The 15th Annual Meeting
The Korean Society for Psoriasis

PROGRAM

September 24, 2011

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 제15차 학술대회를 맞이하여 그 동안 성원하고 지원하여 주신 회원 여러분들께 깊은 감사의 말씀을 드립니다. 올해 15차를 맞이하는 대한건선학회 연례 학술대회는 건선 및 관련 질환에 관심이 있는 여러 회원님들의 지속적인 참여와 격려를 바탕으로 발전해 왔으며 앞으로도 성원 속에 더욱 발전해 나갈 것을 믿어 의심치 않습니다.

금년도 학술대회에는 일본 Kagoshima University, Takuro Kanekura 교수의 “Treatment of pustular psoriasis and neutrophilic dermatoses” 특별강연과 캐나다 Pobity Medical Research Inc. 소속 Kim Alexander Papp의 “New Paradigm in the Treatment of Psoriasis-Role of anti-IL12/23”를 주제로 하는 초청 강연을 준비하였습니다. 또한 교육강연으로 Topical treatment of psoriasis를 주제로 준비하여 건선의 국소치료에 관하여 보다 더 깊은 이해를 하실 수 있도록 하였습니다.

이번 제15차 학술대회를 준비하는데 수고하신 건선학회 임원 여러분과 동참하여 주신 해외 및 국내 초청 연자, 좌장, 발표자 여러분께 다시 한번 깊은 감사를 드립니다. 여러 회원님들의 관심 속에 금번 15차 학술대회가 건선 및 관련 면역학 분야에서 유익한 학술교류의 장이 될 것을 믿어 의심치 아니하며 저희 집행진은 대한 건선학회의 발전을 위하여 성심을 다할 것을 여러 회원님들께 약속드립니다.

2011. 9. 24

대한건선학회 회장 **최 지 호**

INFORMATION

◆ **Advance Registration**

Not available

◆ **On-site Registration**

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

◆ **Official Language**

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

◆ **Venue: COEX InterContinental 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**

Please be advised that slide projection has been completely replaced by beam projection and will be no longer available. Those who would like to use beam projection are advised to use Microsoft PowerPoint (version 2000 or compatible). Double slide projection or overhead projection is not available for the presentation.

- Suggested duration of presentation:

Free communications	7 minute presentation	+ 1 minute discussion
Educational lectures	13 minute presentation	+ 2 minute discussion
Special lectures	50 minute presentation	+ 5 minute discussion

▶ Preview Booth: Located in Registration Area (Harmony Level)

All the presenters are required to submit their presentation material at least 1 hour prior 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**

Cocktail party (free admission, 17:30-18:30) is ready for all the participants.
Please enjoy tasty cuisine and beverage with your colleagues and friends.

PROGRAM

MORNING SESSION

09:30-09:55 등 록

09:55-10:00 개회사 **최지호** (대한건선학회 회장)

축 사 **윤재일** (대한피부과학회 회장)

10:00-11:00 **자유연제 (1)** 좌장: **김낙인** (경희의대)

11:00-12:00 **[Special Lecture 1]** 좌장: **최지호** (울산의대)

12:00-13:30 **점심식사 및 평의원회**

AFTERNOON SESSIONS

13:30-14:30 **[Special Lecture 2]** 좌장: **윤재일** (서울의대)

14:30-15:30 **자유연제 (2)** **좌장: 안규중** (건국의대), **김태윤** (가톨릭의대)

FC-20 Loss of hTid-1 Expression and Aberrant Actin Cytoskeleton Organization in Psoriatic Skin ····· 44

CHOI Ji Hye[1], CHOI Dae-Kyoung[2], KWAK Sang Su[1], SUK Jinkyu[1], LIM Jong-Soon[3], HONG Dong-Kyun[2], LEE Jeung-Hoon[2], JOE Cheol O[1]
[1]Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Daejeon;
[2]Department of Dermatology, School of Medicine, Chungnam National University, Daejeon;
[3]Institute of Traditional Medicine and Bioscience, Daejeon University, Daejeon, Korea

FC-21 Autophagy Negatively Regulates Keratinocyte Inflammatory Responses via Scaffolding Protein p62/SQSTM1 ····· 45

LEE Hye-Mi[1,2], SHI Ge[3], SHIN Dong-Min[1,2], CHOI Dae-Kyoung[3], PARK Seung-Bae[3], HUANG Mei[2,4], KIM Jin-Man[2,4], KIM Chang Deok[3], LEE Jeung-Hoon[3], JO Eun-Kyeong[1,2]
Departments of [1]Microbiology, [2]Infection Signaling Network Research Center, Departments of [3]Dermatology and [4]Pathology, College of Medicine, Chungnam National University, Daejeon, Korea

FC-22 Brn2 is a Transcription Factor Regulating Keratinocyte Differentiation with a Possible Role in the Pathogenesis of Lichen Planus ····· 46

SHI Ge[1], SOHN Kyung-Cheol[1], CHOI Dae-Kyoung[1], KIM Soo Yeon[1], LEE Young Ho[2], LEE Young[1], SEO Young-Joon[1], KIM Chang Deok[1], LEE Jeung-Hoon[1]
[1]Department of Dermatology and Research Institute for Medical Sciences, School of Medicine, Chungnam National University, Daejeon;
[2]Department of Anatomy, School of Medicine, Chungnam National University, Daejeon, Korea

15:30-16:00 *Coffee Break*

16:00-17:00 **교육강연** 좌장: **김광중** (한림의대)

Topical Treatment of Psoriasis

EL-1 Deltanoid **최용범** (건국의대)····· **19**

EL-2 Retinoid **윤상웅** (서울의대)····· **20**

EL-3 Calcineurin Inhibitor **송해준** (고려의대)····· **21**

17:00-17:30 폐회 및 총회

17:30- 간친회

SPECIAL LECTURES

CURRICULUM VITAE

Takuro Kanekura, M.D., Ph.D.
Professor and Chairman
Department of Dermatology, Kagoshima University, Graduate School of Medical and Dental Sciences, Kagoshima, Japan

Education:

1991.9	Ph.D., Kagoshima University (Medical Science)
1983.3	M.D., Kagoshima University Faculty of Medicine, Japan

Professional Training and Appointments:

