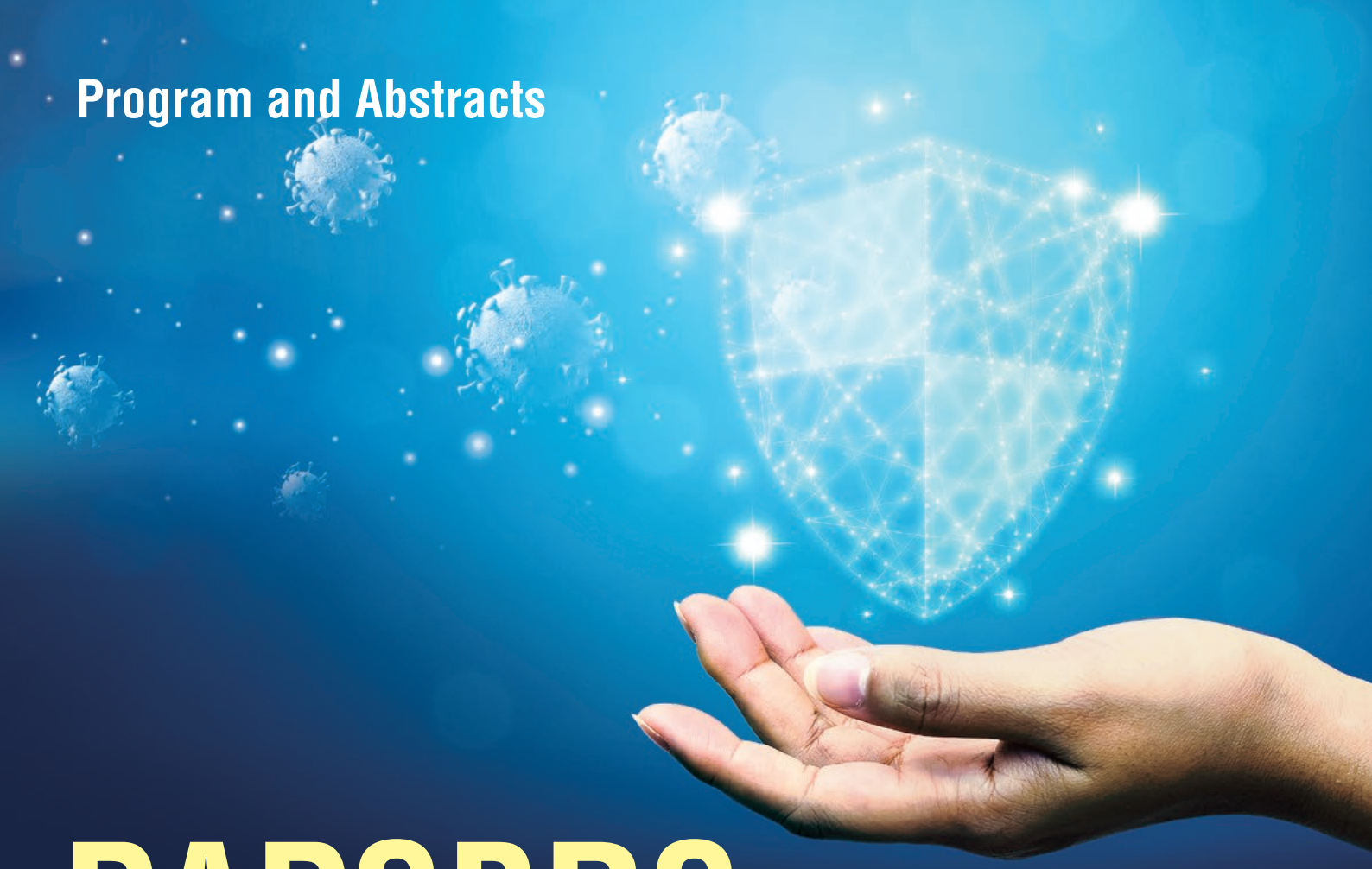
Program and Abstracts



PAPSBRS

The 11th Annual Congress of Pan Asian-Pacific Skin Barrier Research Society

ISID 2023 Tokyo Satellite Symposium

Date : **May 10 (Wed), 2023 / 12:00-14:45**

Venue : **Harmony, 44F Keio Plaza Hotel, Tokyo**

President :

Yutaka Hatano, M.D., Ph.D. Department of Dermatology, Faculty of Medicine, Oita University

Vice-President :

Yutaka Takagi, Ph.D. Faculty of Pharmaceutical Sciences, Josai University

Secretary-General & Society Secretariat :

Takashi Sakai, M.D., Ph.D. Department of Dermatology, Faculty of Medicine, Oita University

The 11th Annual Congress of Pan Asian-Pacific Skin Barrier Research Society (PAPSBRS)

Luncheon Special Lecture

Date：Wednesday, May 10, 2023 / 12:05-12:50
Venue：Harmony, 44F Keio Plaza Hotel Tokyo
2-2-1 Nishi-Shinjuku, Shinjuku-Ku, Tokyo 160-8330

Theme

Skin permeability barrier formation by ceramides

Chair

Dr. Toshifumi Nomura
Professor and Chair, Department of Dermatology,
Institute of Medicine, University of Tsukuba

Speaker

Dr. Akio Kihara
Professor, Faculty of Pharmaceutical Sciences,
Hokkaido University

Co-sponsored: The 11th Annual Congress of Pan Asian-Pacific Skin Barrier Research Society (PAPSBRS)
Sanofi K.K.

