International Pachyonychia Congenita Consortium (IPCC) Symposium

May 15, 2024 | 8:00 am - 12:30 pm
DeSoto Room at the Hilton Anatole, Dallas, TX
Many thanks to our symposium supporters

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PC Project
Pachyonychia Congenita Research & Patient Support Project
WELCOME TO THE 20TH IPCC SYMPOSIUM

Over the past 20 years, the International Pachyonychia Congenita Consortium has collaboratively and lovingly dedicated time, expertise, and resources to assist PC Project, a patient advocacy organization with a mission to find effective treatments and ultimately a cure for pachyonychia congenita, a painful and often debilitating genetic skin disease.

The IPCC's science-based efforts have resulted in remarkable strides for this previously unknown and misunderstood condition. These experts have literally changed what was known about PC, and because of their dedication, patients are being helped, cutting-edge research continues to advance, and meaningful treatments are becoming a real possibility.

“Driven by love, guided by science" perfectly epitomizes the efforts of these physicians and scientists. They know that behind every research endeavor are patients yearning for relief, and the IPCC works toward this goal with unwavering commitment and genuine care.

As we mark this 20-year milestone, we extend our deepest gratitude to each consortium member for their selflessness and tremendous service. We eagerly look forward to a promising future as we continue to work together to achieve even more greatness.

Our Vision:
A day when those who suffer from PC will live without excruciating pain, isolation, and embarrassment.
The Love-to-Science Session  

Chair: Eli Sprecher, MD, PhD

8:00 AM  20 Years Strong: advancing the registry, research, education and patient support  
Janice Schwartz, BA, Executive Director, Pachyonychia Congenita Project  
C. David Hansen, MD, University of Utah Department of Dermatology, Principal Investigator, International PC Research Registry

8:20 AM  Advances in the structure and function of intermediate filaments and what it means for PC patients  
Christopher G. Bunick, MD, PhD, Associate Professor of Dermatology, Program in Translational Biomedicine, Yale University

8:35 AM  Thoughts of a NIAMS (NIH) Program Director on facilitating research into rare skin diseases  
Peter J. Koch, PhD, Program Director, Epidermis, Dermis and Skin Senses Program (NIAMS/National Institutes of Health NIH)

8:50 AM  Discussion

The (PC) Science Session  

Chair: David Kelsell, PhD

8:55 AM  The TOC mouse - a new model of palmoplantar keratoderma  
Diana Blaydon, PhD, Lecturer, Centre for Cell Biology and Cutaneous Research, Blizard Institute, Queen Mary University of London

9:10 AM  Stress keratin function in skin epithelia, and its relevance to Pachyonychia Congenita  
Pierre A. Coulombe, PhD, G. Carl Huber Professor and Chair, Department of Cell & Developmental Biology, University of Michigan Medical School

9:25 AM  Inhibition of stress keratin induction by interfering with mechanotransduction pathways  
Joshua Tam, PhD, Wellman Center for Photomedicine, Massachusetts General Hospital Department of Dermatology, Harvard Medical School, Affiliate Faculty, Harvard-MIT Health Sciences and Technology

9:40 AM  Discussion

9:45 AM  GROUP PHOTO

9:50 AM  BREAK
### The (PPK) Science Session

**Chair: Robyn Hickerson, PhD**

10:10 AM  **Autoinflammatory disease with painful calluses and epithelial abnormalities caused by novel NLRP1 variants in 4 families**  
Alain Hovnanian, MD, PhD, Professor and Director, Laboratory of Genetic skin diseases IMAGINE Institute for Genetic Diseases, INSERM UMR 1163, Department of Genomic Medicine of rare diseases at Necker hospital, Department of Dermatology at Saint-Louis hospital, University of Paris Cité

10:25 AM  **Epidermal Differentiation at a Single Cell Level**  
Bogi Andersen, MD, Professor, Departments of Medicine and Biological Chemistry School of Medicine, University of California, Irvine

10:40 AM  **Role of the keratin-endoplasmic reticulum contact site in epidermolysis bullosa simplex**  
Navaneetha (Nav) Krishnan Bharathan, PhD, Researcher, Department of Dermatology, Penn State College of Medicine, Hershey

