# The 9<sup>th</sup> Annual Meeting The Korean Society for Psoriasis



May 14, 2005 COEX InterContinental Hotel Seoul, Seoul, Korea Organized by The Korean Society for Psoriasis Co-sponsored by The Korean Dermatological Association The Korean Society for Investigative Dermatology

# 인사말씀

대한건선학회 제9차 학술대회를 맞이하여 그 동안 성원하고 지원해 주신 회원 여러분들게 심심한 감사를 드립니다. 우리 학회가 지난 8년 동안 개최한 연례 학술대회는 이제 건선 분 야의 연구업적의 발표 및 학술교류의 장으로 굳게 자리 매김을 하였습니다. 건선 및 관련 질 환에 대한 회원들의 다양한 증례 발표는 임상 경험의 공유로 이어졌으며 건선의 발병 기전으 로부터 면역학적, 분자생물학적 치료에 이르기까지 폭 넓고 심도 있는 연구결과는 진료의 발 전으로 연결되어왔다고 자부하고 있습니다.

매년 알찬 프로그램을 선보이고 있는 대한건선학회 연례학술대회에 올해도 두 분의 저명한 특강 연자를 모시게 된 것을 기쁘게 생각합니다. 여러 회원들도 잘 아시는 영국 Manchester 대학의 Christopher Griffiths 교수는 각종 생물학적제제를 중심으로 하는 현대 건선 치료법을 "The Modern Management of Psoriasis"라는 제목으로, 일본 니혼대학의 Tadashi Terui 교수는 건선 연구의 최신 지견을 "Recent Advances in Research on Psoriasis with a Special Attention on T Cell Activation and Aseptical Neutrophil Accumulation"라는 제목으로 특별강연을 해주시게 되었습니다. 작년에 이어 금년에도 구진인설성질환 전반에 관 한 일반연제를 [자유연제 2]에서 다루고자 하오니 많은 연제를 발표하여 주시기 바랍니다. 또 한 개원의 선생님들과 전공의 선생님들에게 실질적인 도움이 되고 있다는 평가를 받고 있는 교육강연에서는 한국인의 자외선치료에 있어서 현장에서 부딪치는 문제에 대한 전문가들의 견해를 들으실 수 있는 귀한 시간이 될 것입니다.

이번 9차 학술대회를 준비하는데 힘써 주신 건선학회 임원 여러분 그리고 동참해 주신 해 외 및 국내 초빙 연자, 좌장 및 발표자 여러분에게 깊은 감사를 드립니다. 또한 앞으로도 여 러 회원들의 지속적인 후원과 지도 편달을 바라며, 회원 여러분 가정에 만복이 함께 하시고 건강하시기를 기원합니다.

2005. 5. 14

대한건선학회 회장 김 광 중

# PRESIDENT'S MESSAGE

I would like to take this opportunity to express my warmest gratitude to the members of the Korean Society for Psoriasis (KSP) and colleagues of the Korean Dermatological Association for the sincere support for our society and annual meetings. For the past 8 years, annual meetings of the KSP have provided us with great opportunities to share clinical experiences and to obtain comprehensive knowledge in many aspects of psoriasis. The remarkable progress in the field of immunology and molecular biology presented in the annual meetings of the KSP has offered great leverage in the psoriasis management.

The scientific program for this year has been arranged for the best interest of our members. We are delighted to announce that we have two great international scholars for our meeting. Dr. Christopher Griffiths, Professor and Chairman, Dermatology Centre, University of Manchester, UK, will show us how to do integrated management of psoriasis in the era of biologics. Dr. Tadashi Terui, Professor and Chairman, Department of Dermatology, Nihon University, Japan, will update us with recent advances in psoriasis research and treatment. Our attempt to expand our scope to the whole variety of papulosquamous disorders will be maintained again this year in *free communications* 2. Educational lectures covering practical issues in the phototherapy of psoriasis will be greatly helpful especially for young doctors and practicing physicians.

I would like to extend my appreciation to those who present their valuable work in our annual meeting, invited speakers, chairpersons and all the members and directors of the KSP. I cordially ask all of you to continuously support us as ever. I hope the best for every single member of the KSP.

Looking forward to seeing you all in Seoul soon.

Thank you very much.

Sincerely,

**Kwang-Joong Kim**, M.D. President of the KSP

# PROGRAM

09:30 - 09:55	Registration
09:55 - 10:00	Opening Remark
10:00 - 11:00	Free Communications 1
11:00 - 12:00	Free Communications 2
12:00 - 13:30	Lunch / Council Meeting
13:30 - 14:30	Special Lecture 1
14:30 - 15:15	Case Reports
15:15 - 15:30	Coffee Break
15:30 - 16:30	Special Lecture 2
16:30 - 17:30	Educational Lectures
18:00 - 19:00	Cocktail Party

# **INFORMATION**

Advance Registration Not available

#### On-site Registration

Physicians: 20,000 W (including annual membership) Residents: free

### Official Language

Oral presentations will be made in Korean language. <u>However, all the presentation</u> <u>material should be prepared in English.</u> Non-Korean participants are allowed to use English language in oral presentations.

## ▶ Venue: COEX InterContinental Hotel Seoul

159 Samsung-dong, Gangnam-gu Seoul 135-975, South Korea Tel: +82 2 3452 2500, Fax: +82 2 3430 8000 E-mail: coexseoul@interconti.com

#### Presentation

Choice of presentation method between beam projection and slide projection should be notified to us at the time of abstract submissions. Those who would like to use beam projection are advised to use Microsoft PowerPoint (version 97 or compatible). Double slide projection or overhead projection is not available for the presentation.

• Suggested duration of presentation:

Free communications	7 minute presentation+3 minute discussion
Case reports	5 minute presentation+2 minute discussion
Educational lectures	13 minute presentation+2 minute discussion
Special lectures	50 minute presentation+5 minute discussion

<u>All the presenters are required to submit their presentation material at least 1 hour prior</u> to the scheduled presentation time. Recommended media for digital files are CD-ROM or USB type memory. Digital files in presenter's notebook computers will not be accepted.

#### Social Program

Standing cocktail party (free admission 6:00-7:00) is planned for all the participants. Please enjoy tasty cuisine and beverage with your colleagues and friends.

# ACADEMIC PROGRAMS

Free Communications 1 (10:00~11:00) Chairs: Drs. Nack-In Kim / Kyu-Wang Whang

1. PROFILING OF DIFFERENTIALLY EXPRESSED GENES IN PSORIATIC SKIN LESIONS

- 2. GENE EXPRESSION PROFILES OF SERUM--INDUCED ABNORMAL KERATINOCYTE DIFFERENTIATION AND REGULATION OF B7-H1 BY INF-GAMMA
- 3. DQCAR AND TNFD MICROSATELLITE ARE SIGNIFICANT MARKERS OF SUSCEPTIBILITY TO PSORIASIS IN KOREAN POPULATION

LIM Myoung<sup>1</sup>, KIM Chang-Deok<sup>1</sup>, LEE Sang-Keun<sup>2</sup>, KIM Byoung-Soo<sup>2</sup>, SEO Sam-Hwa<sup>2</sup>, KANG Jung-Soo<sup>2</sup>, LIM Jong-Soon<sup>2</sup>, LEE Jeung-Hoon<sup>1</sup> <sup>1</sup>Department of Dermatology, School of Medicine, Chungnam National University, Daejeon, <sup>2</sup>Korea Institute of Traditional Medicine and Biogiana Davier

Medicine and Bioscience, Daejeon University, Daejeon, Korea

<u>LEE Sang-Keun</u><sup>1</sup>, KIM Byoung-Soo<sup>1</sup>, SEO Sam-Hwa<sup>1</sup>, LEE Young<sup>2</sup>, KIM Chang-Deok<sup>2</sup>, LEE Jeung-Hoon<sup>2</sup>, KANG Jung-Soo<sup>1</sup>, LIM Jong-Soon<sup>1</sup>

<sup>1</sup>Institute of Traditional Medicine and Bioscience, Daejeon University, Daejeon, Korea, <sup>2</sup>Department of Dermatology, School of Medicine, Chungnam National University, Daejeon, Korea

## <u>CHOI Eun-Jung</u><sup>1</sup>, CHOI Hee-Baeg<sup>2</sup>, KIM Su-Yeon<sup>1</sup>, YOON Ho-Yeul<sup>1</sup>, PARK Min-Ji<sup>1</sup>, KIM Tae-Yoon<sup>3</sup>, KIM Tai-Gyu1<sup>2</sup>

Department of <sup>1</sup>Microbiology, <sup>2</sup>Catholic Hemapoietic Stem Cell Bank, <sup>3</sup>Department of Dermatology, College of Medicine, The Catholic University of Korea