sanofi

President of Pan-Asian Pacific Skin Barrier Society (PAPSBARS)

President: Mao-Qiang Man (Dermatology Service Veterans Affairs Medical Center, Department of Dermatology, University of California, San Francisco, USA; Dermatology Hospital of Southern Medical University, China)

Honorary President: Seung H. Lee

Honorary President: Peter M. Elias

International board members and contributors for conference programming

Eung Ho Choi (President of Korean Society for Investigative Dermatology; Yonsei University Wonju College of Medicine, Korea)
John Common (President of Skin Research Society of Singapore; A*STAR Skin Research Labs, Singapore)
Li He (Kunming Medical University, China)
Haekwang Lee (President of Korean Society for Skin Barrier Research; P&K Skin Research Center, Korea)
Hyun-Jung Kim (Chairperson of Korean Society for Skin Barrier Research; Chungnam National University, Korea)
Sekyoo Jeong (Vice president of Korean Society for Skin Barrier Research; Incospharm Corp, Korea)
Chih-Hung Lee (Kaohsiung Chang Gung Memorial Hospital, Taiwan)
Tzu-Kai Lin (Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Taiwan)
Jason M. Meyer (Vanderbilt University Medical Center, USA)
Tingting Zhu (Soochow University, China)

Organizing and host program committee members in the 11th PAPSBARS

President: Yutaka Hatano (Oita University, Japan)
Vice president: Yutaka Takagi (Josai University, Japan)
Secretary general: Takashi Sakai (Oita University, Japan)

Masashi Akiyama (Nagoya University, Japan)
Akemi Ishida-Yamamoto (Asahikawa Medical University, Japan)
Akiharu Kubo (Kobe University, Japan)
Shin Morizane (Okayama University, Japan)
Toshifumi Nomura (University of Tsukuba, Japan)
Yasuko Obata (Hoshi University, Japan)
Shigetoshi Sano (Koch University, Japan)
Yoshikazu Uchida (Hallym University, Korea)

Please note that registration for ISID2023 is mandatory for participation in the 11th PAPSBRS.

WELCOME

President of PAPSBRS: Mao-Qiang Man (Dermatology Service Veterans Affairs Medical Center, Department of Dermatology, University of California, San Francisco, USA; Dermatology Hospital of Southern Medical University, China)

Dear Colleagues

More and more evidence has shown the crucial role of epidermal permeability barrier function in regulation of cutaneous and extracutaneous function. Epidermal dysfunction contributes, at least in part, to the development of inflammatory skin disorders and some systemic disorders. Understanding the underlying mechanisms and the efficacy of products that regulate epidermal permeability barrier will advance the development of approaches in the management of epidermal permeability barrier dysfunction and its associated disorders. In these aspects, much progress has been made over the recent years. We all know that meeting provides an incomparable opportunity for scientists to exchange information in their research, in addition to meeting their old friend and making new ones. However, we have missed three annual meetings due to the COVID pandemic. Finally, we have this opportunity to meet again at the 11th annual meeting of Pan-Asian Pacific Skin Barrier Research Society (PAPSBRS) in Tokyo, Japan.

On behalf of the PAPSBRS, it is with great pleasure that I welcome you to enjoy the exciting meeting and beautiful scenery on May 10, 2023, in Tokyo. Also, I would like to express my sincere appreciation to the members of meeting organizing committee, especially professor Yutaka Hatano at Oita University, for their efforts in organizing this event. I am extremely grateful to the speakers for their generosity and willingness to share their work with us at the meeting. I am very thankful to attendees for their participation.

Once again, I sincerely welcome you to the 11th PAPSBRS meeting. I hope you will enjoy both the scientific program and scenery of Tokyo, and appreciate the opportunity to connect with friends.

Sincerely yours,

Mao-Qiang Man, MD.
The president of PAPSBRS

WELCOME

President of the 11th PAPSBARS: Yutaka Hatano (Oita University, Japan)

Dear Friends and Colleagues,

It is my great pleasure to welcome you to the 11th Annual Congress of the Pan Asian–Pacific Skin Barrier Research Society (PAPSBRS) on May 10, 2023, in Tokyo. In fact, this conference was scheduled to be held in Nagoya in December 2020, as a satellite of the 45th Annual Meeting of the Japanese Society for Investigative Dermatology. However, we decided to cancel the event because we considered that the purpose of the conference was to be a platform for colleagues, researchers, and friends to meet face-to-face to share our academic research and enjoy being among friends. Thanks to plenty of encouragement, contributions, and help from our friends and colleagues, we decided to hold this conference and finally get together in Tokyo to discuss science and renew our connections. Although the conference is much smaller than it used to be, we can look forward to hearing interesting lectures regarding important scientific topics. These lectures reflect that skin barrier function research covers a wide range of areas such as permeability, antibacterial properties, and immunity and is closely related to various physiological phenomena, including itch, inflammation, and immunity, among others. In addition, understanding skin barrier function improves our understanding of various diseases, and is becoming an important and attractive field for both researchers and clinicians. We hope that all attendees will enjoy the conference and contribute to the development of this field. I also hope that this conference will bring together skin barrier researchers from around the world and serve as an inspiration for young researchers. I would like to express my sincere gratitude to all those who were involved in the preparation of this conference.

