Drugs of the Future 2008, 33(10): 911-915
Copyright 2008 Prous Science, S.A.U. or its licensors. All rights reserved.
CCC: 0377-8282/2008

Meeting Report

Highlights from International Investigative Dermatology 2008

E. Ferrer
Prous Science, Provenza 388, 08025 Barcelona, Spain

CONTENTS

Abstract

The fifth joint meeting of the Japanese Society for Investigative Dermatology (JSID), the Society for Investigative Dermatology (SID) and the European Society for Dermatological Research (ESDR) was held this year in Kyoto (Japan) on May 14-17. This meeting, which takes place every 4 years, is focused on the latest information on cutaneous biology and skin diseases, covering basic and clinical fields of dermatology. New data related to psoriasis, atopic dermatitis, acne, skin inflammation and cutaneous T-cell lymphoma have been selected for this report.

Psoriasis

J.G. Krueger from The Rockefeller University (New York, USA) delivered a talk on psoriasis and how different information obtained from genetics, genomics, cell biology and innovative biological treatments has transformed psoriasis to a pathology where relevant translational research is performed (1). Everything began when wide gene expression profiling was performed comparing skin from psoriatic patients (lesional and nonlesional) and healthy controls, allowing the identification of genes highly expressed in psoriatic lesions (2). Most of those genes were related to immune signaling pathways involved in dendritic cell and T-cell function. Dendritic cells have attracted much of the attention in psoriasis since they are the source of relevant mediators, such as IL-23 and TNF-α, that have been validated clinically by biological treatments targeting these cytokines. IL-23 is involved in Th17 cell survival and differentiation. Th17 cells produce IL-17 and IL-22, IL-22 being able to induce hyperplasia of the epidermis, dermal inflammation and activation of STAT3 in vivo (3). It is considered that inhibition of IL-22 constitutes a promising therapy for psoriasis based on recent data using an IL-22-neutralizing antibody in a mouse model of psoriasis (4).

K. Miyoshi from the Department of Dermatology of Kochi Medical School, Kochi University (Nankoku, Japan) presented a proof-of-concept study in psoriatic patients with a small-molecule inhibitor of STAT3 (5). It has been shown in an animal model of psoriasis that STAT3 activation is required for the generation of psoriatic changes, and that topical treatment with STAT3 decoy oligonucleotides suppressed the development of psoriatic changes. Ochromycinone (STA-21) is an antibiotic that was identified as a STAT3 inhibitor by virtual database screening (6). STA-21 inhibits STAT3 dimerization and DNA binding and prevents translocation of the protein to the nucleus —processes which are essential for its activation. Five patients with psoriasis were treated with 0.2% STA-21 ointment for 2 weeks. Four of 5 patients showed a significantly favorable response to STA-21 compared with vehicle controls.

R. Abe from Hokkaido University (Japan) presented proof of concept for the use of pigment epithelium-derived factor (PEDF) peptides in psoriasis (7). PEDF has strong antiangiogenic activity and for this reason low-molecular-weight PEDF peptides were identified and tested topically in human psoriatic skin grafted onto severe combined immunodeficient (SCID) mice. The PEDF peptides (1 mM) were applied to the grafted site each day for 10 days. After 2 weeks of treatment, topical application of all peptides significantly reduced the epidermal thickness of the grafted area.

New data on biological treatments for psoriasis were also presented at the meeting. F. Wang from the Department of Dermatology, University of Michigan (Ann Arbor, USA) presented new results on the mechanism of action of etanercept in psoriasis (8). Lesional gene expression of IL-19, IL-20, IL-22 and IL-24 decreased significantly after 1 week of treatment before clinical improvement of lesions was evident. These results suggest that the therapeutic mechanism of etanercept may involve suppression of IL-20-related cytokines prior to clinical improvement. Because suppression of these cytokines preceded that of reduced K16 expression in keratinocytes, it is considered that IL-20-related cytokines

may represent an important bridge between inflammation (leukocyte activation) and phenotypic changes (epidermal hyperplasia) in psoriasis.