- 4. EFFECTS OF KERATINOCYTE GROWTH FACTOR (KGF), EPIDERMAL GROWTH FACTOR (EGF), AND EXTRACELLULAR CALCIUM ON THE GROWTH OF CULTURED PSORIATIC KERATINOCYTES
  - 5. PREFERENCE OF NEAR-ERYTHEMOGENIC NARROW-BAND UVB PHOTOTHERAPY IN PSORIASIS AND ITS IMPLICATION OF DENDRITIC CELLS/CHEMOKINES
  - 6. THE STUDY OF CERAMIDES AND CELL SIGNALING MOLECULES IN PSORIATIC EPIDERMIS: REDUCED LEVELS OF CERAMIDES, PKC-a, AND JNK
  - 7. EXPRESSION OF NEUROPEPTIDES IN PSORIATIC LESIONS WITH OR WITHOUT PRURITUS USING CONFOCAL LASER SCANNING MICROSCOPY
  - 8. PROTECTIVE EFFECT OF PROHIBITIN AGAINST ANTHRALIN INDUCED CELL DEATH

<u>KIM Hong-Seok<sup>1</sup></u>, KU Bon-Seok<sup>1</sup>, KWON Oh-Eon<sup>1</sup>, KIM Ji-Yeon<sup>2</sup>, YOON Tae-Jin<sup>3</sup>, LEE Chea-Wook<sup>1</sup>, KIM Ki-Ho<sup>1</sup>

<sup>1</sup>Department of Dermatology, Dong-A University College of Medicine <sup>2</sup>Department of Biotechnology and Bioengineering, Bukyong National University, Busan, <sup>3</sup>Department of Dermatology, Gyeongsang National University, Jinju, Korea

#### KIM Hong-Seok, KWON Oh-Eon, KU Bon-Seok, LEE Chea-Wook, KIM Ki-Ho

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

#### <u>LEW Bark-Lynn<sup>1</sup></u>, CHO Yunhi<sup>2</sup>, KIM Nack-In<sup>1</sup>

Department of <sup>1</sup>Dermatology, College of Medicine, <sup>2</sup>Department of Medical Nutrition, Graduate School of East-West Medical Science, Kyung Hee University, Seoul, Korea

#### <u>CHANG Sung-Eun</u><sup>1</sup>, JUNG Hae-Jin<sup>2</sup>, MOON Kee-Chan<sup>1</sup>, KOH Jai-Kyoung<sup>1</sup>, CHOI Jee-Ho<sup>1</sup>

Department of <sup>1</sup>Dermatology, Asan Medical Center, <sup>2</sup>Asan Institute for Life Science, College of Medicine University of Ulsan, Seoul, Korea

## <u>KIM Soon-Young</u>, HA Hye-Yeong, KIM Tae-Yoon

Department of Dermatology, College of Medicine, The Catholic University of Korea

## Free Communications 2 $(11:00 \sim 12:00)$

Chairs: Drs. Kyu-Suk Lee / Jee-Ho

Choi

1. THE EFFECT OF ACITRETIN TO THE EXPRESSION OF ANGIOGENIC FACTOR IN PSORIASIS

#### KIM Chi Yeon<sup>1</sup>, <u>NAM Young Ho</u><sup>1</sup>, KIM Gun Do<sup>2</sup>, YOUN Tae Jin<sup>1</sup>, OH Chee Won<sup>1</sup>

<sup>1</sup>Department of Dermatology, College of Medicine, Gyeongsang National University, Chinju <sup>2</sup>Department of Microbiology, Pukyong

National University, Pusan, Korea

#### JUN Hyung-Oh<sup>1</sup>, SEONG Young Rim<sup>3</sup>, HONG Soon-Sun<sup>1</sup>, PARK Jeong-Ae<sup>1</sup>, HA Hye-Yeong<sup>3</sup>, KIM Young Hoon<sup>3</sup>, KIM Kyu-Won<sup>1</sup>, SHIN Jongheon<sup>2</sup>, KIM Tae-Yoon<sup>3</sup>

<sup>1</sup>Research Institute of Pharmaceutical Sciences and College of Pharmacy, Seoul National University, Seoul, Korea <sup>2</sup>Natural Products Research Institute, College of Pharmacy, Seoul National University, Seoul, Korea <sup>3</sup>Laboratory of Dermatology, Catholic Research Institute of Medical Science, College of Medicine, The Catholic University of Korea, Seoul, Korea

#### YOON Hyun-Sun, JO Seong-Jin, YOUN Jai-Il

Department of Dermatology, Seoul National University College of Medicine, Seoul, Korea

#### <u>JO Seong-Jin</u>, YOON Hyun-Sun, YOUN Jai-Il

Department of Dermatology, Seoul National University College of Medicine, Seoul, Korea

#### <u>JO Seong-Jin</u>, YOON Hyun-Sun, YOUN Jai-Il

Department of Dermatology, Seoul National University College of Medicine, Seoul, Korea

2. ANTIANGIOGENIC ACTIVITY OF WONDONIN TARGETTING HYPOXIA-INDUCIBLE FACTOR 1

- 3. THE EFFECT AND SAFETY OF COMBINATION THERAPY USING NARROW-BAND UVB PHOTOTHERAPY AND CALCIPOTRIOL
- 4. TIME COURSE OF TANNING INDUCED BY NARROW-BAND UVB PHOTOTHERAPY IN KOREAN PSORIASIS PATIENTS
- 5. CALCITRIOL OINTMENT FOR THE TREATMENT OF FACIAL PSORIASIS

- 6. AN ATTEMPT AT A NEW SYSTEMIC TREATMENT REGIMEN WITH CYCLOSPORIN BASED ON ITS PHARMACOKINETICS IN PSORIASIS
- 7. CYCLOSPORINE TREATMENT EXPERIENCE IN MILD TO MODERATE PSORIASIS PATIENTS

#### UMEZAWA Yoshinori, AKASAKA Emiko, MABUCHI Tomotaka, OHTA Yukinori, MATSUYAMA Takashi, and OZAWA Akira

Department of Dermatology, Tokai University School of Medicine, Isehara, Kaganagawa, Japan

## LEE Kwang-Jun, KIM Won-Serk, LEE Dong-Youn, YANG Jun-Mo, LEE Eil-Soo, LEE Joo-Heung

Department of Dermatology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

8. CLINICAL AND LABORATORY CHARACTERISTICS OF SMALL PLAQUE PSORIASIS VULGARIS LEW Wook

Department of Dermatology, Yonsei University College of Medicineorea

**Special Lecture 1**  $(13:30 \sim 14:30)$ 

Chair: Dr.

Kwang-Joong Kim

RECENT ADVANCES IN RESEARCH ON PSORIASIS WITH A SPECIAL ATTENTION ON T CELL ACTIVATION AND ASEPTICAL NEUTROPHIL ACCUMULATION

**TERUI Tadashi** Department of Dermatology, Nihon

University School of Medicine, Itabashi-ku, Japan

**Case Reports** (14:30~15:15)

Chairs: Drs. Tae-Yoon Kim / Ki-Ho Kim

1. A CASE OF COEXISTENCE OF MORPHEA AND PSORIASIS PARK Hyun-Je, JANG Ho-Sun, JANG Bong-Seok, KIM Moon-Bum, OH Chang-Keun, KWON Kyung-Sool DDepartment of Dermatology, College of Medicine, Pusan National University, Busan, Korea

2. HYPOCALCEMIA-INDUCED PUSTULAR PSORIASIS-LIKE SKIN ERUPTION LEE Young, LEE Jeung-Hoon, PARK Jang-Kyu, SEO Young-Joon Department of Dermatology, School of Medicine, Chungnam National University, Daejeon, Korea

7. LOW DOSE CYCLOSPORIN: A TREATMENT IN GENERALIZED PUSTULAR PSORIASIS

CHANG Sung-Eun, LEE Mi-Woo, CHOI Jee-Ho, MOON Kee-Chan, KOH Jai-Kyoung Department of Dermatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

AHN Soo-Jin, OH Sang-Hyun,

LEE Jeong-Hoon, YUN Sook-Jung, LEE Jee-Bum, KIM Seong-Jin, WON Young-Ho, LEE Seung-Chul Department of Dermatology, Chonnam National University Medical School, Chonnam, Korea

4. THE KOEBNER PHENOMENON DUE TO INFLUENZA VACCINATION IN A **PSORIASIS PATIENT** 

5. A CASE OF RECALCITRANT EXFOLIATIVE DERMATITIS CAUSED BY **PSORIASIS** 

6. A CASE OF INFANTILE PSORIASIS

PIMECROLIMUS AND LOW DOSE

WITH ACRODERMATITIS CONTINUA

NARROWBAND UVB PHOTOTHERAPY

SUCCESSFULLY TREATED WITH TOPICAL

3. A CASE OF THE EYELID PSORIASIS

YOON Hyun-Sun, JO Seong-Jin, YOUN Jai-Il Department of Dermatology, Seoul National University College of Medicine, Seoul, Korea

YOON Hyun-Sun, JO Seong-Jin,

Department of Dermatology, Seoul National

University College of Medicine, Seoul, Korea

YOUN Jai-Il

### KIM Hei-Sung, KIM Sei-Yeon, KIM Heesu, KIM Gyoung Moon, KIM Si-Yong Department of Dermatology, The Catholic University of Korea, Seoul, Korea

**Special Lecture 2**  $(15:30 \sim 16:30)$ 

THE MODERN MANAGEMENT OF PSORIASIS

GRIFFITHS Christopher E.M.