2006.9-present	Professor and Chairman, Department of Dermatology, Kagoshima University Graduate School of Medical and Dental Sciences
2001.1-2006.8	Associate Professor, Department of Dermatology, Kagoshima University Graduate School of Medical and Dental Sciences
1993.4-2000.12	Assistant Professor, Department of Dermatology, Kagoshima University Faculty of Medicine
1991.4-1993.3	Chief of the Department of Dermatology, Miyakonojo National Hospital
1985.1-1991.3	Instructor, Department of Dermatology, Kagoshima University Faculty of Medicine
1983.6-1985.1	Resident in Dermatology, Kagoshima University Hospital

Major Research Appointments:

1996.4-1998.3	Visiting Researcher, Department of Medicine, University of Tennessee College of Medicine, Memphis, Tennessee
1988.1-1990.1	Visiting Trainee, Department of Biochemistry, Kagoshima University Faculty of Medicine

Certification and Licensure:

1983.6	M.D. Licence, Japan #277897
1992.7	Board Certified Dermatologist, #4484 Japanese Dermatological Association

Selected Membership in Professional Societies

Japanese Dermatological Association
Japanese Society for Investigative Dermatology
Society for Investigative Dermatology

Japanese Skin Cancer Society
Japanese Society for Psoriasis Research
Japanese Society for Apheresis
Japan College of Rheumatology
Japanese Cancer Association
Japanese Society of Allergology
Japanese Biochemical Society
Japanese Society of Lymphoreticular Tissue
Japanese Society for Immunology

Awards and Honors

2006.9 Visiting Professor,
Xiang Ya Hospital, Central South University, Changsha, China

Research Interests

Neutrophilic dermatoses, Collagen Disease,
Molecular and Cellular Biology of the Skin

SL-1

Treatment of Pustular Psoriasis and Neutrophilic Dermatoses

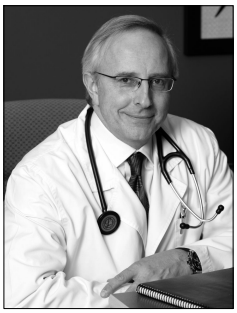
Takuro Kanekura

Department of Dermatology, Kagoshima University,
Graduate School of Medical and Dental Sciences, Kagoshima, Japan

Pustular psoriasis and neutrophilic dermatoses including Sweet's syndrome, Behçet's disease, pyoderma gangrenosum, and so forth are characterized by the dense infiltration of activated neutrophils into the lesions histopathologically. They often have systemic involvement and are intractable. In this lecture, I will first review the clinical features and treatment. Next, I will introduce granulocyte and monocyte adsorption apheresis (GCAP), a new and novel treatment for neutrophilic dermatoses.

GCAP is an extracorporeal apheresis instrument that uses a column containing cellulose acetate (CA) beads designed to remove pathogenic granulocytes and was approved initially for treating ulcerative colitis. We conducted the study of the clinical effectiveness of GCAP for various recalcitrant skin diseases attributable to activated granulocytes and obtained excellent results in patients with pustular psoriasis, psoriatic arthritis, ulcers of Behçet's disease, pyoderma gangrenosum, leg ulcers of rheumatoid arthritis, and so forth. We demonstrated that the expression of the adhesive molecule, integrin Mac-1 (CD11b/CD18), was increased on the patients' peripheral neutrophils and activated neutrophils were selectively removed by the binding of complement component on CA beads and Mac-1 expressed on the activated neutrophils. Based on the remarkable clinical outcomes and *in vitro* observations, we suggest that GCAP is a promising tool for treating patients with intractable skin diseases attributable to activated neutrophils.

CURRICULUM VITAE



Kim Alexander PAPP, M.D., Ph.D., FRCPC
President, Probity Medical Research Inc.,
K. Papp Clinical Research Inc.,
Waterloo, Ontario, Canada

Degrees

1985 M.D. University of Calgary __ Calgary, Alberta
1980 Ph.D. (Physics) York University __ North York, Ontario
1976 M.Sc. (Physics) York University __ North York, Ontario
1974 B.Sc. Hon (Physics) University of Calgary __ Calgary, Alberta

Postgraduate Training

1987-1989 Resident Dermatology, Internal Medicine, University of Toronto-Toronto, Ontario
1986-1987 Resident Dermatology / Internal Medicine
McMaster University-Hamilton, Ontario
1985-1986 Intern Internal Medicine, Mount Sinai Hospital-Toronto, Ontario
1980-1981 Postdoctoral Fellowship Department of Physics, University of Chicago-Chicago, Illinois

Professional Appointments

2006-2007 Tariff Representative Ontario Medical Association, Dermatology Division
2001-2008 Assistant Clinical Professor Department of Medicine, University of Western, Ontario, London, Ontario
2001-2006 Section Head Ontario Medical Association, Dermatology Division
2000-2009 President Instore for a Cure-Waterloo, Ontario, Nonprofit organization, fund raising for cancer research
1989-2002 Consultant JETP Consultants (Computer Hardware and Software) Waterloo, Ontario
1987-1989 Physician Part-time Private Practice-Toronto, Ontario
1986-1987 Part-time Emergency Toronto, Ontario; Simcoe, Ontario; Physician Fergus, Ontario
1981-1982 Assistant Professor Physics, University of Waterloo-Waterloo, Ontario
1978-1980 Instructional Assistant Astronomy, York University-North York, Ontario
1978-1980 Instructor Numerical Methods and Statistical Analysis, York University-North York, Ontario
1978-1980 Tutorial Leader Numerical Methods, Statistical Analysis, Astronomy and Physics, York University-North York, Ontario

1975-1978	Laboratory Instructor Physics, York University-North York, Ontario
1975-1981	Private Consultant Toronto, Ontario
1974	Consultant Algas Engineering-Calgary, Alberta

Awards and Honors

1983	Vice-President's Travel Award
1982-1985	Nat Christie Medical Entrance Award
1980-1981	NATO Postdoctoral Fellowship
1978-1979	Province of Ontario Graduate Scholarships
1976-1978	NRC Post Graduate Scholarships
1976	Province of Ontario Graduate Scholarship
1974	Honorable Mention, Gravity Research Foundation
1973	Honorable Mention, Gravity Research Foundation
1970	Queen Elizabeth Scholarship, University of Calgary

SL-2

New Paradigm in the Treatment of Psoriasis-Role of anti-IL12/23

Kim Alexander PAPP, M.D., Ph.D., FRCPC

President, Probity Medical Research Inc., K. Papp Clinical Research Inc., Waterloo, Ontario, Canada

Psoriasis is one of the most accessible human diseases in which to examine both the cellular and molecular pathogenesis of T-cell inflammatory response mechanism. Over the last decade there have been considerable breakthroughs in the treatment of psoriasis utilizing immunosuppressive mechanism, including the use of biological agents that exert their effects either by inhibiting cytokines from acting on the skin or through the suppression of inflammatory cells. Many controlled studies have demonstrated the safety and efficacy of biologic agents in the treatment of psoriasis.