10:55 AM  **Regulation of cell adhesion and cytoskeletal dynamics in epidermal barrier formation and maintenance**  
Carien M. Niessen, PhD, Department Cell Biology of the Skin, CECAD, and Center for Molecular Medicine Cologne, University Hospital of Cologne, University of Cologne

11:10 AM  **Discussion**

### The Science-to-Love Session

**Chair: Pierre Coulombe, PhD**

11:15 AM  **Skin in health and disease through the lens of single-cell and spatial-seq technologies**  
Johann E. Gudjonsson, MD, PhD, Arthur C. Curtis Professor of Skin Molecular Immunology, Professor, Dept. of Dermatology, Professor, Dept. of Internal Medicine, Division of Rheumatology, Taubman Medical Research Institute, University of Michigan

11:30 AM  **Tools for clinical trials (clinical and research)**  
Edel O’Toole, MD, PhD, FRCP, Professor of Molecular Dermatology, Co-Director of HARP PhD Programme for Health Professionals, Queen Mary University of London

11:45 AM  **Monogenic disorders: the end of an era?**  
Eli Sprecher, MD, PhD, Professor and Chair, Division of Dermatology, Deputy Director General for R&D and Innovation, Tel Aviv Sourasky Medical Center, Frederick Reiss Chair of Dermatology, Department of Human Molecular Genetics & Biochemistry, Vice Dean for Clinical Affairs, Faculty of Medicine, Tel Aviv University

12:05 PM  **Full group discussion: next steps for the IPCC**

12:30 PM  **Lunch for pre-registered attendees & meeting adjourned**

1:15 PM  **Meeting for PC Medical and Scientific Advisory Board - By Invitation Only**
The Love-to-Science Session

Chair: Eli Sprecher, MD, PhD, IPCC Chair

Professor and Chair, Division of Dermatology  
Deputy Director General for R&D and Innovation  
Tel Aviv Sourasky Medical Center  
Frederick Reiss Chair of Dermatology  
Department of Human Molecular Genetics & Biochemistry  
Vice Dean for Clinical Affairs  
Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

8:00-8:20 AM

Janice N. Schwartz, BA

Janice received a B.A. in Communications with an emphasis on advertising from Brigham Young University. She raised four children (two who have PC) and was a founding board member and patient advocate for PC Project for nearly twenty years. In 2017, Janice stepped up to fulfill the Executive Director position and donates her time and each painful step to continue to push the cause forward and bring hope to all who meet her. And although she was motivated in the beginning to help her own children with PC, she quickly became driven by love for her other ‘children’ of all ages who have PC.

C. David Hansen, MD

Dr. Hansen completed his residency training in dermatology at the University of Michigan then returned to the University of Utah where he joined the clinical faculty in dermatology. He is a board certified dermatologist with focus on management of acne, psoriasis, and skin cancer. Research interests include the use of oral retinoids for acne and disorders of keratinization. Diagnosis and management of genetic skin disorders including pachyonychia congenita. In 2004, he participated in the first IPCC symposium involving many of the scientists who continue to work with PC Project today. Since then, he has been privileged to continue to associate with PC Project, helping with patient consultations, patient support meetings, taking numerous biopsies and collaborating with other medical, scientific and industry professionals. He is a member of PC Project’s Medical and Scientific Advisory Board and Board of Trustees and is currently the PI for PC Project’s International PC Research Registry.
IPCC Top 20 Accomplishments and Ongoing Projects

International Collaborative Group
1. In 2004, a group of bright and brilliant researchers and physicians dedicated to finding a cure for PC was formed: The International Pachyonychia Congenita Consortium. And this working group is still going strong today, led by a dedicated Steering Committee.

International PC Research Registry
2. Created and continue to maintain and grow the patient reported, physician verified International Pachyonychia Congenita Research Registry (IPCRR).
3. CLIA-verified genotyping of patients with all cases reviewed monthly by IPCC Genetics Team.
4. Accurately defined the various manifestations of PC and uncovered hitherto unknown features.
5. Reclassified PC into sub-types based on the specific genes affected.
6. Continue to utilize the data to gain new insights about PC and the 10-12 other conditions represented in the registry.