Chair: Dr.

The Dermatology Centre, Hope Hospital, University of Manchester, Manchester, UK.

Jai-Il Youn

## Educational Lectures (16:30~17:30)

- 1. NBUVB THERAPY IN KOREAN PSORIASIS PATIENTS
- 2. PUVA THERAPY FOR PSORIASIS IN COMPARISION WITH NBUVB

Chairs: Drs. Sang-Tae Kim / Young-Ho Won

YOUN Jai-Il Department of Dermatology, College of Medicine, Seoul National University, Seoul, Korea

KIM Tae-Yoon Department of Dermatology, College of Medicine, The Catholic University of Korea, Seoul, Korea

- 3. COMBINATION OF RETINOID WITH ULTRAVIOLET LIGHT THERAPY: IMPLICATION IN THE TREATMENT OF PSORIASIS PATIENTS WITH DARK SKIN
- 4. TREATMENT OF PSORIASIS WITH 308 NM XENON-CHLORIDE (XE-CL) EXCIMER LASER

LEE Joo-Heung Department of Dermatology, Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Korea

KIM Nack-In Department of Dermatology, Kyunghee University School of Medicine, Seoul, Korea

# **SPECIAL LECTURE**

SL-1

# CURRICULUM VITAE

Full Name	:	TERUI Tadashi, M.D., Ph.D.
Sex	:	Male
Date of birth	:	March 28, 1955
Place of birth	:	Japan
Marital status	:	Married
Nationality	:	Japanese
Mailing address	:	Department of Dermatology,
		Nihon University School of Medicine,
		30-1 Oyaguchi-Kamimachi, Itabashi-ku, Japan
		Tel: +81-3-3972-8111 (Ext 2502)
		Fax: +81-3-5995-9841
		E-mail: terui@med.nihon-u.ac.jp

Education	
1975-1981	School of Medicine, Tohoku University: Awarded the degree of MD
1991	Awarded the degree of PhD in cutaneous immunology: Work
	supervised by professor Hachiro Tagami

Clinical and research experience	
1981-1983	Resident at Department of Dermatology, Tohoku University School of Medicine, working under professor Makoto Seiji
1983-1984	Resident at Department of Dermatology, Tohoku Rosai Hospital
1985-1988	Assistant professor at Department of Dermatology, Tohoku University School of Medicine, working under professor Hachiro

Tagami

1988-1991	Research associate at Department of Pathology, University of Utah,
	working under professor Raymond A. Daynes
1991-2000	Lecturer at Department of Dermatology, Tohoku University School
	of Medicine
2000-2004	Associate professor at Department of Dermatology, Tohoku
	University School of Medicine, working under professor Hachiro
	Tagami
2005-Present	Professor and chairman at Department of Dermatology, Nihon
	University School of Medicine

## Board members

Japanese Society for Investigative Dermatology from 1998 Japanese Society for Inflammation (and Regeneration) from 2000 Japanese Society for Dermatoallergology from 2003 Tokyo Division of Japanese Dermatological Society from 2004

# RECENT ADVANCES IN RESEARCH ON PSORIASIS WITH A SPECIAL ATTENTION ON T CELL ACTIVATION AND ASEPTICAL NEUTROPHIL ACCUMULATION

#### TERUI Tadashi

Department of Dermatology, Nihon University School of Medicine, Itabashi-ku, Japan

Psoriasis is a remitting and relapsing inflammatory skin disease with a chronic natural course, and while its true pathogenesis remains uncertain, it can be understood as having a dual nature, one derived from genetic factors and one from environmental factors. As regards its pathophysiology, because it is an inflammatory dermatitis characterized by proliferation of the epidermis, psoriasis was initially thought to be a disease of abnormal keratinocyte differentiation and proliferation. Subsequently, it has been shown that the onset of psoriasis is associated with HLA antigens, that numerous T cells and macrophages are infiltrated in psoriatic lesions, and that the importance of T cells in the pathophysiology of psoriasis is being elucidated from the analysis of blood or lesional skin obtained from patients, and by the presentation of animal models of psoriasis. Such a theory is supported by the excellent results obtained with the new selective treatments for psoriasis that target specific molecules. Superantigens and M protein derived from bacteria have been cited as a promising candidate, but opposing views have also been reported. Thus, at the present time, it must be conceded that the identity of the antigen that induces activation of T cells is not clear. There is growing evidence that T cell activation is mediated by an appropriate antigen presentation via peptide/MHC and T cell receptor interactions in conjunction with signals mediated by costimulatory molecules expressed by antigen presenting cells (APCs). Before then, the APCs must be stimulated to become mature cells by so-called danger or alarm signals. Recent research revealed that environmental factors have a close connection with the danger or alarm signals. As to the pathogenesis of psoriasis having a genetic background, there is no doubt that certain disease-sensitive genes are involved, but it may yet take some time before all the specific genes are identified. In this lecture, I would like to introduce recent advances in research on psoriasis deciphering the relationship between abnormal immune function and genetic factors related to its pathogenesis. I also present the mechanism by which an aseptical neutrophil accumulation occurs in active psoriatic lesions mainly based on our experimental results.

# SL-2

# CURRICULUM VITAE

## Name : GRIFFITHS Christopher

Professor of Dermatology, University of Manchester, Manchester, United Kingdom

Christopher Griffiths, MD, FRCP, FRCPath, is Foundation Professor of Dermatology, University of Manchester, UK and Head of the Greater Manchester Dermatology Centre, Manchester, UK. He received his BSc (1st Class Hons) MB and BS degrees from St Thomas' Hospital Medical School, London University and his MD also from London University. He trained in dermatology at St Mary's Hospital, London and the University of Michigan where he was on faculty in the department of dermatology. He developed the "hub-and-spoke" model of dermatology services for Greater Manchester and instigated the North West Regional Dermatology Training Scheme. He introduced a multidisciplinary clinic for severe psoriasis - the Manchester Psoriasis Service awarded Hospital Doctor Dermatology Team of the Year Award 2002. He has received many awards and honours; named lectureships at national and international meetings include the 1998 Dowling Oration and 2003 St John's Oration. He is a past Chairman of the British Society for Investigative Dermatology and is currently President of the British Association of Dermatologists. He is on the editorial boards of 8 scientific journals, including the British Journal of Dermatology and Clinical and Experimental Dermatology; author of 262 research articles in peer-reviewed journals and 150 articles in non-peer reviewed journals and is a co-editor of the premier international textbook of dermatology - Rook's Textbook of Dermatology. He has a long-standing interest in psoriasis and his research includes immunological mechanisms of psoriasis, immunotherapy (including the new biological agents) and the "brain-skin axis".

# THE MODERN MANAGEMENT OF PSORIASIS

#### **GRIFFITHS** Christopher E.M.

The Dermatology Centre, Hope Hospital, University of Manchester, Manchester, UK.

Biologicals are defined as proteins, derived from human or animal, which have pharmacological activity. They are not new; porcine insulin is a good example of a biological. Modern recombinant DNA technology has allowed considerable advance in this area with production of agents such as erythropoietin. The use of biologicals for inflammatory disease has been pioneered in rheumatology and gastroenterology. Knowledge of the key immunological pathways in psoriasis has allowed development of selectively targeted biologicals for this disease. There is an unmet need for systemic therapies which are able to clear psoriasis without risk of organ toxicity. Biologicals for psoriasis take two main forms: (i) T-cell-targeted namely alefacept an LFA-3 fusion protein, and efalizumab, anti-CD11a; and (ii) TNF- $\beta$  blockers - etanercept, a recombinant soluble TNF receptor and infliximab - monoclonal antibody to TNF- $\beta$ . Alefacept is administered as an intramuscular or intravenous injection once weekly for a 12 week cycle - 75% improvement in Psoriasis Area Severity Index (PASI 75) is seen in approximately 20% of patients. Alefacept is associated with a peripheral CD4 lymphopenia. Efalizumab is self-administered by subcutaneous injection once weekly initially for 12 weeks and long term continual therapy is recorded beyond 2 years. Approximately 23% of patients achieve, PASI 75, monitoring is minimal. Infliximab is administered as 3 intravenous loading doses over 6 weeks and then long-term either on disease relapse or 2 monthly. Response is rapid and high with 85% of patients achieving, PASI 75. Etanercept administered subcutaneously twice weekly, produces approximate 30% improvement after 12 weeks and can be used long-term. Both infliximab and etanercept are associated with reactivation of TB, demyelination and increased incidence of lymphoma. All four biologicals are considerably more expensive than currently available pharmaceuticals. The short-term (<16 weeks) efficacy of pharmaceuticals is overall better than for most biologicals eg ciclosporin 5mg/kg/day and PUVA - 70% of patients achieve PASI 75 and methotrexate - 60% of patients achieve PASI 75. It would appear that the advantage of biologicals (other than infliximab) could be for long-term treatment, indeed they may be more suitable for a chronic, currently incurable condition such as psoriasis although methotrexate has an enviable track record.