The study of various cytokines, particularly interleukins (IL)-12 and IL-23, has led to novel advances in the treatment of this disease. IL-12 and IL-23 are related cytokines that share a p40 subunit, but IL-12 stimulates mainly a Th1 T-cell response (cells that produce gamma interferon on activation), where IL-23 stimulates mainly a Th17 response (cells that produce IL-17 on activation). Psoriasis lesions contain dendritic cells that over-produce IL-12 and IL-23 and activated T-cell subsets that are present in skin lesions include Th1 and Th17 T-cells. Blockade of IL-12 and IL-23 biological activity in psoriasis lesions with an antibody targeted to the common p40 subunit (ustekinumab) leads to significant attenuation of Th1 and Th17 T-cell activation. Human monoclonal antibodies that block IL-12/23 have been shown to be highly efficacious in treating moderate to severe plaque psoriasis in North American, European and Asian Patients.

EDUCATIONAL LECTURES

EL-1

Deltanoids

CHOE Yong-Beom

Department of Dermatology, School of Medicine, Konkuk University

Psoriasis is a relatively frequent chronic skin disorder which presents in a variety of forms. Although it usually involves knee and elbow, psoriasis can victimize any area of the skin. Pathophysiologically, impaired differentiation and increased proliferation of epidermal keratinocytes are key features in psoriatic lesions together with a local activation of T lymphocytes. The active form of vitamin D_3 (1,25-dihydroxyvitamin D_3) is known to play an important role in the regulation of intestinal calcium absorption, bone mineralization and prevention of rickets. In addition to these actions, vitamin D_3 promotes differentiation and inhibits proliferation on various cells. Therefore, it is not surprising that vitamin D_3 is effective on psoriasis. This idea was given by chance when a old male patients with long standing psoriasis and osteoporosis was given oral 1 α-hydroxy vitamin D_3, and noticed his skin lesions improved dramatically. This observation, together with evidence that the bioactive form of vitamin D_3 and its analogs (termed deltanoids) inhibits keratinocytes proliferation and promotes keratinocytes differentiation, led to a new era in topical anti-psoriatic agents.

Vitamin D_3 derivatives act by inhibiting proliferation and facilitating differentiation of epidermal kerationocytes. Immunologically, it inhibits the production of nuclear factor NK-κB protein in lymphocytes, leading to a reduced transcription of IL-2. Also, it can inhibit production of IL-6 in cytokine-stimulated human dermal microvascular endothelial cells and reduce the antigen-presenting function of Langerhan's cell. Less than 1% of topical vitamin D agent is absorbed through skin, and rapidly metabolized. It has minimal effect on calcium metabolism, and does not show skin atrophy and telangiectasia, which are common side effects of steroid. On the other hand, it can cause local irritation and facial dermatitis.

The present review deals with molecular actions, clinical efficacy and safety of vitamin D_3 analogues in psoriasis.

EL-2

Topical Retinoids

YOUN Sang Woong

Department of Dermatology, Seoul National University College of Medicine, and Seoul National University Bundang Hospital

Topical medication is the first line treatment for psoriasis. Topical retinoids have been used for psoriasis since it was approved for use in US in 1997. Tazarotene is the first topical retinoid for psoriasis. It selectively binds to the ɣ and β retinoic acid receptor. It is converted *in vivo* to tazarotenic acid, biologically active metabolite. Tazarotene is believed to normalize keratinocyte differentiation, inhibit keratinocyte proliferation and anti-inflammatory effects. It is available as a 0.1% or 0.05% cream or gel. It is effective for psoriasis as a monotherapy applying once a day. Its side effects are associated with local irritation: erythema, burning, peeling, stinging, dryness and itching. It could be combined with topical corticosteroids resulted with better efficacy and less local irritation side effects. It is chemically compatible with corticosteroids but stability issue beyond two weeks is not solved. Thus, mixed use of tazarotene and corticosteroids is not recommended. Patient should be careful when they use tazarotene for face, neck, genital area or intertriginous area. It is potentially teratogenic and childbearing aged women should have a pregnancy test before use or use adequate contraception during retinoid therapy.

EL-3

Calcineurin Inhibitors

SONG Hae-Jun

Department of Dermatology, Korea University

Activation of T cells leads to an increase in cytoplasmic calcium concentration, activation of calmodulin, and finally activation of calcineurin. Calcineurin dephosphorylates the ncuclear factors of activated T cells (NFATs) and enables NFATs to enter the nucleus. NFATs combine with their nuclear subunits and resulting in the transcription of pro-inflammatory cytokines (IL-2/4, IFN-ɣ, TGF-β). Calcineurin inhibitors including systemic cyclosporine (CsA) and topical tacrolimus and pimecrolimus all bind to immunophilins (cyclophilin, FKBP12) and interfere with the activation of calcineurin. They also affect epidermal keratinocytes in a similar way as T cells. Therefore they can be used as therapeutics for Psoriasis.

