40th Annual Meeting of the **European Society for Dermatological Research**

08-11 September 2010, Helsinki, Finland

Abstract Table of Contents

Square brackets beside poster numbers denote [ORAL] Presentations: [001-026] are Plenary, [027-113] Concurrent

JOURNAL OF INVESTIGATIVE DERMATOLOGY

www.jidonline.org

The *Journal of Investigative Dermatology (JID)* is published by Nature Publishing Group, a division of Macmillan Publishers Ltd on behalf of the Society for Investigative Dermatology.

SCOPE

The Journal of Investigative Dermatology is published monthly in print and online. The journal provides an international forum for the publication of high-quality, original articles. *JID* features information on all aspects of cutaneous biology and skin disease.

This journal is covered by Adonis, BIOSIS, CAB Abstracts, Chemical Abstracts Databases, Current Contents/Clinical Medicine, Current Contents/Life Sciences, Derwent Journals Abstracted, EBSCO, Embase/Excerpta Medica, Global Health, Index Medicus/MEDLINE, International Pharmaceutical Abstracts, PASCAL, Reference Update, Science Citation Index, SciSearch/SCI Expanded, Sociedad Iberoamericana de Información Científica (SIIC) Database.

EDITORIAL

All correspondence should be addressed to: Elizabeth Blalock, Managing Editor for The *Journal of Investigative Dermatology*, 920B Martin Luther King Jr. Blvd., Suite 216, Chapel Hill, NC 27514. Tel: +1 919 843 3094. Fax: +1 866 929 4601. E-mail: JIDoffice@sidnet.org. All manuscripts should be submitted online at: http://jid.manuscriptcentral.com.

PUBLISHER

All business correspondence and inquiries should be addressed to:
The *Journal of Investigative Dermatology*, Nature Publishing Group,
75 Varick Street, 9th Floor, New York, NY 10013-1917.
Tel: +1 212 726 9214. Fax: +1 646 563 7057.
Publishing Manager: Steven Ottogalli
Production Editor: Faith Hill

SOCIETY

For information, contact the Society for Investigative Dermatology at: sid@sidnet.org or the European Society for Dermatological Research at office@esdr.org. Detailed instructions to authors are available at the journal website (www.jidonline.org) and in print in the first issue of the year.

2010 SUBSCRIPTIONS

INSTITUTIONAL SUBSCRIPTIONS

New institutional policy: NPG has moved to a site license policy for institutional online access, using prices based on Full-Time Equivalents (FTE) or Research and Development (R&D) staff. Institutions may also purchase a separate print subscription.

Subscribing to a site license: Contact your local sales representative for a tailored price quote for your institution. You will be required to complete a NPG site license agreement. More information, contact details and FTE/R&D definitions are available at http://npg.nature.com/libraries.

Institutional print subscriptions: Orders can be placed with your regular subscription agent or through NPG—either online or by contacting our customer service department. Prices are as follows (excluding Japan): The Americas $998.00, Europe €1229.00, UK/Rest of World £793.00. For prices applicable in Japan, please contact: institutions@naturejpn.com.

PERSONAL SUBSCRIPTIONS

Personal customers who pay by personal check or credit card receive a combined print plus online subscription. Prices are as follows: The Americas $682.00, Europe €863.00, UK/Rest of World £557.00

CONTACT INFORMATION

SITE LICENSES

The Americas: Tel: +1 800 221 2123. Fax: +1 212 689 9711. E-mail: institutions@us.nature.com

Asia Pacific (excluding South Asia, Australia and New Zealand): Tel: +81 3 3267 8769. Fax: +81 3 3267 8746. E-mail: institutions@naturejpn.com

Australia and New Zealand: Tel: +61 3 9825 1160. Fax: +61 3 9825 1010. E-mail: nature@macmillan.com.au

India: E-mail: npgindia@nature.com

The rest of the world: Tel: +44 (0) 20 7843 4759. Fax: +44 (0) 20 7843 4998. E-mail: institutions@nature.com

PRINT SUBSCRIPTIONS (including single-issue purchases)

All customers (excluding Japan, Korea and China): Customer Service Department, Nature Publishing Group, Houndmills, Basingstoke, Hants, RG21 6XS, UK. Tel: +44 (0) 1256 329 242. Fax: +44 (0) 1256 812 358. E-mail: subscriptions@nature.com

Japan, Korea and China: NPG Nature Asia-Pacific, Chiyoda Building, 2-37, Ichigayatamachi, Shinjuku-ku, Tokyo 162-0843, Japan.
Tel: +81 3 3267 8751. Fax: +81 3 3267 8746. E-mail: institutions@naturejpn.com

Prices are applicable in the following regions: US dollars ($) for North, Central, South America and Canada; Euros (€) for all European countries (excluding the UK); Yen (¥) for Japan; Sterling (£) for UK and rest of world. Please ensure you use the appropriate currency. All prices, specifications and details are subject to change without prior notification. Single issues of The *Journal of Investigative Dermatology* are available.