M. Del Giglio from the Department of Dermatology and Venereology, University of Verona (Italy) presented data from a randomized, controlled trial comparing the efficacy and safety of the association of acitretin and etanercept in the treatment of moderate to severe chronic plaque psoriasis (9). A 24-week, randomized, controlled, investigator-blinded trial was conducted in 60 adult patients with moderate to severe chronic plaque psoriasis. The combined therapeutic regimen of etanercept 25 mg once weekly and acitretin 0.4 mg/kg/day was as effective as etanercept 25 mg twice weekly and more effective than acitretin alone.

Prediction of biological treatment efficacy based on genetic markers is also of interest for biologicals in psoriasis. A. Costanzo from the University of Rome Tor Vergata (Rome, Italy) reported Cw6 as a potential predictive marker for response to efalizumab treatment (10). HLA-Cw6 haplotyping in 82 patients with moderate to severe plaque psoriasis treated with either efalizumab (34 patients) or etanercept (48 patients) demonstrated that the response to efalizumab, but not etanercept, was strictly linked to the presence of the HLA-Cw6 allele.

New information on the topical phosphodiesterase PDE4 inhibitor AN-2728 in psoriasis was presented. AN-2728 is novel boron-containing antiinflammatory drug that inhibits the release of TNF-α. AN-2728 inhibits PDE4 enzyme activity in human U-937 cells with an IC_{50} of 0.49 mM, inhibiting all four PDE4 isoforms equally. AN-2728 has been shown to be a competitive inhibitor of the substrate cAMP, as determined by enzyme kinetic analysis. AN-2728 also inhibits PDE7 with an IC_{50} of 0.73 μM, but does not significantly inhibit PDE1, 2, 3 or 5. K. Beutner from Anacor Pharmaceuticals (Palo Alto, USA) presented data from a microplaque study with AN-2728 in psoriasis (11). Two active formulations of AN-2728 (5% ointment and cream) and two vehicles were tested and lesions were treated over 12 days. Examination of the infiltrate thickness showed that treatment with AN-2728 led to a relevant and clear improvement.

Atopic dermatitis

Reduced production of antimicrobial peptides in atopic dermatitis (AD) lesions is considered to contribute to the susceptibility to skin infections in this condition. Different studies presented at the meeting were evaluated to identify new therapeutic approaches that can restore antimicrobial production in AD. Focusing on the human cathelicidin antimicrobial protein hCAP-18, M. Stahle from the Karolinska Institutet (Stockholm, Sweden) showed that topical vitamin D treatment upregulated hCAP-18 expression in lesional as well as nonlesional AD skin (12). Cultured primary keratinocytes from nonlesional skin of psoriasis and AD and healthy skin all upregulated hCAP-18 mRNA following treatment with vitamin D in vitro. This suggests that topical treatment with vitamin D might aid in reducing skin infections in AD. T.R. Hata from the Division of Dermatology, University of California San Diego (USA), studied whether local dysregulation of cathelicidin in atopic subjects could be corrected with oral vitamin D (13). Supplementation with oral vitamin D (cholecalciferol) at 4000 IU/day was given for 21 days and lesional skin was analyzed and showed a statistically significant increase in cathelicidin expression compared with normal skin after supplementation, suggesting that supplementation with oral vitamin D can induce cathelicidin production only in AD lesional skin. S. Jeong from the Research Division of NeoPharm (Daejeon, South Korea) presented a new molecule, K6-L19, identified after screening molecules with stimulatory activity on antimicrobial synthesis in epidermis (14, 15).

Another hallmark of AD is the inherited defect in permeability of the cutaneous barrier structure. Epiceram™ cream is a ceramide triple-lipid mixture in an optimized ratio designed to correct the lipid biochemical abnormality in AD. Epiceram™ was recently approved by the FDA. J.L. Sugarman from the University of California at San Francisco (USA) presented a clinical trial where the efficacy of Epiceram™ cream was comparable to fluticasone (Cutivate®) cream in 113 children with moderate to severe AD (16). E.L. Simpson from the Department of Dermatology of the Oregon Health & Sciences University (Portland, Oregon, USA) performed a prospective, randomized, investigator-blinded study in 38 children with AD for 4 weeks (17). Epiceram™ appeared to be safe and effective in pediatric patients with mild to moderate AD, with no significant difference compared to tacrolimus at the end of treatment.