Sincerely yours,

Yutaka Hatano, MD, PhD
Professor and Chairman,
Department of Dermatology,
Faculty of Medicine,
Oita University

WELCOME

Vice President of the 11th PAPSBARS: Yutaka Takagi (Josai University, Japan)

Dear Friends and Colleagues

It is a great pleasure to have the 11th Annual Congress of Pan Asian-Pacific Skin Barrier Research Society as ISID 2023 Tokyo Satellite Symposium. I am very happy that we can gather and discuss about skin barrier function with many friends and colleagues from many countries over the COVID-19 disaster.

About 30 years ago, I started to study cutaneous barrier function in Dr. Elias Group. On that time, I belonged to a company and tried to develop and launch skin-care products which enhance cutaneous permeability barrier function. Many people recognized that cutaneous barrier is important and some severe cutaneous disease cause barrier perturbation, however, they believed that most people had healthy barrier function and no need a particular care. Thus, it was quite hard to convince of the importance of taking care of barrier function with skin care materials.

In the last thirty years, various new findings about cutaneous barrier function have been reported by many researchers. The tight junction in the epidermis, the relationship between permeability barrier and immune system, importance of skincare on neonatal period to prevent development of atopic dermatitis, and so on. Of cause, the research about ceramides, one of the crucial factors of barrier function, have made great progress, such as ceramide components are analyzed in detail generally, the metabolism of ceramides becomes clearly including the finding of metabolizing enzymes, and various functions of sphingolipids on cutaneous metabolism have been reported. Accompanied with these findings, the awareness of people about the importance of cutaneous barrier function have been increased and many people worry about their own and family's cutaneous barrier conditions.

Fortunately, I could attend the predecessor meetings of PAPSBRS, Korean Symposium of Skin Barrier Research (KSSBR), 1st annual congress of PAPSBRS in Dalien in China (in this congress, only Prof. Hatano and I were Japanese participants). I am very grad that this PAPSBRS is expanding more and more and there are many exciting presentation and reports on this 11th congress. I believe that all of you will be able to enjoy this congress and connect to further development of your research.

Vice President, Yutaka Takagi, Ph.D.
Professor, Department of Pharmaceutical Sciences
Josai University

WELCOME

International board members and contributors for conference programming: Haekwang Lee (President of Korean Society for Skin Barrier Research; P&K Skin Research Center, Korea)

As a president of Korean Society for Skin Barrier Research, I would like to express my sincere gratitude to Professor Yutaka Hatano, Professor Takashi Sakai, and all the other members of program committee for organizing the 11th Annual Congress of Pan-Asian Pacific Skin Barrier Research Society. During the last a few years, all of us suffered the unprecedented world-wide pandemic situation and missed many academic events, including PAPSBRS. However, this year, with invaluable efforts by Japanese members, we can re-start the congress again and I'm so honored to be able to give a message for this congress. The PAPSBRS congress is not only an academic meeting, but also a great platform for social gathering and networking for barrier research members. It continues to grow up both in quality and numbers of participants, and I am sure that PAPSBRS is a cornerstone event for every skin barrier research member. Now skin barrier function is considered as a keyword for investigative dermatologist and cosmetic researchers, and we will keep our best efforts to make this event being open for every participant and, most of all, to stimulate the research for skin barrier function. Again, I would to appreciate all of the program committee members for their efforts and sincerely hope that all of the participants can enjoy this event.

Haekwang Lee
President of Korean Society for Skin Barrier Research; P&K Skin Research Center, Korea

WELCOME

International broad members and contributors for conference programming: John Common (President of Skin Research Society of Singapore; A*STAR Skin Research Labs, Singapore)

It is my great pleasure to give a warm welcome to all the participants of the 11th Annual Congress of the Pan Asia-Pacific Skin Barrier Research Society (PAPSBRS). We are delighted to be hosting another Congress of PAPSBRS after an enforced break during the pandemic, and as the board member representing Singapore, I hope that all the delegates attending enjoy the science and discussions.

This congress provides a unique forum for the Asia-Pacific region, bringing together research scientists, clinician scientists and our colleagues from industry, with a shared interest in skin barrier research. We are continuing to witness a steady growth of interest in the skin as a research system and there are many new and fascinating topics emerging in barrier research that highlights the complexity and intricacy of our connection with the external environment. The PAPSBRS Congress hopes to capitalize on this interest in the skin barrier and provide research lectures that offer up-to-date information with a broad interest and strong lean towards translational research.

Many people have worked very hard to get this PAPSBRS Annual Congress together and I thank them all sincerely for their efforts. We are also very fortunate that the format of the ISID allows for dedicated satellite symposia, providing a fantastic opportunity to get together again, in person, to passionately share our new research on the skin barrier. It would therefore not be possible without the amazing work of the ISID organizers that provide the foundations for all the satellite symposia that are taking place adjunct to the main meeting this year. Singapore is a proud member of the PAPSBRS and we hope that many other members will join us in the future.

John Common
Senior Principal Investigator, A*STAR Skin Research Labs, Singapore
President, Skin Research Society of Singapore
Board member and Singapore representative, PAPSBRS

WELCOME

International board members and contributors for conference programming: Chih-Hung Lee (Professor, Department of Dermatology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan)

A message to the investigators and attendees for the 11th Pan Asian Pacific Skin Barrier Research Symposium (PAPSBRS)

Skin is the largest organ that delineates the boundary between host body and the environment. Skin barrier integrity and its function are vital to the skin homeostasis in different physiological aspects, including immune networks, environmental interactions, neurovascular regulations, and etc. Hence, abnormal skin barrier contributes to the pathophysiological process in a variety of skin diseases, including environmental skin diseases, allergic skin diseases, infections skin disease, and so on. In parallel, as a large reservoir, skin provides a useful model for drug absorption and delivery. These unique features of skin barrier grant the skin barrier research a great platform for the interdisciplinary investigations. With fruitful collaborations and discussions among the investigators and attendees from different disciplines, I am sure the 11th PAPSBRS will be a huge success, not only to foster the collaborations but also to harvest the young investigators.