Advertising: Inquiries concerning print and web advertisements should be addressed to: Alf Anderson, Advertising Manager. Tel: +1 617 475 9231. Fax: +1 617 494 4960; E-mail: a.anderson@us.nature.com

Supplements: Inquiries concerning supplements should be addressed to: Michelle Libby, Commercial Projects Executive. Tel: +1 617 475 9230. Fax: +1 617 494 4960; E-mail: m.libby@us.nature.com

Reprints and permissions: For reprints or production rights, please go to http://www.nature.com/reprints

ISSN 0022-202X EISSN 1523-1747

Printed on acid-free paper, effective with Volume 126, Issue 1, 2006

Printed and bound in the US by Sheridan Press, Hanover, PA, US.

The *Journal of Investigative Dermatology* (ISSN: 0022-202X) is published monthly by Nature Publishing Group, 75 Varick Street, 9th Floor, New York, NY 10013-1917. Periodicals postage paid at New York, NY, and at additional mailing post offices.

POSTMASTER: send address changes to The *Journal of Investigative Dermatology*, Nature Publishing Group, 342 Broadway PMB 301, New York, NY 10013-3910.

349

An appraisal of oral retinoids in the treatment of pachyonychia congenita

Robert Gruber[1], Roger L Kaspar[2], Sancy A Leachman[3], Michael Edlinger[4], Matthias Schmuth[1] *[1]Department of Dermatology, Innsbruck Medical University, Innsbruck, Austria, [2]TransDerm, Inc., Santa Cruz, California, United States, [3]Department of Dermatology, Huntsman Cancer Institute, University of Utah, Salt Lake City, Utah, United States, [4]Department of Medical Statistics, Informatics and Health Economics, Innsbruck Medical University, Innsbruck, Austria*

Pachyonychia congenita (PC), a rare autosomal-dominant keratin disorder caused by mutations in keratin (KRT) genes *KRT6A/B*, *KRT16* or *KRT17*, is characterised by painful plantar keratoderma and hypertrophic nail dystrophy. Available studies assessing oral retinoid treatment for PC are limited to a few case reports and case series. In a questionnaire-based retrospective cross-sectional survey of 30 genotyped PC-patients on oral retinoids at doses between 10 to 50 mg/day for 0,5 to 240 months, we here determined clinical score, visual analog pain scale (VAS) and side effects. 50% of patients reported that treatment was effective and plantar hyperkeratoses had improved. Only 14% observed an amelioration of their pachyonychia. While 33% experienced decreased plantar pain, 27% reported increased pain with oral retinoid treatment. All patients experienced adverse effects, most commonly dry lips, eyes and skin. A risk/benefit analysis favoured lower retinoid doses of ≤25 mg/d (significant mean overall satisfaction score) for more than 5 months, compared to higher doses of >25 mg/d for a shorter time. Acitretin was slightly more effective than isotretinoin in terms of overall change in calluses. In summary, therapy with oral retinoids at doses of ≤25 mg/d for greater than 5 months is superior to higher doses, shorter treatment duration or no therapy in PC. Further prospective studies are needed to confirm these findings.

350

Treatment of refractory melasma with combination of topical 5% magnesium ascorbyl phosphate and fluorescent pulsed light in Asian patients

Zafar Shaikh, Dilawar Abbas, Ashar Ahmed *Army Medical College / National University of Sciences & Technology (NUST), Rawalpindi, Pakistan*