It is advisable to choose calcineurininhibiotrs as a special option for the treatment of mild to moderate degree of psoriasis, for which topical steroids and vitamin D_3 is usually applicable. Due to their weak penetration potential, topical calcineurin inhibitors were unsuccessful for plaque type psoriasis. To overcome this limitation, descaling of thick scales by salicylic acid before applying topical calcineurin inhibitors and occlusion method was recommended. Consequently topical calcineurin inhibitors (0.1% tacrolimus, 1% pimecrolimus) have been used in body area showing better penetration such as face and flexural parts (inverse psoriasis). In these areas, they are highly effective and safe for short-term therapy even for children. Combination use of topical corticosteroids and calcineurin inhibitors appears useful. Maintenance treatment using calcineurin inhibitors with intermittent rescue therapy with topical corticosteroids has been suggested as an alternative way to reduce the long-term complications of prolonged corticosteroid use. Combination of UV therapy and topical calcineurin inhibitors is not advised due to concern and warning about increased photocarcinogenicity. Though calcineurin inhibitors showed its efficacy in treatment of psoriasis and newer studies indicate that the risk of cancer promotion risk is not increased by topical use, they have to be closely monitored in future studies.

FREE COMMUNICATIONS

FC-1

Psoriasis with Crohn's Disease, Stomach Cancer and Stroke

NA Sun Jae, KWON Hyuck Hoon, YOUN Jai Il

Department of Dermatology, Seoul National University Hospital

Recent findings in psoriasis research have shown that psoriasis is not just a skin disease but frequently associated with systemic comorbidities. However the exact pathomechanism linking psoriasis and the comorbities remains to be determined. We report a case of psoriasis in a 58-year-old Korean man. He presented with erythematous scaly papules of scalp and buttocks after the diagnosis of Crohn's disease, stomach cancer and stroke. He was given subtotal gastrectomy for stomach cancer and there was no evidence of recurrence. Crohn's disease was under control with medication. His cutaneous symptom was relieved after the use of topical vitamin D derivative and steroid.

FC-2

Five Cases of Eczematous Psoriasis

NA Sun Jae, KWON Hyuck Hoon, YOUN Jai Il

Department of Dermatology, Seoul National University Hospital

In the psoriasis clinic, there are some cases with features of significant overlap between psoriasis and the eczematous dermatoses. Often the suspicion of psoriasis in chronic eczema is key to the diagnosis of eczematous psoriasis. The diagnosis of eczematous psoriasis has profound prognostic and therapeutic significance. We report 5 cases of eczematous psoriasis. Each patient had been diagnosed as either chronic eczema or nummular eczema and treated with high potency steroid ointment. The patients were referred to our psoriasis clinic due to the recalcitrant disease course. They were treated with topical vitamin D derivative and steroid ointments.

FC-3

New-onset of Palmoplantar Pustulosis while on Adalimumab Treatment for Ankylosing Spondylitis

LEE Yu-Na, PARK Hyun-Jung, HWANG Young-Ji, LEE Yang-Won, CHOE Yong-Beom, AHN Kyu-Joong

Department of Dermatology, School of Medicine, Konkuk University

Adalimumab, a kind of anti-tumor necrosis factor-α (anti-TNF-α) agents, has been widely used for effective treatment of chronic inflammatory conditions, such as psoriasis, rheumatoid arthritis, and inflammatory bowel disease. Targeted therapy with biological agents has provided new therapeutic options for patients with moderate to severe psoriasis, but paradoxically, there have been reported of new-onset psoriasis or pustular erupion in patients treated with TNF-α inhibitors, although the exact mechanism remains unclear.

We herein report a case of new-onset palmoplantar pustulosis occurred in a 57-year-woman after administration of adalimumab. She had nearly 10-year-history of ankylosing spondylitis (AS), treat with subcutaneous adalimumab 40 mg, once a month. Three months after injection, numerous pustules were developed on her palms and soles. We recommended to discontinuing adalimumab and switching to other agent.

FC-4

Diagnosis of Nail Psoriasis and Psoriatic Arthritis in a Patient with Recurrent Distal Interphalangeal Arthritis

RYU Hyeong Ho, NA Sunjae, NA Se Young, PARK Hyun Sun, LEE Jong Hee, CHO Soyun

Department of Dermatology, Seoul National University Boramae Hospital, Seoul, Korea

Psoriatic arthritis (PsA) is an inflammatory arthropathy occurring in patients with psoriasis. The prevalence of PsA in patients with psoriasis varies widely, from 1% to 39% in previous reports. In a Korean study, the prevalence was 9%. In western countries peripheral PsA is the most frequent pattern, but in Korea axial PsA is the predominant pattern. Approximately 15% of PsA patients develop arthritis more than 1 year before Psoriasis. Recent diagnostic criteria of PsA permit the diagnosis of PsA despite RF positivity or the absence of psoriasis, as long as other typical features of PsA are present. A 43-year-old man with no personal or family history of psoriasis was referred to our clinic from orthopedic surgery department for evaluation and treatment of recurrent dactylitis and distal interphalangeal arthritis. Upon examination, multiple onycholysis and oil spots were found, and hence the diagnosis of nail psoriasis was entertained. After whole body physical examination, we found a scalp psoriatic lesion. Blood test for rheumatoid factor was negative. Imaging studies demonstrated enthesitis, bone erosion at right thumb digital phalanx, and increased uptake at bilateral thumb interphalangeal joint and left ankle in bone scan. Based on CASPAR criteria, we diagnosed this case as PsA with nail psoriasis and started treatment with methotrexate.

FC-5

Aggravation of Preexisting Psoriasis during Adalimumab Treatment for Psoriatic Arthropathy

RYU Hyeong Ho, CHOI Jae Woo, KIM Hyo Jin, PARK Kyoung Chan, YOUN Sang Woong

Department of Dermatology, Seoul National University College of Medicine and Seoul National University Bundang Hospital

Adalimumab, a fully human, recombinant, immunoglobulin G1 monoclonal antibody that binds specially to TNF, is used to treat a wide spectrum of moderate to severe inflammatory conditions, including psoriasis, psoriatic arthropathy, and inflammatory bowel disease. Paradoxically, there have been many reports of de novo or worsening psoriasis associated with adalimumab therapy in western countries. In Korea, there was a report about recurred palmoplantar pustulosis after adalimumab therapy. We present a case of worsening psoriasis with injection site reaction by adalimumab in a 40-year-old man. He was treated by adalimumab for psoriatic arthritis in July 2011. During 2 weeks after the first injection, his psoriasis had been aggravated. The skin lesion improved after therapy with oral cyclosporine and the injection site reaction also improved.