Education and awareness
7. Increases the visibility of PC and educates audiences worldwide.
9. Helps with annual PC Patient Support Meetings around the world.
10. Provides ongoing support for doctors managing PC patients.
11. Provides ongoing support for patients and families.
12. Conducted an Externally Led-Patient Focused Drug Development Meeting for PC: the PC Voice of the Patient Report is now on public record at FDA.

Research and Drug Development
13. Holds annual IPCC Symposiums for sharing research and stimulating collaborations.
14. Published and continues to publish a vast number of PC-related articles in peer-reviewed, respected journals.
15. Conducted a large in-person dermatology exam and pain study in Edinburgh, Paris, and Newark.
16. Continually collaborates for special clinical and research projects.
17. Explores methods to deepening understanding, such as mouse models for PC and delivery methods to skin.
18. Supports clinical and research studies: First-in-human siRNA Clinical trial, statins, sirolimus, erlotinib, botulinum toxin, capsaicin, etc.
19. Facilitates and funds research grants for PC.
20. Partners with and advises companies initiating clinical trials. (Of note, a phase 2 and phase 3 trial was fully enrolled in 8 months and 10 months.)
Christopher G. Bunick, MD, PhD

Dr. Bunick is an associate professor of dermatology and physician-scientist at Yale University School of Medicine’s Department of Dermatology. He leads a structural biology research program where he performs unique dermatologic research studying the 3-dimensional structures of skin-related proteins using x-ray crystallography and cryo-electron microscopy. As an undergraduate at Vanderbilt University, Dr. Bunick studied filamentous plant viruses, sparking his interest in long, filamentous systems, and leading to his current research on intermediate filaments, particularly keratin function in human skin.

Advances in the structure and function of intermediate filaments and what it means for PC patients

Mutations in keratins, particularly K6A, K6B, K6C, K16, and K17, underlie the pathogenesis of pachyonychia congenita. It is important, therefore, to understand the structure-function relationship of keratins containing patient-derived pathogenic sequence variants. New insights into the higher-order organization of intermediate filaments provide clues as to how and why PC-causing mutations harm keratin function. This data, plus biochemical insights into the early tetramerization process of keratins, will be discussed.

Peter J. Koch, PhD

Dr. Koch served as a tenured Professor for 12 years and as a department chair for 2 years. He has been a NIAMS-supported investigator for 23 years. At NIAMS, he now supports investigators interested in basic and translational research into skin biology and skin diseases (Peter Koch, Ph.D. | About NIAMS | nih.gov).

Thoughts of a NIAMS (NIH) program director on facilitating research into rare skin diseases

I will discuss the role of Program Directors (PD) / Program Officers in the mission of NIAMS to support skin research. A major focus of the presentation will be on how PDs support new and established investigators in developing research projects.
After obtaining a PhD in Molecular Genetics from University College London, Dr Blaydon joined David Kelsell’s group at Queen Mary University of London to study rare, inherited skin conditions and helped to identify novel genes associated with several genodermatoses, including palmoplantar keratodermas (PPKs) and peeling skin. As a Lecturer, Dr Blaydon’s research interests remain centered around understanding the molecular mechanisms underlying skin barrier integrity, particularly in response to stress, primarily through the study of proteins associated with PPKs and how palmoplantar skin differs to hairy, body skin.

The TOC mouse - a new model of palmoplantar keratoderma

Palmoplantar skin on our palms and soles is quite different to the skin covering the rest of the human body. To gain insight into the molecular mechanisms underlying conditions, such as palmoplantar keratoderma (PPK), that specifically manifest in this skin site we need a better understanding of these differences. Furthermore, mouse models of PPK are used to recapitulate human disease phenotypes despite limited exploration into how well mouse paws model human palmoplantar skin. Using transcriptomic data, we have compared gene expression differences between mouse paw and back skin with published transcriptional differences in matched human palmoplantar and body skin. After verifying the reliability of mouse paws as a model of human palmoplantar skin, we have examined transcriptomic differences in TOC mouse paw skin – a new model of focal PPK – to deepen our understanding of the role of iRhom2 variant protein in palmoplantar keratoderma.
Stress keratin function in skin epithelia, and its relevance to pachyonychia congenita

Pachyonychia Congenita is caused by mutations affecting the coding sequence of the type II keratins 6A-C or the type I keratins 16 and 17. These keratins are exquisitely responsive to various types of environmental stress and exhibit properties that differ from the keratins normally expressed in healthy interfollicular (thin) epidermis. The outcome of laboratory experimentation over the last 20 years and of computational analyses of high throughput data sets produced in the recent past converge in showing that stress keratin expression reflects altered pathways of keratinocyte differentiation in the epidermis, along with a state of inflammation and differential engagement of the innate immune system in the skin. Such findings have clear implications for the pathophysiology of pachyonychia congenita.