It is yet to be determined as to how biologicals will be integrated into our current standard of care for severe psoriasis - they may be used in combination with currently available pharmaceuticals particularly acitretin and perhaps short-term in combination with ciclosporin; in the case of alefacept/efalizumab combination could enhance speed of response.

# FREE COMMUNICATIONS 1

# PROFILING OF DIFFERENTIALLY EXPRESSED GENES IN PSORIATIC SKIN LESIONS

# LIM Myoung<sup>1</sup>, KIM Chang-Deok<sup>1</sup>, LEE Sang-Keun<sup>2</sup>, KIM Byoung-Soo<sup>2</sup>, SEO Sam-Hwa<sup>2</sup>, KANG Jung-Soo<sup>2</sup>, LIM Jong-Soon<sup>2</sup>, LEE Jeung-Hoon<sup>1</sup>

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Psoriasis is recognized as the most common T cell-mediated inflammatory disease in humans. Genetic linkage to as many as six distinct disease loci has been established but the molecular etiology and genetics remain unknown. To begin to identify psoriasis disease-related genes and construct in vivo pathways of the inflammatory process, a genome-wide expression screen of psoriasis patients was performed. Experimental scheme was designed to the comparison of total RNA obtained from uninvolved skin with that of involved skin. Microarray analysis revealed that the approximately 500 genes (360 over-expressed and 140 under-expressed) were differentially expressed at least twofold in involved skin compared with uninvolved skin. Some of up-regulated genes have been already reported to the correlation with psoriasis including S100 family, proteinases and their inhibitors, antagonists of apoptosis, and differentiation markers. Also, there have been numerous genes showing increased expression of which functions do not have been established or identified in psoriasis. Subsequently, the relative expression levels of randomly selected genes evaluated by reverse-transcriptase polymerase chain reaction were found to be consistent with the microarray data. Although our results could provide a new insight into the understanding of psoriasis pathogenesis, other methods are need for understanding of mRNA profiles shown in psoriatic skin lesions.

# GENE EXPRESSION PROFILES OF SERUM—INDUCED ABNORMAL KERATINOCYTE DIFFERENTIATION AND REGULATION OF B7-H1 BY INF-GAMMA

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Keratinocytes have been reported to show psoriatic differentiation when induced to be differentiated in the presence of fetal bovine serum. To predict the procedures of abnormal keratinocyte differentiation, we compared the gene expression profiles of normal keratinocytes cultured without growth factors with those cultured in the presence of fetal bovine serum after 1, 3, 6, and 24 h using cDNA microarray. As a result, the expression of inflammatory cytokines and chemokines was induced rapidly in the early stage of differentiation, whereas the precursor proteins of the cornified envelope and proteases increased in the late stage, which mirrors the general appearance seen in the psoriatic epidermis. Interestingly, a T-cell co-stimulatory molecule, called as programmed cell death ligand 1 (B7-H1) that might influence lymphocyte activity during the process of skin inflammation was found to show much increased expression at the early stage of abnormal keratinocyte differentiation. Moreover, IFN-y, one of the most potent pro-inflammatory cytokines in the skin, strongly enhanced B7-H1 expression in human dermal fibroblasts and NF-kB binding motif was very important for B7-H1 expression by IFN-y. Because IFN-y also stimulated the transient phosphorylation of ERK1/2 and PI3K in dermal fibroblasts and eventually translocated NF-kB to the nucleus, NF-kB transcription factors mediate the induction of B7-H1 expression via the transient phosphorylation of ERK1/2 and PI3K when cells are stimulated by IFN-y. In summary, our results provide evidence that initiation of keratinocyte differentiation by FBS might reflect the conditions of hyperkeratotic dermatoses in vivo, and B7-H1 is a possible candidate as a novel target for clinical intervention in T-cell mediated inflammatory skin diseases like psoriasis.

# DQCAR AND TNFD MICROSATELLITE ARE SIGNIFICANT MARKERS OF SUSCEPTIBILITY TO PSORIASIS IN KOREAN POPULATION

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Psoriasis is believed to be a multigene disease, the expression of which is partially dependent on external factors. The association between HLA-Cw6 and psoriasis has been found in different populations and extended chromosome 6 haplotypes, such as HLA-A2, B13, Cw6, DR7, DQA1\*0201 (DQ2) and A1, B17, Cw6, DR7, DQA1\*0201 (DQ2) have also been described in Korean. However, it remains uncertain as to whether the genetic factor is the HLA-Cw6 antigen itself or a closely linked unidentified locus. Therefore, we have investigated HLA region microsatellite polymorphisms in psoriasis which are known to be associated with HLA-C locus in the Korean population. one hundred eighty four patients with psoriasis and 88 controls were employed for this study, in which DQCAR, D6S291 and TNFd microsatellite typing were performed. DQCAR 3 (RR=3.56, p<0.000002), DQCAR 5 (RR=2.84, p<0.006), DQCAR 9 (RR=2.0, p<0.004) and DQCAR 11 (RR=2.25, p<0.02) frequencies were significantly increased in the psoriasis group compared with control group. The frequencies of DQCAR 7 (RR=0.15, p<0.04) and DQCAR 14 (RR=0.6, p<0.01) were significantly decreased in patients with psoriasis. Also, TNFd 2 (RR=15.54, p<0.0000003), and TNF 4 (RR=13.67, p<0.0000006) frequencies were significantly increased in the psoriasis group compared with control group. The frequency of TNFd 7 (RR=0.59, p<0.02) was significantly decreased in the psoriasis group. These results suggest that microsatellites in HLA gene region may be used as good susceptibility markers for psoriasis in Korean.

# EFFECTS OF KERATINOCYTE GROWTH FACTOR (KGF), EPIDERMAL GROWTH FACTOR (EGF), AND EXTRACELLULAR CALCIUM ON THE GROWTH OF CULTURED PSORIATIC KERATINOCYTES

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We investigated the effects of KGF and EGF, together with extracellular calciums, on the growth of cultured psoriatic keratinocytes as an effort to establish a new chemically defined medium for culturing psoriatic keratinocytes by some modifications of MCDB 153 media. We compared the cell growth pattern under various culture conditions, including growth factors (KGF or EGF), and extracellular calcium concentrations, attachment and/or matrix factors (type I collagen coating or 3T3 fibroblast layering), culture durations, and types of cultured cells such as normal human epidermal keratinocytes (NHEK) or psoriatic keratinocytes. In order to achieve the above objective, semiquantitative RT-PCR for K16 mRNA, direct immunofluorescence with K8.12 as the markers of regenerating keratinocytes, and microscopic observation for cell colony formation were performed.

The results are summarized as follows:

- 1. Psoriatic keratinocytes were grown optimally at 0.15 mM calcium, irrespective of growth factors or even in free control. And they were grown well under the 20 nM KGF-added condition.
- 2. KGF and/or EGF played an active role in cell growth, especially in 5 days' culture, and the growth stimulatory effect of EGF was suppressed by 0.5 mM calcium, but the effect of KGF was sustained even at the very calcium concentration(0.5 mM). Furthermore, KGF exhibited a cell survival effect for such long duration as 18 days on type I collagen coating and also in 12 days' culture on 3T3 fibroblast layering
- 3. Cultured psoriatic keratinocytes were more vulnerable to extracellular calcium than in NHEK from the point of optimal calcium concentrations; they grew best at 0.15 mM, which

was much lower than 1.5 mM in NHEK.

4. 3T3 fibroblasts exerted a favorable effect on the cell growth and survival, especially in 12 days' culture, maybe due to paracrine effect of endogenous KGF from the 3T3 feeder cells, and cell reattachment/pile-up properties.

To improve the culture methods for psoriatic keratinocytes, the authors think that we should consider the optimal extracellular calcium concentration, introduce the feeder cells layering to increase cell reattachment/pile-up, and supplement the mesenchymal paracrine growth factors such as KGF to exert a favorable effect on the cell growth and survival.

# PREFERENCE OF NEAR-ERYTHEMOGENIC NARROW-BAND UVB PHOTOTHERAPY IN PSORIASIS AND ITS IMPLICATION OF DENDRITIC CELLS/CHEMOKINES

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Background: Now, NB (narrowband)-UVB phototherapy is prevalent in psoriasis treatment all over the world. Some evidences allegedly suggest that near-erythemogenic doses, considering the necessity for effective broadband therapy, are not required for NB-UVB, so as to decrease the risk of burn with this therapy. But recent study proved that the NBUVB phototherapy starting with near-erythemogenic dose, will be preferable to the far-erythemogenic dose methods.