FC-6

Regulation of Skin Inflammation and Angiogenesis by EC-SOD via HIF-1alpha and NF-kappaB Pathways

KIM Byung-Hak, KIM Tae-Yoon

Department of Dermato-Immunology, Catholic Research Institute of Medical Science, The Catholic University of Korea, Seoul, Korea

Extracellular superoxide dismutase (EC-SOD) is an antioxidant enzyme that breaks down superoxide anion into oxygen and hydrogen peroxide in extracellular spaces and plays key roles in controlling pulmonary and vascular diseases in response to oxidative stresses. We aimed to investigate the role of EC-SOD in angiogenesis and inflammation in chronic inflammatory skin disorders such as psoriasis. Overexpressed EC-SOD reduced expression of angiogenic factors and pro-inflammatory mediators in hypoxia-induced keratinocytes and in ultraviolet B-irradiated mice, whereas the expression of the anti-angiogenic factor tissue inhibitor of metalloproteinase-1 (TIMP-1) and anti-inflammatory cytokine interleukin-10 (IL-10) were increased. EC-SOD decreased new vessel formation, epidermal edema, and inflammatory cell infiltration in UVB-irradiated transgenic mice. Moreover, cells treated with recombinant human EC-SOD inhibited endothelial tube formation and cell proliferation. Overall, the anti-angiogenic and anti-inflammatory effects of EC-SOD might be due to suppression of **hypoxia-inducible factor**-1α (HIF-1α), protein kinase C (PKC), and nuclear factor-kappaB (NF-κB) expression. Furthermore, EC-SOD expression in tissue from psoriasis patients was markedly decreased in psoriatic lesional and non-lesional skins from psoriasis patients in comparison to normal skin from healthy volunteers. Together, EC-SOD may provide a novel therapeutic approach for angiogenic and inflammatory skin diseases such as psoriasis.

FC-7

Extracellular Superoxide Dismutase Inhibits IL-23-mediatated Skin Inflammation in Mice

LEE Yun Sang, KIM Tae-Yoon

Laboratory of Dermatology-Immunology, Catholic Research Institute of Medical Science, The Catholic University of Korea, Seoul, Korea

Psoriasis is a common chronic and complex autoimmune inflammatory skin disorder. The histological characteristics of psoriasis are epidermal hyperplasia, increased infiltration of mononuclear leukocytes into the dermis, and increased angiogenesis. Immune cell infiltration is seen in psoriatic lesions and is one of the major causing factors for psoriasis. In addition, it was previously reported that extracellular superoxide dismutase (EC-SOD) has anti-chemotactic activity. Therefore, we hypothesized that EC-SOD could ameliorate psoriasis. To investigate the hypothesis, we induced psoriasis-like IL-23-mediated skin inflammation by intradermal injection of IL-23 in wild type, EC-SOD transgenic and EC-SOD knock-out (KO) mouse ears, and determined the characteristics of IL-23-mediated skin inflammation. The result showed that ear skin was thickener in EC-SOD KO mice and thinner in EC-SOD transgenic mice compared to wild type mice. Additionally, the infiltration of CD4+ T cells, macrophages, and dendritic cells into IL-23 injection sites was increased in EC-SOD KO mice and decreased in EC-SOD transgenic mice. Expression level of IL-17 was also increased in EC-SOD KO mice, while its expression was decreased in EC-SOD transgenic mice. Furthermore, we demonstrated that EC-SOD KO dendritic cells express more MHCII and treatment of recombinant EC-SOD rescue over-expressed MHCII. These results suggest that EC-SOD may inhibit IL-23-induced psoriasis-like inflammation through inhibition of immune cell infiltration and immune responses. These findings reveal an anti-inflammatory effect of EC-SOD and imply that EC-SOD could be a possible candidate for the management of skin inflammatory diseases such as psoriasis.

FC-8

Epidermal CCR6+ γδ T Cells are Major Producers of IL22 and IL17 in a Murine Model of Psoriasiform Dermatitis

Mabuchi Tomotaka[1,2], Akasaka Emiko[1], Hiruma Azusa[1], Kojima Tomoko[1], Manabe Yasuaki[1], Kato Masayuki[1], Ikoma Norihiro[1], Tamiya Shiho[1], Ozawa Akira[1], and Hwang Sam T.[2]

[1]Department of Dermatology, Tokai University School of Medicine, Kanagawa, Japan
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Cytokine components of Th17 pathway play vital roles in human psoriasis. Although much is known about T cell receptor (TCR) αβ T cells in psoriasis, the role of unconventional T cells, including γδ T cells, is unclear.

Herein, using an IL23 skin injection model of psoriasiform dermatitis in mice, we demonstrate that IL22, IL17A, and the IL23 receptor were highly enriched in a population of CCR6+, TCR γδ-low expressing (GDL) T cells that accumulated in the epidermis after IL23 injections. GDL T cells were distinct from resident TCR γδ-high, Vγ3+, CCR6- T cells in the epidermis that did not change appreciably in numbers following IL23 injection. Large numbers of CCR6+ cells were detected at or above the level of the epidermal basement membrane by confocal microscopy five days after repeated IL23 injections at the same time GDL T cells increased in numbers in the epidermis. TCR δ- deficient mice (lacking γδT cells) exhibited decreased ear swelling and downregulated expression of IL22 and IL17A in the epidermis following IL23 injection.

Our data suggest that a subset of γδ T cells play a critical role in IL23-mediated psoriasiform dermatitis.

FC-9

A Study of Altered Level of Sphingoshine and Shpinganine in Psoriatic Epidermis

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Background: Ceramides are the main lipid component maintaining the lamellae structure of stratum corneum. Ceramides are a structurally heterogeneous and complex group of sphingolipids in which sphingoid bases are basic structural constitucnts. The changed level of sphingoid bases have been described in skin conditions of dryness and barrier disruption, such as atopic dermatitis.

Objective: The purpose of this study was to investigate the altered levels of sphingoid bases in psoritatic epidermis and their relationship with clinical severity of psoriasis.