Dr. Coulombe, a native of Montréal, Canada, serves as the G. Carl Huber Professor & Chair of the Department of Cell & Developmental Biology at the University of Michigan Medical School. He is jointly appointed in the Department of Dermatology & is a member of the Rogel Cancer Center at the same institution. Dr. Coulombe joined U-M in 2017 following a 25 year-stay on faculty, including 9 years as the EV McCollum Professor & Chair of the Department of Biochemistry and Molecular Biology, at the Johns Hopkins University. Dr. Coulombe received his Ph.D. degree in Pharmacology from the Université de Montréal & pursued postdoctoral training at the University of Chicago. Dr. Coulombe’s research is focused on cell differentiation, tissue homeostasis & response to stress in surface epithelia. His research is relevant to the pathophysiology of rare skin disorders, psoriasis & related conditions, & non-melanoma skin cancer.
Inhibition of stress keratin induction by interfering with mechanotransduction pathways

PC is caused by autosomal dominant mutations in the keratins 6, 16, or 17, with the most problematic manifestation being the development of excessive and debilitatingly painful calluses, predominantly in pressure-bearing skin areas. Keratins 6/16/17 are also known as stress keratins because they are normally absent from the interfollicular epidermis, but become induced when keratinocytes are in distress, such as when skin is injured or compromised by various pathologies. The weightbearing regions of plantar skin are a rare exception to this rule, with constitutive expression of stress keratins reported in previous studies and confirmed in our lab. This unique expression pattern of stress keratins and the proclivity of PC-associated callosity to develop in weightbearing skin areas suggest that mechanical stimulation is likely to play a key role in inducing the pathologic callosity of PC. Cellular signaling mechanisms that convert physical forces into physiologic responses are collectively known as mechanotransduction pathways, and have been extensively characterized and investigated as targets for pharmaceutical intervention, due to their involvement in cancer progression. This has led to many existing small molecule agents targeting various aspects of mechanotransduction pathways. In this presentation I will introduce the concept of reducing/eliminating the induction of stress keratins in response to mechanical stimulation, using previously-developed small molecule inhibitors of mechanotransduction pathways.
Alain Hovnanian, MD, PhD

Alain Hovnanian, M.D, Ph.D, obtained his medical degree at University of Paris and trained in Dermatology and in Genetics in Paris. From 1993-2000, he did his post-doctoral fellowship at the Wellcome Trust Centre for Human Genetics at the University of Oxford, UK where he identified the genes for recessive dystrophic epidermolysis bullosa, Darier disease and Netherton syndrome. He is now Professor of Genetics at the University of Paris and Director of an INSERM research laboratory on genetic skin diseases at the Imagine Institute for genetic diseases where he identified a new gene for Olmsted syndrome (OS). He described EGFR hyperactivation in Pachyonychia Congenita (PC) and showed that the oral EGFR inhibitor Erlotinib was an effective treatment for OS and PC patients. In 2021, he was awarded the “Eurordis Black pearl award” for rare diseases.