The conventional therapies for melasma are often unsatisfactory because of inadequate response and recurrence following cessation of treatment.This study was designed to determine the effectiveness of treating melasma with combination of topical 5% Magnesium Ascorbyl Phosphate(MAP) and Fluorescent Pulsed Light(FPL). Patients with refractory epidermal and mixed melasma were treated for 12 weeks with topical application of 5% MAP at night, and 3 sessions of FPL(570-950nm) at 3, 6, and 9 weeks (fluence 12-14J/cm^2, pulse width 12-15msec, pulse repetition rate 2/3Hz, spot size 3cm^2). Post-treatment follow up was continued for another 12 weeks. Sunscreen (SPF-60) was prescribed throughout period of observation. Determination of treatment efficacy was based on the Melasma Area and Severity Index (MASI), calculated at beginning and then at weeks 6, 12, and 24. The subjective assessment was done by comparing pre and post-treatment photographs by an independent observer and self-assessment by patients at 12th week; using a 4-point scoring scale (1-poor, 2-fair, and 3-good, 4-excellent). Sixty five patients completed the study. The baseline mean MASI score of 14.80 decreased to 4.53 at 12th week (end of treatment), and 6.35 at 24th week (end of follow up). The overall regression of MASI at these end-points was 69.3% and 57% (p<.001). The pre and post treatment photographic evaluation by independent observer and patients' self-assessment at 12th week showed good to excellent response (scores 3 & 4) in 52.3% and 44.6% cases respectively. The combination of 5% MAP and Fluorescent Pulsed Light could be an effective modality in treating refractory melasma in Asian patients.

351

A novel fibronectin derived peptide (P12) limits skin necrosis when delivered iv within 2 hours after burn in swine

Richard Clark, Fubao Lin, Deddy Harsono, Marcia Tonnesen, Adam Singer *Stony Brook University, Stony Brook, NY, United States*

Skin burn injury progresses over several days secondary to continuing tissue cell necrosis and apoptosis. Fibronectin, a 500 kDa glycoprotein, is produced on-demand by most tissue cells during embryogenesis, morphogenesis and wound healing to become a critical component of the provisional extracellular matrix and is deficient in chronic wounds and burn patients. Last year we reported that a 14mer, growth factor-binding peptide (P12) derived from the first fibronectin type III repeat enhanced adult human dermal fibroblast (AHDF) growth and protected AHDF from necrosis and apoptosis secondary to oxidative and cytokine stress. We also showed that P12 reduced burn progression in a rat comb burn model. Now we demonstrate that P12 also limits progressive skin necrosis in a porcine hot comb model. Burns were created on the backs of outbred, 20-25kg Yorkshire swine using a brass comb preheated in boiling water and applied for 30 seconds resulting in four full thickness burns separated by three unburned interspaces. 20 burns with 60 unburned interspaces were created on each animal. Lactated Ringers (control) or 1, 3 or 10mg/kg P12 were infused intravenously at 1 h (one dose), or 1 h and 24 hrs (two doses) after burn over 30 min using a peristalsis pump. By macroscopic and microscopic analysis, necrosis progressed in 90% of interspaces in controls compared to 40 and 50% of interspaces in animals treated with 1 and 3 mg/kg P12, respectively (P<0.001). One dose was as good as two. These data suggest clinical trials with P12 are warranted.

352

Determining the extent to which clinically effective treatment, ustekinumab or etanercept, reverses the molecular disease profile of psoriatic skin: Comparisons of lesional, non-lesional and normal skin

James Krueger[1], Katherine Li[2], Frédéric Baribaud[2], Mayte Suarez-Farinas[1], Carrie Brodmerkel[2] *[1]Rockefeller University, New York, New York, United States, [2]Centocor Research and Development, Inc., Malvern, Pennsylvania, United States*

ACCEPT, a randomized, active-controlled study, compared the efficacy of etanercept and ustekinumab in 903 patients with moderate-to-severe plaque psoriasis through wk12. Skin biopsies were performed in a subset of patients at baseline, wks1 and 12. Microarray analyses (Affymetrix U133+2 array) comparing non-lesional skin (n=85) to lesional skin (n=85) at baseline showed several thousand probe sets differentially expressed (>2-fold change FDR, p<0.05) in lesional skin. An additional 25 healthy skin biopsies were also analyzed. Comparison of nonlesional skin to healthy normal skin showed a series of lesional genes also dysregulated in non-lesional skin (DEFB4, S100A7A, CCL18, SERPINB3). Analyses to understand the impact of p40 cytokine (IL-12/IL-23) or TNF-alpha blockade on resident and inflammatory cells and on the expression of gene circuits that may drive chronic immune activation and inflammation in the skin were completed. In addition analyses to understand the residual molecular profile or „molecular scar" following 12 weeks of treatment were completed. Patients responding to each agent (>=PASI75, n=21 for etanercept, n=19 ustekinumab) had significant changes in ~4000 transcripts compared to untreated lesions, indicating significant resolution of pathological gene circuits back to nonlesional levels. However, genes such as DEFB4, S100A7, CCL18 and SERPINB3 though reduced to levels similar to non-lesional skin were not reduced to that of healthy normal skin by either treatment unlike ADAM10 and HSD3B1. Elucidation of the molecular pathways which remain dysregulated following effective treatment may provide insight into pathological mechanisms that remain active despite appearance of clinical and histologic resolution.