Objective: We compared the therapeutic effects between 70% MED and 50% MED methods in NB-UVB phototherapy of psoriasis. And also, to elucidate the action mechanism of NB-UVB in psoriasis treatment, we performed this study to investigate immunosuppresive effects in the aspects of Langerhans cells, macrophages, and chemokine/chemokine receptors.

Methods: We have investigated the immunosuppressive effects of NB-UVB in the aspects of dendritic cells and chemokines or its receptors in the psoriasis patients undergoing the NB-UVB phototherapy. We performed skin biopsies after 4 times of 1 MED, once of 4 MED, once of 1 MED, along with corresponding controls from the lesional and non-lesional sites. And immunohistochemistry was undertaken with anti-CD1a, anti-CD11b, anti-MCP-1, and anti-CCR2 antibodies.

Results: The results of immunohistochemcial experiments were as follows;

- NB-UVB irradiation decreased the number of CD1a+ Langerhans cells in the epidermis, but increased CD11b+ macrophages in the dermis. CD11b+ macrophages were increased more in the dermis in single high-dose irradiation than repeated small dose irradiations of equivalent total doses.
- 2. MCP-1 was expressed only in the entire epidermis of psoriatic lesion, especially the highest in proliferating keratinocytes of basal and suprabasal layers, and in the papillary dermis to a lesser extent. And CCR2, a receptor for MCP-1, is expressed in the pattern similar to MCP-1. Single high-dose irradiation reduced MCP-1 and CCR2 to moderate degree,

especially in the basal layer, more than repeated low-dose irradiation of equivalent total doses.

Conclusion: Higher NB-UVB decreased CD1a+ Langerhans cells in epidermis, and increased CD11b+ monocytes/macrophages in dermis. And higher NB-UVB downregulated CCR-2 and MCP-1 expression. In relation with the expression patterns of epidermal and dermal APCs and chemokines in this study, NB-UVB have immunosuppressive properties in psoriasis treatment. For the better NB-UVB protocols for psoriasis treatment, rather higher starting doses and incremental doses may be desirable in future.

# The study of ceramides and cell signaling molecules in psoriatic epidermis: reduced levels of ceramides, PKC- $\alpha$ and JNK

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*Background*, Ceramides are the main lipids in the stratum corneum and are generated during cellular stress and apoptosis by de novo synthesis or by the action of sphingomyelinase. In addition, they are lipid second messengers produced by sphingolipid metabolism and trigger important cell responses, including protein kinase C-alpha (PKC-a) activation and the stimulation of signal transduction pathways with apoptosis and stress-activated protein kinases (SAPK), such as c-jun N-terminal kinase (JNK). Thus, ceramides have anti-proliferative and apoptotic effects.

*Objective*, It has already reported that the levels of epidermal ceramides decreased in psoriasis. However, only limited information is available on the alterations in the apoptotic pathway related to ceramides in skin diseases with epidermal proliferation, including psoriasis. This study measured the changes in the levels of epidermal ceramides and ceramide-related apoptotic signaling molecules in patients with psoriasis.

*Methods*; Samples from lesional and non-lesional epidermis were obtained from psoriasis patients. Total ceramides were fractionated using thin-layer chromatography, and the levels of PKC-a and JNK expression were measured using Western blot analysis with specific antibodies.

*Results*, We demonstrated that (1) the level of ceramides was reduced significantly in lesional epidermis with psoriasis, (2) this decrease was associated with the downregulation of apoptotic signaling molecules, such as PKC-a and JNK, and (3) there was a significant correlation between the ceramide level and the clinical severity in mild to moderate psoriasis.

*Conclusion*; These results suggest that the reduction in the ceramide level not only induces a defect in water retention and barrier function but also leads to downregulation of the apoptotic pathway resulting in epidermal proliferation in psoriasis.

# EXPRESSION OF NEUROPEPTIDES IN PSORIATIC LESIONS WITH OR WITHOUT PRURITUS USING CONFOCAL LASER SCANNING MICROSCOPY

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Pruritus is much more commonly complained in patients with psoriasis than generally expected. The clinical features and cause of pruritus in psoriasis are not well known. This study was aimed to examine the prevalence and clinical features of pruritus in psoriasis and the expression of neuropeptides as pruritogenic factors in psoriatic lesions with or without pruritus using immunohistochemistry and confocal laser scanning microscopy. Questionnaire data from 131 psoriatic patients were analyzed and psoriasis severity was evaluated by PASI score. A skin biopsy was obtained from 10 psoriatic patients with pruritus, 10 psoriatic patients without pruritus and 10 normal controls. Immunohistochemistry and confocal laser scanning microscopy with immunofluorescence stainings were performed. Among 131 psoriatic patients, 109 (83%) suffered from pruritus affecting quality of life. The PASI score was higher in psoriatic patients with pruritus than those without pruritus. Exacerbating factors for pruritus were emotional stress, hot bath, sweating and etc. Keratinocytes in the psoriatic lesions with pruritus showed increased expression of nerve growth factor (NGF), NGF receptor (NGFR) and calcitonin gene-related peptide (CGRP) receptor (CGRPR) compared to those in the psoriatic lesions without pruritus and normal controls. NGF was expressed in the entire keratinocytes layer but NGFR and CGRPR were expressed in basal and suprabasal areas. The expression of substance P (SP), SP receptor, CGRP, VIP, somatostatin, PACAP, PACAP receptor and neurotrophin 4 were increased in psoriatic lesions with or without pruritus compared to normal controls. These results indicate that pruritus is a common feature in psoriasis and the lesional increase of various neuropeptides may be involved in the pathogenesis of pruritus, especially, NGF, NGFR and CGRPR.

Key words : Psoriasis, pruritus, NGF, NGFR, CGRPR

# PROTECTIVE EFFECT OF PROHIBITIN AGAINST ANTHRALIN INDUCED CELL DEATH

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The diverse roles of prohibitin have been reported such as repressing cell cycles, anti-apoptosis under stresses, participating as a mitochondrial chaperone, suppressing tumors, and cellular aging in yeast.

From our previous proteomic analysis of skin biopsies from psoriasis patients the expression of prohibitin was increased in lesions than non-lesions, which was confirmed by Western blot analysis. To understand the reason of up regulation of prohibitin in psoriasis lesion, mammalian prohibitin RNAi vector was constructed and transfected to HaCaT to get a stable cell line, PHBi. Under a normal growth condition, the level of the mRNA of prohibitin in PHBi was down regulated, but the amount of prohibitin was not reduced significantly. It was observed that prohibitin localized mainly in peripheral mitochondria and partially in nucleus. The treatment of anthralin, which has been applied for psoriasis treatment, was shown differential expression level and cellular localization between mock and PHBi. Anthralin treatment on HaCaT cleared nuclear prohibitin and mitochondria. Interestingly, the mitochondrial remains were only restricted to perinucleus where prohibitin overlaid. To figure out the role of prohibitin in mitochondria, mitochondrial membrane potential was assessed using mitochondria specific fluorescence dye, JC-1. PHBi expressing less amount of prohibitin showed stronger red emission in peripheral and near perinucleus but mock showed stronger green in perinucleus by confocal analysis. Anthralin induced depolarization of mitochondrial membrane potential showing color changes from red to green in both cell lines. However, at 6hrs after anthralin treatment, it was observed that faster cell death process occurred in PHBi than in mock. This result was in accordance with the viability assay by MTT. The results suggested that prohibitin exhibit protective effect against anthralin induced cell death. These data implicate prohibitin as an important therapeutic target mediating mitochondrial damage in psoriasis.

# FREE COMMUNICATIONS 2

# THE EFFECT OF ACITRETIN TO THE EXPRESSION OF ANGIOGENIC FACTOR IN PSORIASIS

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*Purpose* : Psoriasis is a well known disorder of keratinization. In this disease, several reports revealed that dermal micro vessels are increased and angiogenic factors such as vascular endothelial growth factor (VEGF) are over-expressed. Angiogenesis may play an important role in progression of psoriasis. Acitretin is widely used as an anti-psoriatic drug because of its potent action on keratinocyte growth and differentiation, but the effects to angiogenesis are uncertain. The goal of this immunohistochemical study was to investigate the effects of acitretin to the expression of VEGF in psoriatic lesional skin.

*Materials & Methods*: We compared the expression levels of VEGF between pre- and post-treated acitretin (Neotigason<sup>®</sup>, Roche, Korea) of 10 psoriatic lesional skin, psoriatic lesional skin and 3 normal control.

*Results* : The expressions of VEGF in psoriatic lesional skin were significally higher than in normal control skin. The expressions of VEGF in post-treated psoriatic lesional skin were lower than pre-treated.

*Conclusion* : Acitretin revealed inhibitory effects on angiogenesis by reducing the expression of VEGF in psoriatic lesional skin. We suggest acitretin may be therapeutic approaches to psoriasis could be possible on the aspect of angiogenesis.