Methods: Samples from lesional and non-lesional epidermis were obtained from 8 psoriasis patients. Altered level of sphingoshine (So) and shpinganine (Sa) were ananlyzed by high-performance liquid chromatography. The protein expressions of ceramide synthase (CerS) and ceramidase (CDase), which are related with So and Sa metabolism, were measured using western blot analysis.

Results: Levels of So and Sa in the lesional epidermis were significantly higher than those in the non-lesional epidermis. Although there's no altered protein expressions of CerS and CDase between non-lesional and lesional epidermis, there is a highly significant positive correlation between the % change of CDase, a degradative enzyme of ceramide into So, and PASI score.

Conclusion: The levels of So and Sa are significantly increased in the psoriatic epidermis, and % change of CDase is positively correlated with clinical severity of psoriasis.

FC-10

Comparison of Facial PASI with Facial PLASI Regarding Construct Validity and Reliability

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Background: Assessing the reliability of severity measures in facial psoriasis has been rarely conducted while it is essential to treat patients in clinical practice and to document therapeutic responses in clinical trials.

Objectives: To assess whether facial Psoriasis and Severity Index (fPASI) properly evaluates the severity of facial psoriasis and compare it with facial Psoriasis Log-based Area and Severity Index (fPLASI) with regard to construct validity and reliability.

Methods: The severity of facial psoriasis from 573 patients visiting our clinic was analyzed in the scale of fPASI and fPLASI. Then, using the previous data of two clinical trials involving facial psoriasis treatment, the extent of clinical improvement during whole treatment course was calculated as the percentage change of fPASI and fPLASI (ΔfPASI and ΔfPLASI). And the corresponding values were compared with both physician's global assessment of facial lesions (fPGA) and subjective global assessment of facial lesion (fSGA) during clinical trials respectively.

Results: The distribution of fPASI was clustered in lower score value (8.0 ± 5.9) comparing with systemic PASI (15.9 ± 9.8), mainly because the area grade could not effectively differentiate the facial surface involvement concentrated in narrow range. After applying PLASI system, the mean value and standard deviation (14.1 ± 9.3) increased significantly. In retrospective analysis of clinical trials, the degree of clinical improvement measured by PGA matched better with ΔfPLASI compared with ΔfPASI. ΔfPASI also tended to underestimate clinical improvement comparing with ΔfPLASI in both fPGA and fSGA grading.

Conclusion: As a result of the logarithmic scale for the affected skin surface, fPLASI system could effectively differentiate the clustered area distribution of facial psoriasis. Facial PLASI might be a more reliable and practical measure than fPASI in assessing both disease severity and therapeutic improvement of facial psoriasis.

FC-11

Cross-sectional Study on the Correlation of Serum Uric Acid with Disease Severity in Korean Psoriasis Patients

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Background: Hyperuricemia is a common finding in psoriasis. However, previous studies have reported inconsistent results about the association between serum uric acid concentration (SUAC) and psoriasis severity. Recent studies have also reported that SUAC is associated with metabolic dysregulation.

Objective: To assess any association between SUAC and clinical features of psoriasis, and to evaluate the traits of patients with psoriasis with hyperuricemia compared with patients with normouricemia.

Methods: Cross-sectional data from 198 patients with psoriasis were analyzed. Association of SUAC with clinical features of psoriasis, body mass index (BMI) and various laboratory values was assessed.

Results: The average SUAC of patients with psoriasis was not significantly different from that of the healthy population. There was a positive correlation between SUAC and PASI and BMI in patients with psoriasis. There was no association with age of disease onset, family history, or other laboratory values. Of the other factors of disease severity, the extent of body surface involvement was correlated with SUAC although there was no significant relationship with activity of individual lesions. Mean PASI and extent of psoriasis were increased in hyperuricemic compared with normouricemic patients.

Conclusion: SUAC in patients with psoriasis is positively related with PASI, extent of skin involvement and BMI for both genders independently.

FC-12

Pathogenic Roles of Wnt Ligand and Notch Signaling in Psoriasis

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Background: Psoriasis is characterized by uncontrolled hyperproliferation, aberrant differentiation and dermal infiltration of immune cells, specifically, a Th17-subset of T cells. Recent studies have shown that Notch1, a determinant of keratinocyte terminal differentiation, is markedly decreased and Wnt5a signaling is increased in psoriasis.

Objectives: Our goal was to investigate the expression and interaction of Wnt5a and Notch signaling in psoriasis in relation to T-cell-mediated epidermal hyperproliferation.

Patients/Methods: Psoriatic skin biopsies were used for immunohistochemistry for the expression of Wnt5a / Notch1 signaling-related factors. In primary normal human keratinocytes (NHKs) treated with Wnt5a, cell proliferation and the expression of Wnt5a / Notch1 signaling-related factors were assessed.

Results: Wnt5a expression was increased and Notch1 expression was decreased in lesional samples compared to non-lesional samples of psoriatic and normal skin. Treatment with recombinant Wnt5a (rWnt5a) increased the proliferation of NHKs. Exposure of NHKs to a cytokine environment containing IL-1α, TNF-α, TGF-α, and IFN-γ downregulated Notch1 and HES1 and increased Wnt5a expression. Treatment of NHKs with rWnt5a increased the expression IL-23, IL-12 and TNF-α. Finally, overexpression of Wnt5a downregulated Notch1and HES1.

Conclusion: Our data strengthen the notion that Wnt5a and Notch signaling exert counteracting influences on each other and are involved in the central pathomechanism of psoriasis. Increased Wnt5a signaling and decreased Notch1 signaling may be associated with defects in terminal differentiation and enhanced proliferation of keratinocytes while Wnt5a may be a pathogenetic link between dermal infiltration of immune cells and abnormalities of keratinocytes in psoriasis.

FC-13

Implication of TRPVs in Psoriasis

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TRPV (transient receptor potential vanilloid), one of the seven TRP channel superfamily, might have a central role in the pathogenesis of pruritus and also involved in epidermal cell proliferation or differentiation. The purposes of this study were to investigate the expression of TRPV1 and TRPV3 in psoriatic skin and the pathophysiologic association.

Clinically, we obtained patients' Psoriasis Area and Severity Index (PASI) score and pruritus scale. The expression of TRPV1 and TRPV3 were evaluated by immunohistochemistry, real time RT-PCR, western blot in the biopsied skin. *In vitro* study, epidermal cell proliferation and differentiation were examined with TRPV3 agonist and antagonist.