Chih-Hung Lee, MD, PhD
Professor, Department of Dermatology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan

WELCOME

International board members and contributors for conference programming: Jason M. Meyer (Vanderbilt University Medical Center, USA)

Message for the 11th Annual Pan Asian-Pacific Skin Barrier Research Society (PAPSBARS) Symposium

Dear Colleagues and Friends,

I am honored to accept an invitation to share my research at the 11th Annual Pan Asian-Pacific Skin Barrier Research Society Symposium. My interest in the skin barrier stems from my clinical work as a dermatologist and my laboratory research on skin barrier formation. Recently, I have contributed to a research project with Dr. Alan Brash at Vanderbilt University to study the enzymatic activity of PNPLA1, a protein that is essential for skin barrier function via its role in ceramide and fatty acid metabolism. I hope you will find this research project as interesting and enjoyable as I have.

This project is part of a larger research effort carried out by many investigators across the world to define the molecular basis of skin barrier function (and dysfunction). My former postdoctoral mentor, Dr. Peter Elias, told me a few years ago that there has never been a better time to be involved in skin barrier research, based on a decades-long solid foundation plus a promising future with many opportunities for applications to medicine and industry. This 11th PAPSBARS Symposium promises to provide an engaging snapshot of the current field, with representatives from across the world and from diverse backgrounds and areas of expertise. I am very excited to be part of this symposium, and I'm looking forward to my first trip to Japan, to seeing old friends and making new acquaintances. See you soon in Tokyo!

Sincerely,

Jason Meyer, MD, PhD
Instructor and Attending Physician
Vanderbilt Dermatology
Nashville VA Medical Center
Nashville, TN, USA

Schedule and Program of The 11th Annual Congress of Pan Asian-Pacific Skin Barrier Research Society (PAPSBRS)

Date: May 10, 2023

Venue: KEIO PLAZA HOTEL TOKYO (room: Harmony 44F)

10:00-11:00 **Business meeting** (room: Comet 43F)

12:00-12:03 **Opening remarks:**

Yutaka Hatano (President of the 11th PAPSBARS; Oita University, Japan)

12:05-12:50 **Luncheon Special Lecture** (Lecture 40min; Q&A 5min.) *sponsored by Sanofi K.K.

Title: Skin permeability barrier formation by ceramides

Speaker: Akio Kihara (Hokkaido University, Japan)

Chair: Toshifumi Nomura (University of Tsukuba, Japan)

Short Break

12:53-13:11 **Lecture 1** (Presentation 15min. Q&A 3min.)

Title: Purified recombinant PNPLA1 catalyzes the synthesis of acylceramides and acylacids of the mammalian skin barrier

Speaker: Jason M. Meyer (Vanderbilt University Medical Center, USA)

Chair: Matthias Schmuth (Medical University Innsbruck, Austria)

13:11-13:29 **Lecture 2** (Presentation 15min. Q&A 3min.)

Title: Antimicrobial peptides enhance skin barrier function: therapeutic implications in atopic dermatitis

Speaker: François Niyonsaba (Juntendo University, Japan)

Chair: Shin Morizane (Okayama University, Japan)

13:29-13:47 **Lecture 3** (Presentation 15min. Q&A 3min.)

Title: Topical autophagy activator enhances the epidermal permeability barrier function through SIRT1-mediated ceramide synthesis

Speaker: Sekyoo Jeong (Incospharm Corp, Korea)

Chair: Haekwang Lee (P&K Skin Research Center, Korea)

Short Break

13:50-14:08 **Lecture 4** (Presentation 15min. Q&A 3min.)

Title: Laser-mediated drug delivery to overcome the skin permeation barrier

Speaker: Jia-You Fang (Chang Gung University, Taiwan)

Chair: Chih-Hung Lee (Kaohsiung Chang Gung Memorial Hospital, Taiwan)

14:08-14:26 **Lecture 5** (Presentation 15min. Q&A 3min.)

Title: Skin physiology related changes associated with natural moisturising factors in the stratum corneum

Speaker: Stephen Wearne (A*STAR Skin Research Labs, Singapore)

Chair: Koh Li Fang (A*STAR Skin Research Labs, Singapore)

14:26-14:44 **Lecture 6** (Presentation 15min. Q&A 3min.)

Title: Molecular insight of topical emollient on the development of atopic dermatitis and atopic march in a mice model

Speaker: Jiayi Zhang (Shanghai Jiao Tong University, China)

Chair: Li He (Kunming Medical University, China)

14:44-14:45 **Closing Remarks:**

Yutaka Takagi (Vice president of the 11th PAPSBARS; Josai University, Japan)

12:05-12:50 **Luncheon Special Lecture** (Lecture 40min; Q&A 5min.) *sponsored by Sanofi K.K.
Skin permeability barrier formation by ceramides
Speaker: Akio Kihara (Hokkaido University, Japan)
Chair: Toshifumi Nomura (University of Tsukuba, Japan)