# ANTIANGIOGENIC ACTIVITY OF WONDONIN TARGETTING HYPOXIA-INDUCIBLE FACTOR 1

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Angiogenesis is associated with the various skin disorders like psoriasis. Hypoxia-inducible factor alpha (HIF-1a) is a key transcription factor that can regulate genes involved in angiogenesis process. Recently, HIF-1a has been reported as a target for anti-angiogenic therapy. In this study, we addressed whether wondonin, a new bis (dihydroxystyryl)imidazole purified from an association of the sponges *Poecillastra wondoensis* and *Jaspis* sp, might have a novel antiangiogenic function that inhibit HIF-1a activity in HaCaT cells. When wondonin was added to HaCaT cells under a hypoxic condition, it inhibited activity of HIF-1a activated in response to hypoxia by strengthening of binding HIF-1a to VHL. Moreover, it was followed that the expression of vascular endothelial growth factor (VEGF) was suppressed, suggesting that wondonin could contribute to the inhibition of angiogenesis. The Effect of wondonin on angiogenesis was performed through in vivo and in vitro assay systems. It was shown that Wondonin decreased neovascularization of chick embryos in the choriallantoic membrane assay, and also reduced the tube formation, the migration and the invasion of human umbililical vein endothelial cells. Taken toghther, our data indicate that wondonin has the potential to become the antiangiogenic agent to target HIF-1a and could be one of the candidates for the treatment of skin diseases.

# THE EFFECT AND SAFETY OF COMBINATION THERAPY USING NARROW-BAND UVB PHOTOTHERAPY AND CALCIPOTRIOL

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Narrow-band ultraviolet B (NBUVB) phototherapy has appeared to be effective in clearing psoriatic lesions. Calcipotriol has been combined with a number of systemic antipsoriatic treatments, improving efficacy or reducing the systemic treatment required.

In psoriasis clinic at Seoul National University Hospital, 91 psoriasis patients were treated with the calcipotriol-NBUVB. Phototherapy was done once daily three times a week and the dose was gradually increased. Calcipotriol ointment was applied twice a day. The PASI score was used to evaluate the effects of the treatment and the patients were classified to clearance, improvement, and failure. The therapeutic results showed 48.3% of clearance, 36.3% of improvement and 15.4% of failure. Of 91 patients, 60 patients experienced variable adverse effects, but there was no significant adverse effect to discontinue the therapy. The most common adverse effect was itching sense. The total number of irradiations, duration of treatment, final UVB dose, and total cumulative UVB dose required to reach grade IV were significantly higher in the extremities than the trunk (p<0.01).

Our results demonstrated that using calcipotriol ointment with NBUVB phototherapy is effective therapeutic method for psoriatic patients.

# TIME COURSE OF TANNING INDUCED BY NARROW-BAND UVB PHOTOTHERAPY IN KOREAN PSORIASIS PATIENTS

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Narrow-band (TL-01) UVB lamps have been increasingly used for phototherapy of psoriasis and other dermatoses for their excellent effect. In Korea, however, many patients receiving phototherapy have complained about the tanning effect of ultraviolet radiation and prefer bright skin to dark one. The aim of this study was to know the time-course of pigmentation induced by phototherapy during and after narrow-band UVB treatment.

Of psoriasis patients receiving narrow-band UVB phototherapy, the changes of skin color were recorded during phototherapy in 40 patients and after the end of treatment in 20 patients. All patients were evaluated using two different reflectance spectrophotometers every seventh day for 10 weeks. The results were presented by E (erythema)- and M (melanin)-index as well as values converted to the L\*a\*b\* system recommended by the CIE (Commission Internationale de l'Eclairge) and ITA(Individual Typology Angle). The L\* values which indicate luminance decreased continuously until 5th week and then showed plateau during the phototherapy, and it slowly recovered throughout the whole observation-period of 10 weeks after the end of treatment. The patterns of a\* and b\* values were compatible with that of L\* values both during and after the therapy. The mean ITA also showed similar pattern to L\* values. The E-index and M-index changed slowly both during and after phototherapy. In addition, analyzing data according to skin type, respective values showed the similar pattern to their mean value. But, L\* value, ITA and M-index of skin type III recovered faster than those of skin type IV and V.

From this study, it was found that pigmentation induced by narrow-band UVB phototherapy increased continuously for 5 weeks during the therapy and recovery needed 10 weeks or more. These results provide standard data on a time course of narrow-band UVB induced tanning during and after phototherapy in Korean brown skin.

# CALCITRIOL OINTMENT FOR THE TREATMENT OF FACIAL PSORIASIS

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Facial involvement of psoriasis require a different approach than is used for typical plaque psoriasis on other skin areas. Topical corticosteroids are the primary treatment for psoriasis, but the side effects of corticosteroids are magnified on facial skin. Calcitriol, the naturally occurring and hormonally active form of Vitamin D3, may improve the lesion of face without the atrophy or other local side effects associated with the use of topical corticosteroids.

In psoriasis clinic of SNUH, a total of 73 patients were treated with the calcitriol  $3\mu g/g$  ointment (Silkis<sup>®</sup>) for 8 weeks. Efficacy was evaluated with investigator's assessment(worsening, no change, minimal improvement, moderate improvement, marked improvement, almost clearance, and clearance) and area and severity index score on face at 2nd, 4th, and 8th week. Global assessment was also determined into 4 grades of poor, fair, good, and excellent at the 8th week.

A total of 16 patients discontinued prematurely from the study, because of lost to follow-up (n=15) and combined use of topical corticosteroid (n=1). April, 2005 Now, 4 patients were on follow-up. Rest 53 patients showed the response to treatment as follows; excellent (n=8), good (n=24), fair (n=12), and poor (n=9). After 8 weeks treatment of calcitriol oint, clinical improvement was achieved in 83.0%. Among them 60.4% showed excellent (15.1%) or good effect (45.3%) by calcitriol oint. Some patients showed local adverse reaction like erythema, exfoliation, and itching sensation and 2 patients discontinued the treatment due to adverse reaction. No patient, however, showed telangiectasia, skin atrophy, and systemic side reaction.

Our results suggested that calcitriol ointment is an effective treatment for psoriasis of face.

# AN ATTEMPT AT A NEW SYSTEMIC TREATMENT REGIMEN WITH CYCLOSPORIN BASED ON ITS PHARMACOKINETICS IN PSORIASIS

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*Aim.* In our search for a new treatment regimen with cyclosporin for the purpose of acquiring psoriasis patients in the remission and maintenance phases, we have tried to establish a once daily administration of MEPC-cyclosporin for treating psoriasis in the maintenance phase based on its pharmacokinetics.

*Materials and methods*: Seven psoriasis patients in the remission phase received twice daily administration of cyclosporin (stage 1). Then, they received 2/3 of the dose once daily for one month (stage 2). In the next stage, we divided the 2/3 dose and administered it twice daily (stage 3). We monitored the pharmacokinetics in the patients and their skin condition at each stage of the study. Blood sampling was performed hourly for 4 hr after cyclosporin was administered.

*Results*: A change in the treatment regimen from stage 1 to stage 2 produced no change in 6 of 7 patients. However, the change from stage 2 to stage 3 produced significant changes in all the patients. The pharmacokinetic changes were almost identical in the stage 1 and 2 treatment regimens. Patients who received once daily administration of the 2/3 dose had very similar pharmacokinetic values, particularly  $C_{max}$ , to the values obtained with the maintenance dose. However, when the 2/3 dose was divided and administered twice daily, the pharmacokinetic values, particularly  $C_{max}$ , were significantly decreased.

*Conclusions*: These results suggest that in cyclosporin treatment of psoriasis,  $C_{max}$  has a more significant effect on therapeutic efficacy compared to dose. Therefore, administration may be more important than dose in cyclosporin treatment of psoriasis.

# CYCLOSPORINE TREATMENT EXPERIENCE IN MILD TO MODERATE PSORIASIS PATIENTS

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Traditionally systemic therapies for psoriasis were only indicated when the disease is severe. However, with the development of treatment options with less toxicity and with growing emphasis on the quality of life of patients, systemic therapies tend to be considered in cases of mild to moderate psoriasis when it significantly affects patients' quality of life. In this regard, it is of note that patients who have guttate psoriasis (small plaque) were reported to suffer from psychosomatic problems more frequently than those with other types of psoriasis.

Efficacy of cyclosporine in the treatment of psoriasis is well established. However, widespread use of this drug has been limited by concerns over adverse effects, such as renal impairment. However, when treatment guidelines are followed well, the risk of serious adverse effects is not high and reversible especially in the short-course therapy.