Itching and pruritus are clinical signs present in AD. Since there are almost no itching/pruritus-specific treatments for this disease, different investigations are ongoing to identify relevant agents. In AD, C-fibers are involved in itching and semaphorin-3A is an axon guidance molecule that is a potent inhibitor of neurite outgrowth of sensory neurons. J. Takeo-Yamaguchi from the Department of Environmental Immuno-Dermatology, Yokohama City University Graduate School of Medicine (Yokohama, Japan), investigated the effect of recombinant semaphorin-3A administered intracutaneously into the skin lesions of NC/Nga mice, an animal model of AD. Semaphorin-3A dose-dependently improved skin lesions and decreased scratching in the mice (18). Because the interruption of the itch–scratch cycle likely contributes to the improvement of AD-like skin lesions, semaphorin-3A treatment could be of interest for AD. Prostaglandin D_2 (PGD_2) is considered to be an endogenous antipruritic substance, since topically applied drug significantly suppresses scratching in the NC/Nga mouse. Y. Honma from Taisho Pharmaceutical (Saitama, Japan) demonstrated that topically applied PGD_2 significantly suppressed the long-lasting scratching induced by different stimuli in cohabitating BALB/c mice (19).

Some preclinical approaches for AD tested in animal models were also presented at the meeting.

Oligodeoxynucleotides (ODNs) containing CpG motifs (CpG-ODN) are known to reduce Th2-mediated responses by increasing Th1 responses. K. Na from the Dermato-Immunology Department of the Catholic University of Korea (Seoul, South Korea) presented results for a phosphodiester (PO) form of CpG-ODN that decreased Th2 responses without a substantial increase in Th1 responses (20). In a mouse model of ovalbumin (OVA)-induced skin inflammation, pretreatment with PO-CpG-ODN before OVA sensitization prevented the development of Th2-mediated responses, which indicated that PO-CpG-ODNs may be possible candidates for the prevention of AD. J. Kim from the Department of Dermatology at the Seoul National University College of Medicine (Seoul, South Korea) examined the clinical efficacy and therapeutic mechanism of *Actinidia arguta* extract (AAE) in 2-chloro-1,3,5-trinitrobenzene (TNCB)-induced AD-like skin lesions in NC/Nga mice (21). Orally administrated AAE significantly reduced the clinical dermatitis severity. M. Terakawa from Asubio Pharma (Osaka, Japan) investigated the effect of SUN-13834, a specific chymase inhibitor, in a mouse dermatitis model induced by repeated painting with 2,4-dinitrofluorobenzene (DNFB) (22). Oral administration of SUN-13834 (2 mg/kg) once a day decreased skin thickness, accumulation of mast cells and eosinophils and the scratching behavior induced by DNFB at 10 mg/kg and higher.

Acne

Multiple factors are involved in the pathogenesis of acne, including follicular hyperkeratinization, sebum production, hormones, *Propionibacterium acnes* infection and inflammation. J. Kim from UCLA (Los Angeles, USA) presented results linking *P. acnes* with innate immune system activation that may contribute to understanding this pathology and offer new opportunities for therapeutic approaches (23). *P. acnes* can trigger cytokine responses through TLR2 in human monocytes via the production of IL-12 and IL-8 (24). In addition, *all-trans*-retinoic acid (tretinoin), an effective treatment for acne, downregulated TLR2 expression in monocytes in vitro. TLR2 can therefore be considered a novel target for acne treatment.