We found that the expression of TRPV3 increased in psoriatic lesional skin compared with non-lesional skin. Expression of TRPV3 showed correlation between their expression and clinical phenotypes in the aspect of pruritus intensity and PASI score. Epidermal cell proliferation was observed after treating TRPV3 agonist and the proliferation was suppressed after treating TRPV3 antagonist. These findings suggest the activation of TRPV3 may have potential role in the pathogenesis of psoriasis.

FC-14

Epidemiology and Clinical Features of Pediatric Psoriasis in Tertiary Referral Psoriasis Clinic

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Few epidemiological studies about pediatric patients with moderate to severe psoriasis were available although there was no approved systemic therapy for these patients. The aim of the study was to elucidate clinical features of pediatric psoriasis in tertiary referral psoriasis clinic. We analyzed the clinical data of 358 patients under 18 years referred to our clinic from other private clinics and medical centers. Our data showed that male to female ratio was 1.06:1, and the peak age of onset was in the 10- to 11-year-old. Thirty two point four percent of the patients had a positive family history. The most prevalent phenotype was plaque type (67.3%) and the mean PASI score was 17.2 ± 12.7. The most frequently affected body part was trunk (69.5%), followed by legs (65.3%). Sunlight exposure and summer season improved psoriatic lesions, while stress and winter season aggravated the clinical course. Only 26.0% of patients received systemic therapy or phototherapy during the therapeutic course. Oral acitretin (11.2%) was most frequently used followed by UVB phototherapy (7.3%). Childhood group (under age 13) showed higher prevalence of guttate and generalized pustular phenotypes and more severe clinical course compared with adolescent group (between age 13 and 18) (p<.05). In conclusion, our patients showed distinctive features in clinical phenotypes, disease severity and affected body parts compared with previous reports. We also found that clinical application of systemic therapies for pediatric patients were limited considering severe disease state of our patients, demanding a need for more research on treatment of pediatric psoriasis.

FC-15

Clinical Study of Childhood and Adolescent Psoriasis

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Background: Few clinical studies are available on childhood and adolescent psoriasis in Korea.

Objectives: The purpose of this study is to analyze clinical features of childhood and adolescent psoriasis in a referral center in Korea.

Methods: We performed retrospective medical record-based analysis for 255 psoriasis patients younger than 16 years of age at the time of diagnosis at our center from March 2001 to July 2010. Age, sex, onset age, familial history, site of involvement, type of psoriasis, nail involvement, initial PASI score, treatment modality were analyzed.

Results: There was no sexual predominance; mean age of onset was 8.85 years; 17.25% of patients had familial history. Upper extremities, lower extremities, trunk, scalp and face were most commonly involved sites in sequence. Guttate psoriasis (58.90%) was the most common type of psoriasis. Nail involvement was observed in 11.11% of patients. Initial PASI score at the time of diagnosis was 7.9. The most common treatment was topical steroid and topical vitamin D in combination.

Conclusion: Childhood and adolescent psoriasis is not uncommon disease. Larger scale epidemiological study is needed.

Tentative categories: Clinical issues

FC-16

The Inflammatory Cytokine Profile according to Morphological Phenotype in Psoriasis

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Psoriasis is a chronic inflammatory skin disease associated with over-expression of Th-1 and Th17 cytokines. We can observe two kinds of morphological state in psoriasis, one is acute eruptive state characterized by rapidly spreading small papules and the other is chronic stable state characterized by large stable plaques. Many trials have been performed to examine the cytokine profile to better characterize inflammatory process in psoriasis. However, the trial yielded conflicting result, and the studies focusing on the divergence of cytokine levels among various morphological phenotypes within the psoriasis patients has been scarce.

We are trying to investigate the differences of inflammatory cytokine profile according to morphological phenotype using multiplex cytokine analysis through xMAP technology and enzyme-linked immosorbent assay.

FC-17

Proteomics Based Psoriasis Specific Protein Identification and Its Expression Pattern Analysis as Disease Maturation

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In development of psoriasis, there are various complex contributing factors including genetic tendency, immunologic factor, angiogenesis and keratinocyte differentiation. In the present study, we conducted an investigation of different specific proteomes of psoriatic lesional skin and nonlesional psoriatic skin for understanding pathgogenesis of psoriasis. In proteomic analysis, there were increased expressions proteins involved in negative regulation of apoptosis, cell cycle modulation, inflammatory response, regulation of ROS and psoriasin. Psoriatic tissue was categorized to 3 phases that early phase with small scaly papule, plaque phase with maturation, and big plaque phase with scaly big plaque as maturation of disease. And immunohistochemical staining was conducted to identify the locations of protein expression in each phase. In pathologic finding, marked parakeratosis, psoriasiform hyperplasia thinning of papillary dermis was observed as maturation of psoriasis phases, and location of protein expression was different regarging to its phase.

Taken together, through proteomic analysis of specific protein and immunohistochemical study of its location, we would like to perform the further studies of proteins that associated with development of psoriasis and its maturation.

FC-18

A Substitute of Human CD11c^{+}, CD1c^{-} Inflammatory Myeloid Dendritic Cells

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In psoriatic skin, there is a large number of CD11c^{+}, CD1c- myeloid (mostly, TNFα and iNOS producing- [Tip-]) dendritic cells (DCs) in the dermis. These cells produce significant amount of pro-inflammatory cytokines and activate T cells. The origin and the substitute of these inflammatory myeloid DCs in human system are still elusive. Because of similar phenotypic characteristics, monocyte-derived DCs (Mo-DCs) cultured with granulocyte-monocyte colony stimulating factor (GM-CSF) and interleukine (IL)-4 have been generally considered an *in vitro* model of resident dermal DCs. In this study we found that Mo-DCs are functionally more similar to inflammatory myeloid DCs than resident dermal DCs, especially when they were cultured using the IFNɣ-supplemented media. Flow cytometry analysis showed that DCs cultured with GM-CSF and IL-4 expressed HLA-DR, CD11c, CD1c and cytoplasmic iNOS and TNFα. The expression of CD1c molecule was down-regulated by additional treatment with IFNɣ. Moreover triple cytokine (GM-CSF, IL-4 and IFNɣ)-induced DCs (IFNɣ-DCs) secreted significant amount of Th17-inducing cytokines such as IL-1β, IL-6, TNFα and IL-23p40 when activated with LPS and increased IFNɣ, IL-17A-producing Th subsets after co-culturing with allogeneic lineage marker negative T cells. In conclusion, the profile of cytokine production, the expression of intracellular iNOS and TNFα, the expansion of Th1/Th17 subsets and the phenotypic similarity strongly suggest that IFNɣ-DCs can be an *in vitro* substitute of inflammatory myeloid (CD11c^{+}) DCs which are found in various Th17-mediated autoimmune diseases such as psoriasis.