We made a retrospective analysis of mild to moderate psoriasis patients who had been treated with cyclosporine to see whether a short-term cyclosporine therapy can be a safe and worthwhile option in this selected group. Among those who visited Samsung Medical Center between January 2003 and December 2004, 11 patients met the criteria of mild to moderate psoriasis (less than 12 in PASI scores). Male to female ratio of patients was 9:2. Mean duration of cyclosporine administration was  $8.0\pm3.5$  weeks. Average dosage of initial and maximum cyclosporine was  $3.8\pm0.46$ mg/kg and 4.5mg/kg respectively. Initial PASI score of the patients was  $8.8\pm2.0$  (mean+SD). Mean time to PASI50 and PASI75 were  $4.8\pm3.4$  weeks and  $6.4\pm4.0$  weeks respectively. At week 4, PASI50 was reached in 7 patients (63.6%) and at week 8, in 10 patients (90.9%). PASI75 improvement was made in 7 patients (63.6%) at week 8. During the treatment, no patients revealed increase of serum creatinine more than 30% of the baseline. Other side effects associated with cyclosporine use were transient elevation of BP (3), diarrhea (1), hirsutism (1) and folliculitis (3).

Although our study lacks control group and the sample size is limited, we can conclude that cyclosporine therapy could be considered in selected cases of mild to moderate psoriasis where the quality of life of patients can exceed potential risk and cost of this therapy.

## CLINICAL AND LABORATORY CHARACTERISTICS OF SMALL PLAQUE PSORIASIS VULGARIS

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The incidence and clinical manifestations of psoriasis vulgaris vary according to the patients' ethnic backgrounds or geographic locations. It is considered that Korean psoriasis vulgaris is less severe and is composed of smaller sized plaques. Therefore this type of psoriasis vulgaris was reported to be small plaque (SP) psoriasis in comparison with large plaque (LP) psoriasis. To elucidate the mechanism of these clinical characteristics, the psoriasis vulgaris patients were classified into two groups and were evaluated for laboratory markers to be expressed differentially. Expression of interleukin-18 mRNA in the lesions of SP psoriasis was not different from the uninvolved sites of patients, but the expression was decreased in LP lesions. However the expression of matrix metalloproteinase-9 mRNA was low in the uninvolved sites of SP patients, but the expression was high in those of LP patients. In addition, these patients were evaluated for any clinical difference in the well-known factors related to severity or aggravation such as onset age, family history, pruritus, stress (or fatigue), smoking and alcohol intake. Among them, only alcohol intake was significantly correlated as an aggravating factor in the LP patients, but was not in SP patients. Although it is not yet known how these laboratory markers and clinical characteristics are correlated, if more differential laboratory markers or clinical characteristics are known, it seems likely to elucidate the mechanism causing clinical difference. It is also possible to use these markers as therapeutic targets developing new therapy for psoriasis.

## CASE REPORTS

## A CASE OF COEXISTENCE OF MORPHEA AND PSORIASIS

#### PARK Hyun-Je, JANG Ho-Sun, JANG Bong-Seok, KIM Moon-Bum, OH Chang-Keun, KWON Kyung-Sool

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Morphea is sclerosis of the skin characterized by one or multiple circumscribed ivory-white, indurated, sometimes confluent plaques. We herein report a case of coexistence of morphea and psoriasis in a patient. Despite the relatively common occurrence of each disease, the concurrence of two in a patient is extremly rare. A search of the literature revealed only 2 cases of coexistence of morphea and psoriasis internationally. The concomitant occurrence of these two dermatoses may be explained by immunological factors or trauma.

A 38-year old man presented with multiple erythematous scaly patches on both lower legs and brownish, sclerotic, indurated plaques on back. He was diagnosed as psoriasis 5 years ago and has been treated by topical steroid intermittently. 2 months ago, he found the sclerotic lesions on back subsequently. Clinical and histopathological findings confirmed that the lesions of legs were psoriasis and that of back was morphea. He has been treated by acitretin and additionally topical PUVA for morphea lesion. The both lesions of morphea and psoriasis have been improved gradually.

## HYPOCALCEMIA-INDUCED PUSTULAR PSORIASIS-LIKE SKIN ERUPTION

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Psoriasis is an inflammatory skin disorder characterized by keratinocyte hyper-proliferation and altered differentiation. One type of psoriasis, pustular psoriasis of von Zumbusch, is characterized by a generalized pustular, erythematous, painful skin eruption accompanied by fever, leukocytosis, and prostration.

A 70-year-old man presented with hypocalcemia, and the histologic examination was compatible with pustular psoriasis of von Zumbusch. He was treated with calcium carbonate and vitamin D analogues. The pustular skin lesions and erythroderma cleared rapidly as the calcium level reached normal, implicating changes in the serum calcium level in the development or exacerbation of psoriasis.

The relative importance of hypocalcemia or the deficit in parathyroid hormone and vitamin D as factors triggering generalized pustular psoriasis remains unclear. It is uncertain whether hypocalcemia-induced pustular psoriasis can be called psoriasis because its treatment differs completely from that of typical generalized pustular psoriasis, although the histology and pustular-like skin eruption appear like psoriasis. More study of this is required.

### A CASE OF THE EYELID PSORIASIS

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Not a small portion of patients with psoriasis had facial involvement, but eyelid involvement is relatively rare. Eyelid psoriasis is difficult to manage because the eyelids are susceptible to cutaneous adverse effects of usual topical corticosteroids, and the absorption of corticosteroid may induce glaucoma or cataract. A 44-year-old male with 12-year history of psoriasis presented erythematous scaly patches on whole body. Face was more affected than the trunk or extremities. He also presented slightly injected conjunctiva and scaly patches on both upper eyelids. Initially he was treated with 0.03% tacrolimus ointment twice a day, and improvement of the lesion on face was seen after 2 months. However, he felt burning sensation on eyelid and conjunctiva so we discontinued tacrolimus ointment application on this area and started treating the patient with other glucocorticoid containing ophthalmic ointment.

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First described in 1876 as the appearance of psoriatic lesions in the uninvolved skin of psoriatic patients as a consequence of trauma, the Koebner phenomenon has been described in numerous diseases and numerous causes. The causes of koebnerization include allergic reaction, drug reaction, variable dermatoses, and therapeutic modalities. A 33-year-old male with 15-year history of psoriasis presented erythematous and scaly plaque on left upper arm. He had taken influenza vaccination before 10 days. The site of injection became painful and erythematous swelling 1 day after vaccination, and developed psoriatic plaque 4 days after vaccination. Previously he had never experienced the Koebner phenomenon by other vaccinations or injections. The skin lesion improved by application of calcipotriol ointment.

## A CASE OF RECALCITRANT EXFOLIATIVE DERMATITIS CAUSED BY PSORIASIS

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Exfoliative dermatitis is a inflammatory skin disease characterized by generalized erythema and scaling. The majority of cases result from the pre-existing skin diseases or systemic disorders and some cases are caused by drugs. A 58-year-old man visited us with a 10 days history of generalized pruritic erythema, desquamation with edema. He was diagnosed as psoriasis and treated with steroid injection and Diavonex<sup>®</sup> cream at private clinics. His father, brother and sister had a history of psoriasis. On laboratory exam, mild eosinophilia was found, but no specific findings were found on peripheral blood smear. The histopathologic features were compatible with psoriasis. Up to date, he has admitted 8 times during last 3 years, but no internal organ malignancy was found as a underlying disease. He had been treated with prednisolone, narrow band-UVB, acitretin and cyclosporin, but only partial improvement was observed. We report a case of recalcitrant exfoliative dermatitis which was caused by psoriasis.

## A CASE OF INFANTILE PSORIASIS WITH ACRODERMATITIS CONTINUA SUCCESSFULLY TREATED WITH TOPICAL PIMECROLIMUS AND LOW DOSE NARROWBAND UVB PHOTOTHERAPY

### AHN Soo-Jin, <u>OH Sang-Hyun</u>, CHANG Sung-Eun, LEE Mi-Woo, CHOI Jee-Ho, MOON Kee-Chan, KOH Jai-Kyoung

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Psoriasis is a chronic inflammatory papulosquamous disorder that usually starts after puberty. It is a well-described entity in children but is rare in infancy. Psoriasis in infancy is often more therapeutically challenging than adult onset psoriasis. Many treatment modalities such as topical corticosteroids, topical vitamin D, psoralen plus ultraviolet A (PUVA), UVB, oral retinoids, or methorexate have been used for childhood as well as adult psoriasis. An early onset psoriasis usually shows more severe disease, and as psoriasis reveals chronic and relapsing courses, some of aforementioned therapeutic modalities are limited for their long-term side effects in children.

Herein, we report a 5-month-old female infant with widespread psoriasis including acrodermatitis continua, who was successfully treated with the combination therapy of topical pimecrolimus (Elidel<sup>®</sup>) and low dose narrowband UVB phototherapy. Although long-term follow-up will be needed to evaluate the efficacy and side effects, the combination therapy was effective in a short time. So we think that it would be considered as a novel therapy in infantile psoriasis.

