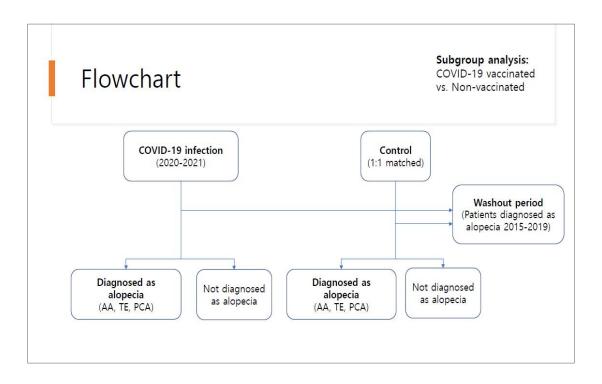




# Objective

- To determine the prevalence of hair loss disorders during the COVID-19 pandemic
- To investigate the relationship between new-onset of alopecia and COVID-19 infection/vaccination





# 대한모발학회 임원명단

(2022년 6월 - 2024년 5월)

• 고 문	노병인	명지병원
• 고 문	박장규	더웰피부과의원
• 고 문	임철완	
• 고 문	강진수	강한피부과의원
• 고 문	김도원	울산대병원
• 고 문	심우영	강동경희대병원
• 고 문	이원수	원주세브란스기독병원
• 고 문	강 훈	은평성모병원
• 고 문	최광성	인하대병원
• 회 장	김문범	부산대병원
• 부 회 장	권오상	서울대병원
• 총무/국제관계이사	허창훈	분당서울대병원
• 학술이사	유박린	강동경희대병원
• 재무이사	김상석	강동성심병원
• 교육이사	이 영	충남대병원
• 기획이사	이양원	건국대병원
• 간행정보이사	김도영	세브란스병원
• 홍보이사	원종현	서울아산병원
• 의무이사	서수홍	고대안암병원
• 대외협력이사	김범준	중앙대병원
• 무임소이사	박병철	단국대병원
• 총무간사	신현태	인하대병원
• 학술간사	최지웅	아주대병원
• 학술간사	박현선	보라매병원

• 재무간사 김민성 조선대병원 이지혜 성빈센트병원 • 교육간사 • 기획간사 박 진 전북대병원 • 기획간사 김정은 은평성모병원 • 기획간사 장용현 경북대병원 신기혁 부산대병원 • 간행정보간사 김효진 인제대백병원 감 사 • 감 사 조성빈 연세세란피부과의원

#### • 이 사

강광영, 김기호, 김창덕, 김효진, 노윤우, 민복기, 박성욱, 박원석, 방철환, 서구일, 성영관, 신기식, 신정원, 오지원, 이상훈, 이세원, 이승용, 이승호, 이인준, 임이석, 장승호, 전지현, 정의현, 조성빈, 조성환, 조항래, 최유성, 허 식, 황성주

# 대한모발학회 Hair Forum 연혁

#### ● 대한모발학회 Hair Forum 소개 ●

2002년 시작하여 해마다 참석하는 인원이 늘어나고 있는 Hair Forum은 모발학회 회원들 간의 격식 없는 모임입니다. 이는 자유로운 토론과 회원 상호간의 친목도모를 위하여 마련되고 있으며, 주로 진단 및 치료가 어려운 증례에 대한 토론, 그동안 연구했던 내용 발표, 해외모발학회 참관기소개 등 다른 회원들과의 의견공유를 위해서 밤늦은 시간까지 진행됩니다. 최근에 개최된 Hair Forum 현황은 다음과 같습니다.