Autoinflammatory disease with painful calluses and epithelial abnormalities caused by novel NLRP1 variants in 4 families

We studied 4 families with very painful punctate-like palmoplantar keratoderma and epithelial abnormalities. We identified novel NLRP1 variants predicted to be pathogenic which co-segregate with the disease phenotype. NLRP1 is one of the receptors used to detect danger signals of microbial origin. It is part of the inflammasome, an important element of the innate immune response, which senses danger signals and whose activation induces caspase 1-mediated activation of pro-inflammatory cytokines Il-1b and Il-18. Germline dominant and recessive gain-of-function mutations in NLRP1 have previously been associated with several rare autoinflammatory diseases (inflammasomopathies).
The 4 families included 8 patients affected over 2 generations. All patients developed early in life very painful calluses of their soles with a punctate, verrucous, and hyperkeratotic appearance, mainly on the forefoot and the heel. Four patients had also a hoarse voice due to laryngeal dyskeratosis, one patient had oral leucoplasia and one patient had a possible corneal dyskeratosis. Nails were normal. All patients suffered from neuropathic pain resistant to analgesics, with a very strong impact on their quality of life. Intriguingly, 3 patients had hidradenitis suppurativa, one of whom also had multiple sclerosis. One patient had a history of cured Hodgkin disease. There was inter- and intrafamilial variability in disease severity.

Exome sequencing and targeted panel next generation sequencing analysis identified 4 heterozygous variants in the NLRP1 gene located in different domains of the molecule. These variants were missense substitutions predicted to have a deleterious effect by in silico analysis. They were not reported and segregated with the disease phenotype in the 4 families. In vitro studies showed that IL-1b and IL-18 levels were significantly increased in the culture media of non-stimulated keratinocytes from one patient, indicating inflammasome activation in the basal state. We therefore concluded that these NLRP1 variants were very likely to be pathogenic and a specific therapy by the IL-1 receptor antagonist Anakinra was proposed to the patients.

These results further illustrate the clinical spectrum of inflammasomopathies due to NLRP1 variants and broadens the variety of NLRP1 mutations. The search for genotype-phenotype correlations will require analysis of other cases. The association of other autoinflammatory diseases (HS and multiple sclerosis) raises the question of the involvement of the IL-1 and IL-18 pathways in the pathogenesis of these conditions in these patients. The possible involvement of NLRP1 should be considered in the case of painful calluses with corneal, laryngeal, or oral dyskeratosis and normal nails. The identification of pathogenic gain-of-function NLRP1 variants offers the possibility of a specific treatment targeting the IL-1b pathway, the efficacy and tolerability of which have yet to be evaluated in this rare condition.

10:25-10:40 AM

Bogi Andersen, MD

Bogi Andersen is a Professor of Medicine and Biological Chemistry at UC Irvine. His research focuses on transcriptional regulation of epidermal differentiation and wound healing and the role for the circadian clock in skin. He is the Director of UCI Skin, an NIH-funded Skin Biology and Diseases Research-based Center.

Epidermal differentiation at a single cell level

I will describe our findings from studies applying single cell RNA sequencing and spatial transcriptomics to understand interfollicular epidermal differentiation in the mouse and human. The presentation will focus on a surprisingly large population of cells transitioning between the basal and spinous layers, and on differences in human volar and non-volar skin.
Navaneetha (Nav) Krishnan Bharathan, PhD

I am employed as Research faculty, working under Dr. Andrew Kowalczyk at the Penn State College of Medicine. I am currently studying the role of a recently discovered complex between keratin filaments and the endoplasmic reticulum in the context of skin disease and development. I will be entering the academic job market this Fall and I am seeking a tenure-track faculty position.

Role of the keratin-endoplasmic reticulum contact site in epidermolysis bullosa simplex

Epidermolysis bullosa simplex (EBS), a skin blistering disease, is caused by mutations in keratins 5 and 14 (KRT5/ KRT14). Prior studies have reported activation of endoplasmic reticulum (ER) stress and inflammatory pathways in EBS cell culture models. However, the molecular mechanisms linking keratin dysfunction to activated stress responses in EBS remain poorly understood. Using electron microscopy and live-cell fluorescence imaging, we find that peripheral ER tubules are in close proximity to keratin filaments and form mirror image arrangements at desmosome cell-cell junctions. Focused Ion Beam Scanning Electron Microscopy (FIB-SEM) and 3D reconstructions reveal intricate nanoscale associations of ER tubules with keratin filaments and the desmosome inner dense plaque. Keratin intermediate filaments align and intertwine with ER tubules at points of contact we term the keratin-ER contact site (KERCS), and stabilize ER membrane. In addition, expression of an EBS-causing keratin 14 mutant, KRT14R125C, leads to changes in ER morphology, converting ER tubules at the cell periphery to ER sheets. Finally, we observed that mitochondria are localized more peripherally in KRT14R125C-expressing cells, preferentially associating with peripheral ER sheets. Our results suggest that keratin filaments regulate the stability and organization of the ER. Further, we propose that KRT14 aggregate-mediated changes in ER morphology alter mitochondrial localization in EBS, with potential downstream effects on mitochondrial function.
Regulation of cell adhesion and cytoskeletal dynamics in epidermal barrier formation and maintenance