Skin permeability barrier formation by ceramides

Akio Kihara, PhD

Faculty of Pharmaceutical Sciences, Hokkaido University

Ceramides play an essential role in the formation of the skin permeability barrier. The stratum corneum contains a wide variety of ceramides, as we recently reported the presence of 23 classes and 1,581 species of ceramides. Ceramides are classified into free and protein-bound ceramides, and the free ceramides are further classified into non-acylated ceramides and acylceramides. The stratum corneum has two structures important for the skin barrier: lipid lamellae and corneocyte lipid envelope (CLE). Free and protein-bound ceramides are major components of lipid lamellae and CLE, respectively. Decreased ceramide levels and altered class composition are observed in atopic dermatitis patients. Mutations in genes involved in the synthesis of acylceramides or protein-bound ceramides cause congenital ichthyosis. We have identified several acylceramide synthesis genes (*ELOVL1, CYP4F22, PNPLA1, FATP4, and ABHD5*). In this seminar, I will describe the molecular mechanisms that produce diverse ceramides, ceramide measurement techniques, and the physiological and pathological functions of ceramides/acylceramides.

Education:

1993 Bachelor of Science in Chemistry; Department of Science, Kyoto University
1995 Master of Science in Chemistry; Graduate School of Science, Kyoto University
1998 Ph. D. in Science; Graduate School of Science, Kyoto University

Research Experience:

1998–1999 Postdoctoral Research Fellow, Japan Society for the Promotion of Science, Kyoto University
1999–2000 Postdoctoral Research Fellow, Japan Society for the Promotion of Science, National Institute for Basic Biology, Okazaki, Japan
2001–2004 Research Associate, Graduate School of Pharmaceutical Sciences, Hokkaido University
2005–2007 Assistant Professor, Faculty of Pharmaceutical Sciences, Hokkaido University
2007–2008 Associate Professor, Faculty of Pharmaceutical Sciences, Hokkaido University
2008–present Professor, Faculty of Pharmaceutical Sciences, Hokkaido University
2021–present Dean, Faculty of Pharmaceutical Sciences, Hokkaido University

12:53-13:11 **Lecture 1** (Presentation 15min. Q&A 3min.)

Purified recombinant PNPLA1 catalyzes the synthesis of acylceramides and acylacids of the mammalian skin barrier

Speaker: Jason M. Meyer (Tennessee Valley Healthcare System, USA)

Chair: Matthias Schmuth (Medical University Innsbruck, Austria)

Purified recombinant PNPLA1 catalyzes the synthesis of acylceramides and acylacids of the mammalian skin barrier

(Jason M. Meyer, William E. Boeglin and Alan R. Brash)

Jason M. Meyer, M.D., Ph.D.

Instructor and Attending Physician, Vanderbilt Dermatology, Tennessee Valley Healthcare System, Nashville, TN, USA

Accumulating evidence indicates an essential role of patatin-like phospholipase domain-containing protein 1 (PNPLA1) in the synthesis of esterified omega-hydroxy acylsphingosine (EOS) and related acylceramides and acylacids of the mammalian skin barrier. However, little is known about the enzymatic properties of PNPLA1. We expressed and purified a soluble, truncated form of PNPLA1 in E. coli, along with the related protein PNPLA2 (ATGL, adipose triglyceride lipase), and co-activator CGI-58. Lipid substrates were prepared as micelles or liposomes, incubated with recombinant enzymes for 0.5 – 24 h and products were analyzed by HPLC-UV and LC-MS in comparison to authentic lipid standards. PNPLA1, like ATGL, catalyzed lipolysis and transacylase reactions from triglyceride or diglyceride substrates. These reactions were rapid (1 – 2 h), with quantitative conversion (nmols per reaction) into free fatty acid and glyceride products. Lipolysis products (monoacylglycerol and free fatty acid) were the most abundant species formed in the reactions with ATGL and were increased by co-incubation with CGI-58. PNPLA1 produced more of the transacylase product triacylglycerol compared to ATGL, and triacylglycerol formation was not increased by CGI-58, in contrast to the lipolysis reaction. PNPLA1 and ATGL also transferred acyl groups from glycerides to omega-hydroxy ceramide and omega-hydroxy fatty acid acceptors to form EOS and acyl acid, respectively, albeit in smaller quantities (pmols per reaction). Similar to triacylglycerol formation, EOS and acyl acid production were not stimulated by the addition of CGI-58. PNPLA1 formed EOS more efficiently than ATGL and exhibited a selectivity for the transfer of linoleate over oleate. Triacylglycerol or diacylglycerol were effective as acyl donors, and omega-hydroxy fatty acid, omega-hydroxy ceramide or glucosyl omega-hydroxy ceramide were effective as acceptors. These results support the hypothesis that PNPLA1 is involved in the synthesis of EOS and other acylceramides and acylacids in epidermis via its role as a transacylase and suggest that the enrichment of these lipid pools with linoleic acid could result in part from the substrate selectivity of PNPLA1.

Research experience

My research is focused on the molecular basis of the skin's permeability barrier. I completed my graduate research training in biochemistry under the mentorship of Dr. Deneys van der Westhuyzen at the University of Kentucky, in which I helped characterize a novel pathway of lipoprotein cholesteryl ester uptake in macrophages. After a medical internship and dermatology residency training, I completed postdoctoral research training in the laboratories of Dr. Peter Elias and Dr. Theodora Mauro at the University of California San Francisco. My postdoctoral research was focused on the roles of PNPLA1 and ALOX12B/12R-lipoxygenase in skin barrier formation and helped to identify specific functions of these proteins in lamellar lipid organization and corneocyte lipid envelope formation. I also participated in multiple collaborative studies on skin barrier formation with investigators in the United States and other countries. In 2021, I moved to Vanderbilt as a junior faculty member to collaborate with Dr. Alan Brash on the enzymatic activity of PNPLA1 and the mechanism of lipid envelope formation. This work has shed some light on the enzymatic properties of PNPLA1and given some clues about how PNPLA1 and other proteins contribute to skin barrier formation.