#### [ 2002 대한모발학회 제1차 Hair Forum ]

일시: 2002년 8월 23일

장소: 대전 유성 리베라 호텔

모발의 색소이상에 나타나는 모구의 변화 외 8건 발표

#### [ 2003 대한모발학회 제2차 Hair Forum ]

일시: 2003년 8월 23일

장소: 대전 유성 리베라 호텔

원형탈모증 환자 400명의 임상적 고찰 외 8건 발표

#### [ 2004 대한모발학회 제3차 Hair Forum ]

일시: 2004년 8월 28일

장소: 대전 유성 스파피아 호텔

모낭유래세포에서의 androgen receptor, estrogen receptor의 발현 양상 외 13건 발표

#### [ 2005 대한모발학회 제4차 Hair Forum ]

일시: 2005년 8월 20일

장소: 대전 유성 스파피아 호텔

원형탈모증 환자 400명의 임상적 고찰 외 8건 발표

#### [ 2006 대한모발학회 제5차 Hair Forum ]

일시: 2006년 8월 19일 장소: 대전 유성 레전드호텔

Acute diffuse alopecia areata 외 11건 발표

#### [ 2007 대한모발학회 제6차 Hair Forum ]

일시: 2007년 8월 18일

장소: 대전 유성 리베라 호텔

모낭유래세포의 특성분석 외 13건 발표

#### [ 2008 대한모발학회 제7차 Hair Forum ]

일시: 2008년 8월 23일

장소: 대전 유성 리베라 호텔

전두탈모증 환자에서 모반 제거후 모발재생의 치료 경험 외 18 건 발표

#### [ 2009 대한모발학회 제8차 Hair Forum ]

일시: 2009년 8월 22일

장소: 대전 유성 리베라 호텔

원형 탈모증 환자에서 스트레스 평가에 대한 예비 연구 외 9건 발표

#### [ 2010 대한모발학회 제9차 Hair Forum ]

일시: 2010년 8월 21일

장소: 대전 유성 리베라 호텔

Differential expression of cytokines and interferone inducible genes in alopecia areata 외 16건 발표

#### [ 2011 대한모발학회 제10차 Hair Forum ]

일시: 2011년 8월 27일

장소: 대전 아드리아 호텔

Retinol-binding protein 4 (RBP4) and anti-RBP4 antibody are increased in alopecia areata 외 12건 발표

#### 2022 대한모발학회 제20차 Hair Forum

#### [ 2012 대한모발학회 제11차 Hair Forum ]

일시: 2012년 8월 18일 장소: 대전 아드리아 호텔

Effects of mycophenolic acid and rapamycin on hair growth 외 12건 발표

#### [ 2013 대한모발학회 제12차 Hair Forum ]

일시: 2013년 8월 17일 장소: 대전 아드리아 호텔

How can we enhance follicular penetration? (In vivo preliminary study) 외 13건 발표

#### [ 2014 대한모발학회 제13차 Hair Forum ]

일시: 2014년 7월 26일

장소: 대전 유성호텔 8층 스타볼룸

털껍질(hair cuticle)이 모발색조에 미치는 영향 외 6건 발표

#### [ 2015 대한모발학회 제14차 Hair Forum ]

일시: 2015년 8월 22일

장소: 대전 유성호텔 8층 스타볼룸

Experience of combination therapy with finasteride and low dose dutasteride in the treatment of male pattern hair loss 외 8건 발표

#### [ 2016 대한모발학회 제15차 Hair Forum ]

일시: 2016년 8월 27일

장소: 대전 유성호텔 8층 스타볼룸

#### [ 2017 대한모발학회 제16차 Hair Forum ]

일시: 2017년 8월 26일(토)

장소: 대전 유성호텔 8층 스타볼룸

#### [ 2018 대한모발학회 제17차 Hair Forum ]

일시: 2018년 8월 18일(토)

장소: 대전 유성호텔 8층 스타볼룸

The effect of ceramide-based essence cream for the damaged hair shaft 외 8편 발표

#### [ 2019 대한모발학회 제18차 Hair Forum ]

일시: 2019년 8월 17일(토)

장소: 대전 유성 호텔 8층 스타볼룸

Impact of alopecia areata on subsequent pregnancy rate: a retrospective cohort study 외 10편 발표

#### [ 2020 대한모발학회 Hair Forum ] (코로나로 취소)

#### [ 2021 대한모발학회 제19차 Hair Forum ]

일시: 2021년 8월 21일(토)

장소: 대전 유성 호텔 8층 스타볼룸

The effect of onset-season in the prognosis of alopecia areata: A retrospective study of 492 cases 외 13편 발표



### 2022 대한모발학회 제20차 Hair Forum

인 쇄 2022년 8월 12일 발 행 2022년 8월 20일

발행처 대한모발학회

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