New data on the potential interest of peroxisome proliferator-activated receptor PPARγ agonists for acne were presented by M. Rivier and A. Jomard from Galderma R&D (Sophia Antipolis, France) (25, 26). The selective PPARγ agonist rosiglitazone dose-dependently decreased the sebaceous gland volume following 4-week topical treatment of *fuzzy* rats. Sebaceous glands and epidermis still revealed a normal structure on histological examination, whereas a potent specific PPARγ antagonist was found to be ineffective. In addition, in the same rat model, potent PPARα antagonists could counteract the effects of the potent androgen dihydrotestosterone (DTH). It is considered that the activation of PPARγ may inhibit sebum excretion in humans and lead to a subsequent beneficial therapeutic effect in acne patients.

Skin inflammation

PGE_2 is a lipid mediator that exerts its effect through four G protein-coupled receptors known as EP_1, EP_2, EP_3 and EP_4. The EP_3 receptor can be an interesting target for skin inflammation. AE-248 is a novel EP_3-selective agonist that can reduce the DNFB-induced contact hypersensitivity response by suppressing cutaneous dendritic cell function (N. Shiraishi, Department of Dermatology, University of Occupational and Environmental Health, Kitakyusyu, Japan) (27). EP_3 receptors are supposedly expressed in keratinocytes and EP_3-deficient mice showed significantly increased ear swelling compared with wild-type mice in a contact hypersensitivity model after repeated hapten application. These results suggest that activation of EP_3 signaling plays an antiinflammatory role in this model by inhibiting keratinocyte activation, and that endogenous PGE_2 signaling also plays a suppressive role in the development of contact hypersensitivity (28).

New information on the potential interest of rhamnoside derivatives in skin inflammation was presented by M. Lévèque from the Pierre Fabre Research Institute (Toulouse, France) (29). He showed that undecylrhamnoside was capable of reducing the transcription factor NF-κB in TNF-α-stimulated human keratinocytes. Pentylrhamnoside has been designed in order to enhance the low epidermal absorption of rhamnose.

Cutaneous T-cell lymphoma (CTCL)

Results from clinical trials for CTCL were presented at the meeting. M. Urosevic from the University Hospital Zurich (Zurich, Switzerland) showed that adenoviral gene transfer of the human interferon gamma gene (*IFNG*) is safe and effective in patients with primary CTCL (30, 31). TG-1042 is a nonreplicating recombinant adenovirus with a human *IFNG* cDNA insert. TG-1042 was evaluated in an open-label, multicenter, dose-escalating phase I/II trial as repeated intratumoral injections in 39 patients with advanced primary CTCL and multilesional B-cell lymphomas. Local clinical response was observed in 19 (57%) of 33 evaluable patients, 9 of which were complete responses and 10 partial responses. Forodesine is a potent inhibitor of purine nucleoside phosphorylase (PNP) that leads to T-cell-selective intracellular accumulation of dGTP, resulting in apoptosis. An open-label, dose-escalating study of oral forodesine (40-320 mg/m^2/day) for 4 weeks was discussed by Y. Kim from Stanford University (Palo Alto, California, USA) (32). Oral forodesine at the optimal dose was well tolerated and demonstrated promising clinical activity in patients with refractory CTCL.

Temozolomide (TMZ) is an oral imidazotetrazine that induces DNA damage by cross-linking, similar to other alkylating agents. The efficacy of TMZ (200 mg/m^2 p.o. for 5 days every 28 days) was evaluated in a phase II trial in 26 patients in advanced stages of mycosis fungoides/Sézary syndrome (MF/SS). The overall response rate was 27%, with a median disease-free survival of 4

Table I: Targets of relevance for dermatological conditions.

Target	Relevance	Indication
Pigment epithelium-derived factor (PEDF)	Topical low-molecular-weight PEDF peptides are effective antiangiogenic agents in animal models of psoriasis	Psoriasis
Reactive oxygen scavengers (ROS)	ROS inhibit IL-23/Th17 signaling	Psoriasis
STAT3	Topical STAT3 inhibition is effective in psoriasis	Psoriasis
Semaphorin-3A	Interesting target for itching	Atopic dermatitis
FABP7	Immunogenic antigen identified by expression profiling	Melanoma
Coding region instability determinant-binding protein (CDR-BP)	RNA-binding protein highly expressed in malignant melanoma	Melanoma
TLR2	*P. acnes* activates innate immune response through TLR2	Acne
PPARγ	PPARγ agonist active in an animal model of acne	Acne
EP_3 receptor	Selective EP_3 agonist inhibits cutaneous inflammation in mice	Skin inflammation

months. The median overall survival of all patients was 24 months (33).