13:11-13:29 **Lecture 2** (Presentation 15min. Q&A 3min.)
Antimicrobial peptides enhance skin barrier function: therapeutic implications in atopic dermatitis
Speaker: François Niyonsaba (Juntendo University, Japan)
Chair: Shin Morizane (Okayama University, Japan)

Antimicrobial peptides enhance skin barrier function: therapeutic implications in atopic dermatitis.

François Niyonsaba, M.D., Ph.D.
Professor, Juntendo University Graduate School of Medicine

The human skin secretes a plethora of antimicrobial/host defense peptides that not only display antimicrobial activities against invading pathogens but also exhibit various immunomodulatory functions, including the cytokine/chemokine production and cell migration, proliferation and differentiation. They also improve angiogenesis, promote wound healing, and suppress inflammation. Among skin-derived antimicrobial peptides, human β-defensins (hBDs), cathelicidin LL-37, S100A7 and antimicrobial peptide derived from insulin-like growth factor-binding protein 5 (AMP-IBP5) enhance the function of both stratum corneum and tight junction (TJ) barriers. In addition, hBD-3 and AMP-IBP5 restore the T helper type 2 (Th2) cytokine-mediated impairment of skin barrier function, implying a possible role of these peptides in the pathogenesis if atopic dermatitis (AD), a skin condition characterized dysfunctional skin barrier, itching and inflammation caused by overproduction of Th2 cytokines. Indeed, both hBD-3 and AMP-IBP5 improved dermatitis-like symptoms, suppressed inflammatory and itch-related cytokines, and improved skin barrier function in AD mice. The ability of AMP-IBP5 to alleviate inflammation and improve skin barrier function in AD mice was abolished in mice treated with an antagonist of the low-density lipoprotein receptor-related protein-1 (LRP1) receptor, while inhibition of the aryl hydrocarbon receptor (AhR) specific antagonist attenuated hBD-3-mediated therapeutic effects in these mice.
We observed that keratinocyte autophagy was restrained in the skin lesions of patients with AD and murine models of AD. Interestingly, hBD-3 and LL-37 induced autophagy activation in keratinocytes through activation of AhR receptor and P2X7 receptor, respectively. While autophagy deficiency impaired epidermal barrier and exacerbated inflammation, administration of hBD-3 attenuated skin inflammation and enhanced the TJ barrier in AD mice through autophagy activation. Importantly, hBD-3-mediated improvement of skin barrier function was abolished in autophagy-deficient AD mice, suggesting a role of antimicrobial peptide-mediated autophagy in regulation of the epidermal barrier and inflammation in AD. Collectively antimicrobial peptides could be used for therapeutic purposes in the treatment of AD through their ability to improve skin barrier function, suppress inflammation and activate keratinocyte autophagy.

Research experience:

François Niyonsaba received his MD in 1994 and Master's degree in Orthopedics (1998) at China Medical University (China). He joined the Department of Biochemistry at Juntendo University Graduate School of Medicine (Japan) and received his PhD in 2003. He was appointed as Instructor (2003), Assistant Professor (2006) and Associate Professor (2007) in the Atopy (Allergy) Research Center at Juntendo University. In 2010, he was assigned as Visiting Associate Professor in the Department of Microbiology and Immunology at the University of British Columbia (Prof R.E.W. Hancock, Canada). In 2015 and 2017, he was respectively promoted to Senior Associate Professor and Full Professor in the Faculty of International Liberal Arts, Juntendo University and became Senior Associate Professor in January 2021 and Full Professor November 2021 in the Atopy (Allergy) Research Center. His numerous awards/honors include the Outstanding Scholar Award, Excellent Young Researchers Overseas Visit Program from the Japan Society for the Promotion of Science, Award for Excellence from the Eastern Asia Dermatology Congress, and Honorary Fellowship of the Asian Academy of Dermatology and Venereology.
His research interests include "Roles of antimicrobial peptides in the skin immunity". He has published more than 100 articles and has more than 20 patents awarded.

13:29-13:47 **Lecture 3** (Presentation 15min. Q&A 3min.)

Topical autophagy activator enhances the epidermal permeability barrier function through SIRT1-mediated ceramide synthesis

Speaker: Sekyoo Jeong (Incospharm Corp, Korea)

Chair: Haekwang Lee (P&K Skin Research Center, Korea)

Topical autophagy activator enhances the epidermal permeability barrier function through SIRT1-mediated ceramide synthesis

Sekyoo Jeong, Ph.D.