Key words: Psoriasis; inflammatory myeloid dendritic cells; CD11+, CD1c- DCs, monocyte-derived dendritic cells

FC-19

In Situ Evidence for CCl20/CCR6 System as a Relevant Contributor to Chronic T Cell-Mature DC Interaction in Psoriasis

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The formation of the ectopic T cell-mature dendritic cells (DCs) cluster is one of the characteristics for chronically inflamed skin, including psoriasis. However, responsible chemokine microenvironments for organizing these structures remain to be elucidated. This study aimed to evaluate whether psoriasis-associated chemokine system, CCL20/CCR6, is involved in the ectopic lymphoid structure in psoriasis. CCL20 is expressed on both epidermal and dermal compartment in lesional psoriasis, and populations of infiltrating T cells are primary sources for dermal CCL20 expression. By flow cytometry, we identified that CCL20 production from CD4+ T cells are restricted to Th1/Th17/Th22, but rarely to Th2 subset. In psoriatic skin, CCR6-expressing cells present typical grouped-features with the marked increased number. Two-color immunofluorescence showed that CCR6 is expressed on the majority of psoriatic T cells and, unexpectedly, DC-LAMP+ mature DCs. Furthermore, DC-LAMP+ mature DCs are found close to CCL20+ cells in situ, suggesting T cells-mature DCs interaction via CCL20/CCR6 in psoriasis lesion. Collectively, our data propose the novel concept that T cell-driven CCL20 may play an important role for recruiting CCR6-bearing mature DCs and further Th17 cells to generate the ectopic lymphoid tissues which lead to persistent T cell activation and chronic nature of psoriasis.

FC-20

Loss of hTid-1 Expression and Aberrant Actin Cytoskeleton Organization in Psoriatic Skin

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A comparative study of hTid-1 expression pattern in psoriatic and normal skin was carried out. Here, we report that the loss of hTid-1expression in psoriatic skin leads to the aberrant actin cytoskeleton organization in the epidermis of psoriatic lesions. The biochemical mechanisms by which hTid-1 regulates actin cytoskeleton organization was investigated in cultured HeLa cells. We found that hTid-1, specifically hTid-1S interacts with MK5, a p38-regulated/activated kinase The binding of hTid-1 with MK5 inhibits MK5 protein kinase activity that phosphorylates its downstream target protein HSP27 known to play a critical role in the regulation of F-actin phosphorylation. Overexpression of hTid-1S resulted in the inhibition of stress fiber formation and cell migration in HeLa cells. Moreover, we found enhanced F-actin polymerization in psoriatic epidermis where hTid-1 expression is suppressed. This study suggests that the failure of hTid-1 expression in psoriatic skin is responsible for the aberrant actin cytoskeleton organization, making hTid-1 as a potential target in the treatment of psoriasis.

FC-21

Autophagy Negatively Regulates Keratinocyte Inflammatory Responses via Scaffolding Protein p62/SQSTM1

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The scaffolding adaptor protein p62/SQSTM1 (p62) has been shown to be an autophagy receptor that acts as a link between the ubiquitination and autophagy machineries. However, the roles of autophagy and p62 in human keratinocytes are not well understood. In this study, we show that the p62 expression is negatively regulated by autophagy pathway, which is thus essential for the prevention of excessive inflammation in human keratinocytes. We found that Toll-like receptors (TLR) 2/6 stimulation robustly activated autophagy pathways and up-regulated p62 expression in human primary keratinocytes. Blockade of autophagy significantly increased the generation of inflammatory cytokines and expression of p62 in primary human keratinocytes. Notably, silencing p62 through RNA interference resulted in a significant decrease in nuclear factor (NF)-κB activation and inflammatory responses in keratinocytes. Epidermal expression of p62 was further found to be significantly higher in psoriatic skin than in those affected by atopic dermatitis or from healthy controls. Collectively, our data provide new insights into the cross talks between autophagy and p62 in controlling cutaneous inflammation.

FC-22

Brn2 is a Transcription Factor Regulating Keratinocyte Differentiation with a Possible Role in the Pathogenesis of Lichen Planus

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Terminal differentiation of skin keratinocytes is a vertically directed multi-step process that is tightly controlled by the sequential expression of a variety of genes. In this study, we investigated the role of the POU domain-containing transcription factor Brn2 in keratinocyte differentiation. Immunohistochemical analysis showed that Brn2 is expressed primarily in the upper granular layer. Consistent with its epidermal localization, Brn2 expression was highly induced at 14 days after calcium treatment of cultured normal human epidermal keratinocytes. When Brn2 was overexpressed by adenoviral transduction, Brn2 led to increased expression of the differentiation-related genes involucrin, filaggrin, and loricrin in addition to inhibition of their proliferation. Chromatin immunoprecipitation demonstrated that Brn2 bound to the promoter regions of these differentiation-related genes. We injected the purified Brn2 adenovirus into rat skin, which led to a thickened epidermis with increased amounts of differentiation related markers. The histopathologic features of adenovirus-Brn2 injected skin tissues looked similar to the features of lichen planus, a human skin disease showing chronic inflammation and well-differentiated epidermal changes. Moreover, Brn2 is shown to be expressed in almost all cell nuclei of the thickened epidermis of lichen planus, and Brn2 also attracts T lymphocytes. Our results demonstrate that Brn2 is probably a transcriptional factor playing an important role in keratinocyte differentiation and probably also in the pathogenesis of lichen planus lesions.

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