Finally, a list of interesting targets presented at the meeting is shown in Table I.

References

1. Zaba, L.C., Fuentes-Duculan, J., Eungdamrong, N.J., Pierson, K., Lowes, M.A., Krueger, J.G. *Identification of a novel dendritic cell subset that could drive Th17 polarization and inflammation in psoriasis vulgaris*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 305.

2. Zhou, X., Krueger, J.G., Kao, M.C. et al. *Novel mechanisms of T-cell and dendritic cell activation revealed by profiling of psoriasis on the 63,100-element oligonucleotide array*. Physiol Genomics 2003, 13(1): 69-78.

3. Zheng, Y., Danilenko, D.M., Valdez, P. et al. *Interleukin-22, a T(H)17 cytokine, mediates IL-23-induced dermal inflammation and acanthosis*. Nature 2007, 445(7128): 648-51.

4. Sano, S., Chan, K.S., Carbajal, S. et al. *Stat3 links activated keratinocytes and immunocytes required for development of psoriasis in a novel transgenic mouse model*. Nat Med 2005, 11(1): 43-9.

5. Miyoshi, K., Nakajima, K., Asao, N., DiGiovanni, J., Sano, S. *An inhibitor of Stat3 activation can be a novel drug for anti-psoriatic strategy*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 373.

6. Song, H., Wang, R., Wang, S. et al. *A low-molecular-weight compound discovered through virtual database screening inhibits Stat3 function in breast cancer cells*. Proc Natl Acad Sci USA 2005, 102(13): 4700-5.

7. Abe, R., Yamagishi, S., Fujita, Y. et al. *Topical application of antiangiogenic peptides based on pigment epithelium-derived factor can improve psoriasis*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 12.

8. Wang, F., Helfrich, Y., Smith, N. et al. *Rapid suppression of IL-20-related cytokines by etanercept decreases regenerative hyperplasia in vivo*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 87.

9. Del Giglio, M., Gisondi, P., Cotena, C., Girolomoni, G. *Combining etanercept and acitretin in the therapy of chronic plaque psoriasis: A 24-week, randomized, controlled, investigator-blinded trial*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 336.

10. Costanzo, A., Talamonti, M., Mazzotta, A., Papoutsaki, M., Climenti, S. *Cw6 allele confers sensitivity to efalizumab treatment in psoriasis*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 416.

11. Beutner, K., Gassmueller, J., Marti, D., Lathrop, A. *AN2728, a novel oxaborole in development for treatment of psoriasis, demonstrates significant activity in a micro plaque study*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 367.

12. Stahle, M., Mallbris, L. Wei, T. et al. *Vitamin D treatment upregulates the antimicrobial protein hCAP18/ILL-37 on atopic dermatitis*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 53.

13. Hata, T.R., Jackson, M., Nguyen, M., Udall, D., Paik, A., Kotol, P., Gallo, R. *Rescue of diminished cathelicidin antimicrobial peptide expression in subjects with atopic dermatitis by administration of oral vitamin D.* J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 368.

14. Jeong, S., Bae, J., Kwon, M., Kim, H., Lee, S. *Newly synthesized molecule, K6-L19, increased antimicrobial peptides (AMPs) expression in cultured keratinocyte and murine skin.* J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 652.

15. Jeong, S., Bae, J., Kwon, M., Kim, H., Lee, S. *Effect of K6-L19, antimicrobial peptides (AMPs) augmenting molecule, in skin barrier function.* J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 653.