Director and CTO, Research Team, Incospharm Corp. Daejeon, Korea. Address: #4, Kukjegwahak0-7-ro, Yuseong-gu, Daejeon, South Korea (ZIP 34000) Contact information: sekyoo.jeong@gamil.com

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Autophagy is an evolutionarily conserved, highly regulated cellular process for self-removal of damaged proteins and organelles, and for the regeneration of cellular energy responding to the nutrient deprivation condition. Recently, autophagy has emerged as a core machinery responsible for maintaining the various skin homeostasis, including epidermal integrity, keratinocyte differentiation, senescence, melanogenesis, and sebogenesis. Previously we have reported that newly synthesized dipeptide derivative (hexacarboxymethyldipeptide-12; HMD-12) stimulated the autophagic flux in epidermal keratinocyte and dermal fibroblast, through the binding of situin 1 (SIRT1) protein, and consequence via deacetylation of forkhead box class O (FOXO) 1. Diversified roles of SIRT1, including stimulating ceramide synthesis in epidermal keratinocytes, prompted us to investigate the potential effects of HMD-12 for epidermal skin barrier function. As results, HMD-12 treated keratinocytes showed increased amount of ceramides production, mainly through the activation of ceramide synthase-2 and -3. Topical application of HDM-12 on healthy human skin further confirmed that relatively-long chain (C22 ~ C26) and even very-long chain (C26-C32) fatty acid-conjugated ceramides are increased in stratum corneum. Acceleration of epidermal barrier restoration after acute skin damage by tape stripping was also observed in clinical study. These results suggest that topical autophagy activator can be used for various skin conditions with skin barrier dysfunction, including atopic dermatitis, psoriasis, and sensitive skin.

Research Experience

Dr. Sekyoo Jeong has been working in skin research field for more than two decades, mostly in private companies. His major area of interest focuses on epidermal permeability barrier function, i.e., how the skin barrier is formed and, once impaired, how the compromised barrier is restored. Sphingolipids biology for ceramides regulation, development of new formulation using ceramides for skin barrier function, and investigation of ceramide-containing formula have been major research themes. He has been working on identifying and evaluating new bioactive molecules for cosmetic and potential pharmaceutical application, including protease-activated receptor (PAR)-2 inhibitor, epidermal anti-microbial peptides (AMPs) synthesis stimulants, epidermal cannabinoid receptor modulating molecules, and autophagy modulating compounds. He is a vice-president of Korean Society for Skin Barrier Research and a member of Korean Society of Investigative Dermatology, Society of Cosmetic Scientists of Korea, and Japanese Investigative Dermatology.

13:50-14:08 **Lecture 4** (Presentation 15min. Q&A 3min.)
Title: Laser-mediated drug delivery to overcome the skin permeation barrier
Speaker: Jia-You Fang (Chang Gung University, Taiwan)
Chair: Chih-Hung Lee (Kaohsiung Chang Gung Memorial Hospital, Taiwan)

Laser-mediated drug delivery to overcome the skin permeation barrier

Jia-You Fang, Ph.D.

Professor. Pharmaceutics Laboratory, Graduate Institute of Natural Products, Chang Gung University, Kweishan, Taoyuan, Taiwan

The laser modality can be used as an effective approach for enhancing drug permeation via the skin. Drug permeation enhancement by lasers allows for more efficacious therapy than passive delivery. The treatment duration of the therapy is possibly shortened. In addition, the applied drug dose can be lowered with less adverse effects. As compared to the other ablation techniques, the laser is capable of controlling the etched depth by energy adjustment in a precise way. Moreover, the skin is exposed by the laser in a non-contact fashion, minimizing the contamination or infection risk. No bio-hazardous waste is produced after the laser application. Laser ablation even sterilizes the entrance to the created pores. Since the superficial ablation of SC or upper epidermis is enough to generate a significant increase in skin absorption, the fluence used for laser-assisted delivery is much lower than that used for cosmetic dermatology or rejuvenation, assuring the safe use of the laser for drug permeation aid. The enhancement mechanisms of laser-assisted drug permeation are the direct ablation of the superficial skin, optical breakdown by a photomechanical wave, and a photothermal effect. This talk describes the development of laser-assisted drug delivery in the recent years. I will systematically introduce the concepts and enhancement mechanisms of the technique, highlighting the potential of the laser approach for increasing drug absorption via the skin. A recent advance of this approach is the use of fractional laser offering limited skin damage and short recovery time. Another sign of progress regarding laser-assisted drug delivery in the recent 5 years is the clinical trials for treating various dermatological disorders. The potential use of the laser-assisted approach affords a novel treatment for topical drug application with significant efficacy. Although many clinical studies have been performed, further studies using a large group for patients are needed to confirm and clarify the findings in the in vitro or animal experiments. The laser-assisted delivery should be optimized to achieve skin targeting without the risk of diffusion into circulation.

Research experience

Over the past 25 years, Prof. Jia-You Fang and his team have made contributions to the understanding of drug delivery, pharmaceutics, pharmacokinetics, nanomedicine, and cosmeceutics. Not only by means of providing academic research in the Pharmaceutics Laboratory of Chang Gung University, but also by the many educational activities for the pharmaceutical, medicinal professionals and trainees, that have expanded the knowledge and management skills that come up from their research, which is extremely translational and oriented toward industrial and clinical practice. Examples of this are the impact of low-energy ablative laser on drug absorption enhancement, a specific technique for assisting drug permeation via skin that emerged from their work, and which is nowadays an attractive enhancement strategy for topical administration. Another example is the passive targeting of nanoparticles to lungs, an area where Dr. Fang and his team have made seminal contributions that have changed the view on the therapy of acute lung injury. Moreover, Dr. Fang and his group have greatly contributed to increase the availability of anti-alopecia drugs for hair follicle targeting, by means of the design of antibody-conjugated lipid nanocarriers. His contributions add up to 310 peer-review articles, more than 10,000 citations and H-index of 61 (Scopus).