How cell shape and mechanics controls tissue turnover and function is still poorly understood. In the squamous stratifying epithelium of the skin, the epidermis, stereotypic changes in cell shape guide the differentiation and upward migration of cells. Using the epidermis as a model system, my laboratory asks how cell shape, fate and position are coordinated, and how integration of adhesion and cytoskeletal mechanics and signalling regulate the formation and renewal of functional compartments within the epidermis in health and disease. I will discuss how adherens junctions control the formation of desmosomes and also affect the organization of the keratin cytoskeleton. Moreover, I will discuss how mechanochemical regulation of junctional and cytoskeletal dynamics enable the formation and regeneration of a resilient epidermal barrier, and how dysregulation of these processes promote disease.
Johann E. Gudjonsson MD, PhD

Dr. Gudjonsson's primary research focus is basic immunological and genetic research on chronic inflammatory skin diseases. He has published over 290 peer-reviewed papers in top-tier journals, including Nature Immunology, Nature Genetics, Immunity, JCI, Science Translational Medicine, and the JID. He received the Young Investigator Award from the American Academy of Dermatology in 2007, and his work has earned several research awards, including awards from the American Skin Association and Doris Duke Foundation, and was selected as the Society for Investigative Dermatology Rising Star Lecture in 2018. He was elected as a member of the American Society for Clinical Investigation (ASCI) in 2020 and the American Association of Physicians (AAP) in 2024 and is a fellow of the American Association for the Advancement of Science (FAAAS). He is the director of an NIH-sponsored P30 Research Core Center at the University of Michigan. He is currently the chair of the NIH ACTS Study Section and on the Board of Scientific Counselors to NIAMS.

Skin in health and disease through the lens of single-cell and spatial-seq technologies

Recent technological advances have revolutionized our ability to understand the biology of the skin. This includes, in particular, technologies that permit the assessment of changes in gene expression and DNA accessibility down to a single-cell level and, in combination with spatial technologies, allow visualization of biological changes in the context of the structure of the skin. Here, we will highlight some of the tools used to analyze such data and how they can be integrated to provide an overview of the different cell types and differentiation states in healthy skin and how these may facilitate and promote the development of a disease state.
Edel O'Toole, MD, PhD, FRCP

I am a clinical academic in the Blizard Institute at Queen Mary University of London with an active research group working on diverse aspects of keratinocyte biology related to rare skin disease. My clinical interests are genetic skin disease (palmoplantar keratodermas and ichthyoses) and pediatric dermatology. I am a co-director of the Wellcome-funded HARP (Health Advances in Underrepresented Populations and Diseases) doctoral training programme. I have been part of the Genetics group of PC Project since 2006 and have been chief investigator for 2 PC trials in the UK.

Tools for clinical trials (clinical and research)

Pachyonychia Congenita (PC) is characterized by plantar pain. In this short talk, I will discuss 2 possible tools to be used in clinical trials.

In the first part of the talk, I will discuss the foot function index (FFI) which is a self-administered questionnaire composed of 23 questions which produces a total score and 3 sub-scale scores (activity limitation, disability and pain). Patients from the International Pachyonychia Congenita Research Registry (IPCRR) with confirmed PC were asked to complete the FFI 3 times over 3 months. As well as the FFI, respondents were asked to document the peak temperature that day. 389 responses were received from 211 patients with PC. The results show a significant impact of PC on foot function. The FFI may be a suitable patient-reported outcome measure in PC clinical trials. In the second part of this talk, I will discuss a pilot study on the use of phospho-proteomics on patient callus parings. Can we predict what drug the patient may respond to?
Eli Sprecher chairs the Division of Dermatology at the Tel Aviv Sourasky Medical Center where he also serves as Deputy Director for Research and Development. He is Frederick Reiss Professor of Dermatology at the Faculty of Medicine, Tel Aviv University. He is president of the European Society for Dermatological Research (ESDR). He has co-authored over 400 scientific publications and has earned several patents. His research focuses on the genetic basis of skin diseases. His group aims at understanding the molecular genetics of both simple and complex traits, deciphering their pathogenesis and then attempting at translating this new knowledge into innovative therapeutic tools.