## LOW DOSE CYCLOSPORIN: A TREATMENT IN GENERALIZED PUSTULAR PSORIASIS

#### KIM Hei-Sung, KIM Sei-Yeon, KIM Heesu, KIM Gyoung Moon, KIM Si-Yong

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Generalized pustular psoriasis is a rare form of psoriasis seldom seen in children. Here we present an 8-year-old boy with generalized lesions consisting of pustular, erythemtaous and scaly follicular papules. Focal pustular lesions appeared since the patient was 5 years old. Although they responded to topical steroid, recurrences were noted from time to time. The generalized eruption of pustules occurred after a 10-day trial with traditional herbal medication, and mostly arose from scratch wounds, gained after a number of fall-downs while playing.

The skin biopsy specimen showed changes compatible with pustular psoriasis, namely acanthosis with rete ridge elongation, parakeratosis and spongiosis with subcorneal and intraepidermal collections of neutrophils.

We initially started with methotrexate (7.5 mg #3, with 12 hours interval/ week for 2 weeks) since the patient was intolerable to cyclosporine. The effect was not dramatic, and with improvement of the patient's general condition, we switched to cyclosporin A (1.0 mg/kg/day) in the form of suspension. Within 2 weeks of therapy, the psoriatic pustules have completely dried off with concurrent desquamation and 4 weeks later, we could only detect mild erythema. No side effects of the drug were observed. During treatment with cyclosporin A, the only topical therapy used was emollients. The patient is currently under treatment with regular follow-ups.

Therapeutic agents used in childhood GPP include systemic and topical steroid methotrexate, etretinate or acitretin and UV therapy. From our recent experience, low dose cyclosporin appears to be an effective alternative treatment.

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# EDUCATIONAL LECTURES

## NBUVB THERAPY IN KOREAN PSORIASIS PATIENTS

#### YOUN Jai-Il

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Narrow hand UVB phototherapy using 311nm wavelength is in widespread use due to its greater efficacy and, safety compared with broad band UVB and PUVA. Action spectrum studies support its use in psoriasis. However, its optimal initial dose and dose increment regimen is not determined till now. Treatment regimen in psoriatic patients with brown skin will be different from white skin.

Various regimen using 311nm narrow band UVB in white skin and Korean brown skin will be discussed in this subject.

It is very clear that narrow band UVB phototherapy represent a major advance in phototherapy of psoriasis in brown skin.

Many patients receiving narrow band UVB phototherapy have complained about tanning effect of UVB especially in dark skinned one. Tanning effect induced by phototherapy may interfere with patient's compliance. Therefore Time course of pigmentation by phototherapy during and after narrow band UVB treatment will be important in brown skin. It was found that pigmentation increased continuously for 5 weeks. The L\* values which indicate luminance decreased continuously until 5th week and then showed plateau during the phototherapy, and it slowly recovered throughout the whole observation-period of 10 weeks after the end of treatment. The patterns of a\* and b\* values were compatible with that of L\* values both during and after the therapy. The mean ITA also showed similar pattern to L\* values. The E-index and M-index changed slowly both during and after phototherapy.

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Oral psoralen photochemotherapy (PUVA) in which a patient ingests soralen and is subsequently exposed to an indoor artificial source of ultraviolet A radiation has been used for treating moderate to severe psoriasis for a long time. However, a careful evaluation of the patient is necessary because PUVA therapy is often a long-term treatment. It is also crucially important for patients to know that almost everyone undergoing PUVA therapy experiences some adverse effects from the treatment and to know what the effects might be.

The most common indication for PUVA therapy is disabling psoriasis unresponsive to topical therapy. Besides, PUVA therapy is indicated in a few patients as the initial treatment because of explosive onset of wide-spread psoriasis and in some patients as they cycle off methotrexate or some other systemic therapy. Recently, narrow band UVB (NBUVB) therapy has been utilized extensively throughout Europe. NBUVB, emitting high-intensity light ranging only from 311-313 nm, is an exciting, new modality that may be a boon not only for treatment-resistant patients or patients for whom other therapies are contraindicated, but also as first-or second-line agent once practitioners become more familiar with it. There are several factors to consider when comparing the two therapies, including efficacy, carcinogenesis, remission rates, and ease of administration. The data in the literatures suggest that PUVA may be better for clearing lesions that are more recalcitrant to therapy and in groups of patients with high PASI score. One major disadvantage of PUVA is the risk of carcinogenesis. NBUVB offers some major logistic advantages over PUVA that may be important when choosing therapy for an individual patient. It is less time-consuming, easier to perform, safe in pregnant women and children, and does not require concomitant administration of a photosensitizer.

When considering the use of PUVA and narrow band UVB (NBUVB) therapies, three important differences must be kept in mind: 1) PUVA therapy might be more effective than NBUVB in clearing psoriasis in most patients, 2) a much more convenient and effective maintenance treatment 3) more penetrating through a greater depth of tissue.

Factors to consider for NBUVB therapy : 1) psoriasis of recent initial onset, 2) a history of

rapid and easy clearance on exposure to sunlight, 3) hotosentivity to UVA, 4) pregnancy, lactation, or intention to become pregnant, 5) young age, 6) skin type I, 7) a past history of x-ray or arsenic treatment, 8) low intelligence, 9) preference for avoiding oral medications.

Factors to consider for PUVA therapy : 1) a long history of psoriasis, 2) thick plaque, 3) involvement of the palms, soles and nail, 4) photosensitivity to UVB, 5) failure to respond to NBUVB phototherapy, 6) active, aggressive disease (erythrodermic, pustular), 7) skin type III and higher, 8) social and occupational factors.

## COMBINATION OF RETINOID WITH ULTRAVIOLET LIGHT THERAPY: IMPLICATION IN THE TREATMENT OF PSORIASIS PATIENTS WITH DARK SKIN

#### LEE Joo-Heung

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Phototherapy is one of the oldest in the history of psoriasis treatment. The fact that many of psoriasis patients experience improvement of their lesions during summer, when the UV exposure is higher than any other seasons suggested that sunlight, more specifically UV therein, can be utilized in the treatment of psoriasis. With the introduction of modern fluorescent lamps emitting UVB or UVA, phototherapy has gained popularity. Although it is substantially efficacious treatment option, it entails hyperpigmentation, which is not only undesirable cosmetically but also could prevent effective UV penetration into the skin. In contrast to the potential for the photocarcinogenesis occurring more frequently in white skin, this adverse effect of UV is more significant in Asian people with dark skin. Therefore, various approaches have been developed in terms of frequency of UV exposure, starting doses, and increment methods.

Retinoid is one of the safest options for the psoriasis treatment among the systemic agents. Although it can be used as a monotherapy, when combined with phototherapy, systemic retinoid is reported to reduce number of exposures, duration of treatment and the total cumulative UV doses, thereby not only being capable of handling very recalcitrant lesions but also decreasing long-term side effect of UV. This feature is considered to reflect the capacity of retinoid to normalize thick stratum corneum and psoriasiform hyperplasia in psoriasis. Although its efficacy in combination therapy with UV is well known, it is still unknown whether retinoid-phototherapy or retinoid-photochemotherapy is as good in Korean psoriasis patients with dark skin as in Caucasians from whom most of the clinical efficacy data has come from. Even if the retinoid combination is useful in the phototherpay of psoriasis in dark skin, reinoid dose and the parameters in UV therapy should be critical in overriding UV-induced hyperpigmentation. Therefore, well-designed prospective study investigating potential benefit of the retinoid combination and optimal paratmeter for the best results is warranted.

## TREATMENT OF PSORIASIS WITH 308 NM XENON-CHLORIDE (XE-CL) EXCIMER LASER

#### KIM Nack-In

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Psoriasis is a chronic disorder characterized by epidermal hyperplaia. Many investigations have been done to develop highly efficacious and safe long-term treatment measures in the management of psoriasis. Phototherapy of psoriasis including PUVA, UVB, narrow band UVB (NBUVB) is performed as monotherapy or in combination with retinoid, cyclosporin, methotrexate to reduce UV doses and side effects.

The most effective wavelength in psoriasis treatment has been known to encompass 311-313 nm and xenon chloride excimer laser using similar wavelength of 308 nm has also been reported to be useful in the treatment of psoriasis. Excimer laser has been utilized in the field of dermatology for the treatment of vitiligo, atopic dermatitis, alopecia areata, lichen planus as well as for psoriasis. Among psoriasis patients, excimer is indicated for those with localized chronic plaque, palmar psoriasis without pustule, scalp and hairline psoriasis. Although the mechanism of 308 nm excimer laser remains to be seen, it is suggested that excimer might have a similar biological action mechanism with 311 nm NBUVB. Since excimer laser can focus on the lesion, sparing normal appearing area, it can reduce total cumulative UV dose for the whole body. Rapid improvement with laser therapy is also a great advantage of excimer laser therapy.

Although treatment parameters and schedules for the excimer laser have been suggested in English literatures, few investigations have been done in Korean psoriasis patients. We reported our treatment experience for psoriasis with excimer laser, however, it indicated less efficacy compared to the previous ones from US or Europe. Therefore, we suggest that optimal parameters should be sought for Korean psoriasis patients with different skin characteristics.

## 대한건선학회 임원 및 평의원

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