16. Sugerman, J.L., Parish, L.J. *A topical physiologic lipid-based, barrier repair formulation (Epiceram™ cream) is highly-effective monotherapy for moderate-to-severe pediatric atopic dermatitis: A multicenter, investigator-blinded trial comparing a barrier repair formulation, Epiceram™, to fluticasone proprionate (Cutivate®) cream*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 319.

17. Simpson, E.L., Berry, T., Tofte, S., Hanifin, J., Eichenfield, L. *Epiceram for the treatment of mild to moderate atopic dermatitis – A pilot study*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 462.

18. Takeo-Yamaguchi, J., Nakamura, F., Aihara, M. et al. *Semaphorin3A alleviates skin lesions and scratching behavior in NC/Nga mice, an atopic dermatitis model*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 47.

19. Mizukawa, Y., Yamazaki, Y., Shiohara, T. *IgE preferentially protects female mice against hapten-induced immunopathology.* J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 1052.

20. Na, K., Jeon, M., Kim, T. *Prevention of atopic dermatitis by pretreatment of phosphodiester-CpG-ODN in mice.* J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 1045.

21. Kim, J., Kim, K. *Effects of orally administered Actinidia arguta extract on 2-chloro-1,3,5-trinitrobenzene (TNCB)-induced atopic dermatitis-like skin lesions in NC/Nga mouse*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 1049.

22. Terakawa, M., Tomimori, Y., Muto, T. et al. *Oral chymase inhibitor SUN13834 ameliorates skin inflammation and pruritus in a 5-week mouse model for atopic dermatitis*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 44.

23. Phan, J., Becker, T., Liu, P., Modlin, R.L., Kim, J. *Propionibacterium acnes induces proinflammatory cytokines and antimicrobial peptides in skin-derived dermal cells*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 1118.

24. Kim, J., Ochoa, M.T., Krutzik, S.R. et al. *Activation of toll-like receptor 2 in acne triggers inflammatory cytokine responses*. J Immunol 2002, 169(3): 1535-41.

25. Rivier, M., Mauvais, P., Boiteau, J., Clary, L., Jomard, A. *Selective PPARgamma agonists but not antagonists decrease sebaceous gland size in the Fuzzy rats*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 884.

26. Jomard, A., Feraille, G., Clary, L., Boiteau, J., Rivier, M. *Selective PPARrgamma agonists antagonize DHT-induced effect on sebaceous glands in the Fuzzy rat*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 886.

27. Shiraishi, N., Kabashima, K., Koga, Y., Tokura, Y. *Prostaglandin E2-EP3 signaling, as a negative regulator of skin immune responses by suppressing cutaneous dendritic cell functions*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 39.

28. Honda, T., Matsuoka, T., Miyachi, Y., Narumiya, S. *Prostaglandin E2-EP3 signaling suppress skin inflammation by inhibiting keratinocyte activation in mouse contact allergy*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 974.

29. Lévèque, M., Castex-Rizzi, N., Charvéron, M. *Potential anti-inflammatory properties of a new undecyl-rhamnoside on human keratinocytes*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 137.

30. Urosevic, M., Dreno, B., Assaf, C. et al. *Adenoviral gene transfer of human interferon-gamma gene is safe and efficacious for patients with primary cutaneous lymphomas*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 328.

31. Urosevic, M., Fujii, K., Calmels, B., Laine, E., Acres, B., Dummer, R. *Response to adenoviral vector participates in the regression of cutaneous lymphoma lesions following adenovirus-mediated interferon-gamma gene transfer*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 439.

32. Kim, Y., Forero-Torres, A., Foss, F., Olsen, E., Pinter-Brown, L., Duvic, M. *Responses to oral forodesine in refractory cutaneous T-cell lymphoma (CTCL): Final results of a phaseI/II study.* J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 353.

33. Querfeld, C., Rosen, S.T., Guitart, J. et al. *Results of a multicenter phase II trial of temozolomide in patients with advanced MF/SS*. J Invest Dermatol [Int Invest Dermatol (May 14-17, Kyoto) 2008] 2008, 128(Suppl. 1): Abst 446.