Monogenic disorders: the end of an era?

Monogenic disorders have traditionally been defined as conditions due to specific genetic variants, those variants being not only necessary but actually sufficient to cause a disease phenotype. The occurrence of marked clinical variability within families seems to contradict the mere definition of monogenic diseases. Recently, it turned out that many clinical manifestations in a steadily growing number of cutaneous inherited conditions result from genetic variants in more than one gene. These discoveries signify the end of our current understanding of the pathogenesis of genodermatoses and pave the way for improved diagnosis and possibly treatment of those diseases.

11:45-12:05 PM

Eli Sprecher, MD, PhD

Monogenic disorders: the end of an era?

12:05-12:30 PM

Full group discussion: next steps for the IPCC

Led by the PC Steering Committee

12:30 PM

Lunch
IPCC WORKING COMMITTEES

Steering Committee: Eli Sprecher (lead), David Hansen, Edel O’Toole, Robyn Hickerson, Pierre Coulombe, Alain Hovnanian, Roger Kaspar
Responsibilities: Decision-making body for “all things PC”, budget oversight, partnership with the PC Medical and Scientific Advisory Board and the Board of Trustees

Research Committee: Pierre Coulombe (lead), Alain Hovnanian, David Kelsell, Robyn Hickerson
Responsibilities: Review grants and requests for funding, define priorities, oversee data sharing; look for sources for outside research funding both in and outside of US

Patient Committee/Genetics Team: David Hansen (lead), Eli Sprecher, Edel O’Toole, Alain Hovnanian, Antoni Gostynski
Responsibilities: Monthly meetings reviewing patient registry submissions, genetic testing, counseling

Membership Committee: Edel O’Toole (lead), Roger Kaspar, Pierre Coulombe
Responsibilities: Recruit patients, physicians, scientists, philanthropists to PC Project.

Communications Committee: Robyn Hickerson (lead), Michael Conneely, Peter Steijlen
Responsibilities: Chart and implement strategy for PC website, newsletters for PC social media platforms

If you are interested in participating on a committee, please email info@pachyonychia.org.

PC Medical & Scientific Advisory Board

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<thead>
<tr>
<th>Pierre Coulombe</th>
<th>Alain Hovnanian</th>
<th>Edel O’Toole</th>
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<tr>
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<td>Joyce Teng</td>
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Attention Researchers!

Now Accepting PC Grant Proposals

May 15, 2024 – Application Period Opens
August 31, 2024 – Application Deadline
November 1, 2024 – Awards Announced

AVAILABLE GRANTS FOR 2024

• **Catalyst Research Grants – up to $50,000.** Designed to support talented early-career scientists on the path toward becoming the next generation of PC thought leaders by supporting hypothesis-driven research projects. (An early-career scientist is someone in a tenure track faculty position at a grant-worthy institution for less than approximately 6 years.)

• **PC Project Champion Research Grants – up to $100,000.** Encourages established researchers to pursue research on ongoing or emerging challenges in PC or to bring their expertise to the field of PC.

Any proposal is welcome that is focused on addressing the genetics, pathophysiology and/or treatment of pachyonychia congenita (PC). Relevance to PC will be considered a defining criterion during the review of the scientific merit of proposals and also when making final decisions regarding funding.

pachyonychia.org/apply-for-a-grant/
If you are planning to attend the ESDR Meeting in Lisbon, consider coming a few days earlier and joining us as our guests. This is an excellent educational opportunity to meet with many rare skin disease patients in one setting—and it’s a lot of fun, too! Contact us for more details if you’re interested.

pachyonychia.org/2024-patient-support-meeting/
Just Calluses? Think Again.

THIS IS PACHYONYCHIA CONGENITA

“I don’t know what a painless day is.”

- PC Patient