353

Augmentation of Lipogenesis and Steroidogenesis-related Enzyme Expression by Gefitinib in Sebaceous Gland Cells *in vitro*

Akira Ito[1], Kenta Yoshida[1], Noriko Akimoto[1], Shin Ohta[2], Masato Wakabayashi[3], Kazuyoshi Nakazawa[3], Ichiro Kurokawa[4], Takashi Sato[1] *[1]Dept of Biochemistry & Molecular Biol, Tokyo Univ of Pharmacy & Life Sciences, Hachioji, Tokyo, Japan, [2]Dept of Pharma Health Care & Sciences, Tokyo Univ of Pharm & Life Sciences, Hachioji, Tokyo, Japan, [3]Dept of Pharma, Nagano Red Cross Hospital, Nagano, Nagano, Japan, [4]Dept of Dermatology, Mie Univ Grad School of Medicine, Tsu, Mie, Japan*

A small-molecule tyrosine kinase inhibitor, gefitinib, which targets the ligand-binding domain of epidermal growth factor (EGF) receptors, exhibits anti-tumorigenic activity in patients with advanced non-small cell lung cancer. Many patients treated with gefitinib develop an acne-like rash on the face and upper body, most likely related to keratinocyte alterations, and hair follicle proliferation and maturation. Although acne is characterized as a functional disorder in sebaceous glands and pilosebaceous units, e.g., excess sebum production, accumulation, and secretion, there have been no reports to date that gefitinib may modulate sebum production in sebaceous glands. In the present study, therefore, we examined whether or not gefitinib directly influenced EGF-mediated cell proliferation, sebum production, and steroidogenesis in hamster and human sebocytes *in vitro*. Western blot analysis showed that EGF receptors were constitutively detectable in hamster sebocytes. In addition, gefitinib was found to dose-dependently inhibit the EGF-mediated sebocyte proliferation. Furthermore, nile-red staining revealed that intracellular lipid-droplet formation was augmented by gefitinib in both hamster and human sebocytes. Moreover, real-time PCR indicated that gefitinib increased the gene expression of cytochrome P450 cholesterol side-chain cleavage enzyme (P450scc) and 5α-reductase in both sebocytes. These results provide novel evidence that gefitinib directly facilitates sebum production along with the augmented gene expression of P450scc and 5α-reductase in sebocytes. These findings are likely to increase the clinical understanding of the side effects of gefitinib.

354

Quantitative and objective area extraction of tinea unguium

Yasuki Hata[1], Hitoshi Iyatomi[2], Sumiko Ishizaki[3], Mizuki Sawada[3], Ken Kobayashi[3], Masahiko Ozeki[3], Masaru Tanaka[3] *[1]Division of Dermatology, Saiseikai Yokohamashi Tobu Hospital, Yokohama-city, Kanagawa, Japan, [2]Department of Applied Informatics, Hosei University, Koganei-city, Tokyo, Japan, [3]Department of Dermatology, Tokyo Women's Medical University Medical Center East, Arakawa-ku, Tokyo, Japan*

Quantitative and objective evaluation of tinea unguium would be helpful for drug efficacy assessments. The aims of this study are to provide a quantitative assessment of the tinea unguium determined by dermatologists and to develop a computer-based quantification method of lesions. We examined a total of 38 clinical images of tinea unguium taken by a digital camera with polarized filters. The six images were clinically easy to identify the lesion areas while the others were rather difficult. The lesions were determined based on color information with the "location mask", which was generated based on a priori knowledge: nail is located near the border of finger and has an ellipse shape. Since the deviation in lesion area determined among dermatologists was large, we needed to define a gold standard for each image for evaluation of the proposed method. Five dermatologists manually drew the border of each lesion with a tablet computer. After an assessment of the extraction by dermatologists, the gold standard was defined as the area that was selected by two or more dermatologists, since the standard deviation of dermatologists' extraction were quite large (28.4%). Our method achieved a precision and recall score of 84.3% and 74.7%, respectively for the 6 clear cases and similarly, 63.8% and 58.3%, respectively for the total 38 cases. Our preliminary method determined the lesions almost accurately for relatively easy cases. Although our preliminary method needs further investigation, we confirmed a computer-based method has the capability to quantize the area of tinea unguium.