14:08-14:26 **Lecture 5** (Presentation 15min. Q&A 3min.)
Skin physiology related changes associated with natural moisturising factors in the stratum corneum
Speaker: Stephen Wearne (A*STAR Skin Research Labs, Singapore)
Chair: Koh Li Fang (A*STAR Skin Research Labs, Singapore)

Skin physiology related changes associated with natural moisturising factors in the stratum corneum

Stephen Wearne, PhD.
Research Fellow, A*STAR Skin Research Labs (A*SRL), A*STAR, Singapore.

Tape stripping of the skin is a non-invasive and efficient method to collect biological material, allowing for analysis of skin barrier function and the microbiome. Until recently, analysis of the skin barrier function through metabolite measurement from tape strips has been a challenge due to the low biomass obtained. In this study, we developed an ultra-high performance liquid chromatography–tandem mass spectrometry (UHPLC-MS-MS) method allowing for both relative and absolute quantification of a targeted panel of metabolites from skin tapes. This panel includes up to 20 amino acids and natural moisturizing factors (NMFs), including the trans and cis isomers of urocanic acid (UCA). Metabolites were extracted with water and formic acid, before separation through an anion-exchange LC column for MS acquisition. The simplicity and reproducibility of this method permits high-throughput analysis of samples even with very low biomass. With this method we analysed samples from a variety of sources including a large Singapore based cohort. From this cohort we observed differences in metabolite profile across varying skin physiological parameters, between sexes but not ethnicity. To further assess this method, we also performed a depth analysis of healthy skin by tape stripping the stratum corneum at various depths to a maximum level of 30 tape strips. Notably, the photo exposed isomer of UCA, cis-UCA, was found at higher levels closer to the stratum corneum surface. This protocol will be utilised to gain further insights on the skin metabolome and probe its dynamic changes with the skin environment.

Research Experience:

I studied Molecular Cell Biology at the University of York (UK), before moving to the University of Nottingham (UK) for my Master's degree which focused on understanding CRISPR-Cas immunity in E.coli. I completed my PhD jointly with the University of Manchester (UK) in the lab of Prof Neil Hanley and at the Institute of Medical Biology (IMB) in A*STAR (Singapore) in Assoc. Prof Ray Dunn's Lab, working on a novel method for the transdifferentiation based generation of pancreatic progenitor cells. Following my PhD, I worked as the project manager for the Asian Skin Microbiome Programme (ASMP), a nascent programme focused on expanding our knowledge of the skin microbiome in Asia. For the past year I have been working as a Research Fellow within Dr. John Common's Lab (A*SRL) in A*STAR. There I have been working on skin barrier and skin microbiome related projects with a specific focus on utilising mass spectrometry-based methods to better understand the metabolome of the skin.

14:26-14:44 **Lecture 6** (Presentation 15min. Q&A 3min.)
Molecular insight of topical emollient on the development of atopic dermatitis and atopic march in a mice model
Speaker: Jiayi Zhang (Shanghai Jiao Tong University, China)
Chair: Li He (Kunming Medical University, China)

Molecular insight of topical emollient on the development of atopic dermatitis and atopic march in a mice model

Jiayi Zhang, undergraduate MD

Dermatologist, Department of Dermatology, Ruijin Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China.

Atopic dermatitis (AD) is usually the initial step of the atopic march. Early intervention aimed at protecting the skin barrier and controlling local and systemic Th2 inflammation may provide a critical opportunity to prevent infants from developing subsequent atopic diseases. Here, we aim to investigate the effect of emollient on atopic march and its mechanism by using a murine model of chronic atopic dermatitis (AD).

Following induction of atopic dermatitis with topical calcipotriol (MC903) and ovalbumin (OVA), one group of mice was treated topically with a linoleic acid-ceramide-containing emollient, while mice without emollient treatment served as controls. Additional group of normal mice served as normal controls. After 28 days, clinical, histological, and transcriptomic analyses were performed in the skin lesions and the lung. Cytokine levels of cytokines were also measured. Treatments of mice with calcipotriol and ovalbumin induced a typical phenotype of AD, accompanied by increased expression levels of Th2 and basophil-related genes in the lung. Topical emollients markedly decreased the severity of skin lesions and inflammatory cell infiltration. Moreover, emollient treatments significantly downregulated expression levels of AD-related genes [286 of 1450 differentially expressed genes (DEGs)], including those related to innate inflammation (S100a8/a9, Il1b, Defb3/6, Mmp12), chemokines (Cxcl1/3, Ccl3/4) and epidermal permeability barrier (Krt2/6b/80, Serpinb12, Lce3e, Sprr2), etc.. Down-regulated genes were enriched in mitochondrial OXPHOS-related pathways, while up-regulated genes were mainly enriched in axon guidance and tight junctions. Moreover, topical emollient treatments decreased total serum levels of IgE and TSLP, along with substantial reductions in IL-4 levels. Furthermore, 187 of 275 upregulated genes in the skin were also significantly downregulated in lung tissue, including those involved in cytokines, cytokine/receptor interaction (Cxcl2/Cxcr2, Ccl2/3, Csf3r, etc.), and basophil activation (Mcpt8, Cd200r3, Ms4a2).

In conclusion, Topical emollient not only reduces skin inflammation, but also mitigates systemic inflammation by decreasing TSLP and IgE levels. Moreover, topical emollient reduces chemokine production, and basophil infiltration and activation in the lung, providing a molecular basis for blocking the atopic march.

Research experience:

- MD from medical school of JiaoTong university of Shanghai (2014-2023)
- master degree in Immunology and Immunopathology at University of Paris (2019-2020)
- 6 months laboratory internship and 1 month course of advanced immunology in Institute of Pasteur in Pairs (2019-2020)