17th Annual International Pachyonychia Congenita Consortium (IPCC) Symposium
May 12-13, 2020
prior to the SID Annual meeting
in Scottsdale, Arizona at the Westin Kierland Resort

Please register at www.surveygizmo.com/s3/5360362/2020IPCC
The registration fee is waived with pre-registration; sessions & meals included.

**SCHEDULE**

Tuesday, May 12
12:00 pm Lunch and welcome
12:30-4:00 pm Presentations
5:30 pm Bus to dinner at the Phoenix Zoo

Wednesday, May 13
7:30 am Breakfast
8:30-12:00 pm Presentations
12:00 pm Lunch & Meeting Adjourns
12:30-2:00 pm PC Project’s Medical and Scientific Advisory Board Meeting

**CONFIRMED SPEAKERS AND ATTENDEES**

Christopher Bunick
Keith Chooate
Michael Conneely
Pierre A. Coulombe
John Doux
Tracy L. Funk
Kathy Green
C. David Hansen
Robyn P. Hickerson
Alain A. Hovnanian
Rich Kang
Roger L. Kaspar

Wesley Kaupinen
David Kelsell
Akiharu Kubo
E. Birgitte Lane
Thomas M. Magin
Edel A. O’Toole
Amy S. Paller
Dennis R. Roop
Liat Samuelov
Braham Shroot
Eli Sprecher
Albert Wu
MESSAGE FROM THE EDITOR

Greetings from a very wet London. There is some concern, as there is everywhere, about COVID-19 virus and I hope you and your families are well.

In this newsletter, the IPCC spotlight shines on David Kelsell who has worked for many years elucidating the genetic basis of palmoplantar keratodermas. There is an update on the VALO trial which has now recruited adequate patients.

The March rare disease issue of the British Journal of Dermatology is now published featuring 1 editorial, 5 commentaries, 2 review articles and 4 research articles and 1 research letter on PC. Thank you to all who contributed.

We look forward to seeing you all at the IPCC meeting in Scottsdale, Arizona prior to the SID meeting.

For more information on VALO, Palvella Therapeutics’ Phase 2/3 study investigating PTX-022 (QTORINTM rapamycin) for pachyonychia congenita, please visit pachyonychia.org/valo/ or clinicaltrials.gov.

PC PATIENT SUPPORT MEETING
JUNE 4-6, 2020, PARIS, FRANCE

There are currently 57 people registered thus far (including 22 PC patients) to attend the European Patient Support Meeting which will be held in Roissy, France (near Paris), June 4-6, 2020.

The France meeting will be held in both English and in French, with translation services. Interested clinicians, researchers and drug developers are invited to attend:

Please register at pachyonychia.org/2020psm/

Many thanks to Le Coeur Au Pied, our French PC advocate group, for the help and support in organizing this meeting with PC Project staff.

It’s All About Love

February was the month of Valentine’s Day in many countries, a time when people express their feelings of love for others. PC Project was established because of love and continues to run because of the service and goodwill of many people, including you.

Here are just a few examples of the selfless, loving acts we’ve observed recently:

• Members of the IPCC continue to collaborate with each other and PC Project to help further research and drug development.

VALO PHASE 2/3 CLINICAL STUDY
FULLY ENROLLED IN RECORD TIME
By Emily Cook, Palvella VP of Clinical Operations

Within a short eight months, the Phase 2/3 study has now been fully recruited! Recognition needs to be made to PC Project for their significant efforts in supporting successful study enrollment. All patients that have participated in the study, in any way, are true medical heroes. Palvella looks forward to sharing top line study results at the end of this year.

With the close of recruitment for the main study, recruitment now opens for the Pharmacokinetic Maximal Usage Sub-Study. The purpose of the sub-study is to look more closely at the pharmacokinetic profile of PTX-022 in up to 16 PC patients with either K6A, K6B or K16 genotyped mutations.

VALO-2, the open-label extension study, is in late stages of start-up and currently undergoing IRB review. Clinic study site activation is underway and everyone is looking forward to enrollment of the first patients eminently.

PO Box 17850, Holladay, UT 84117 · www.pachyonychia.org · 801-987-8758 · info@pachyonychia.org
The IPCC Genetics team donates their time monthly to review cases, discuss genetic testing and assist PC Project with patient needs and research.

Members from the PC Project Medical and Scientific Advisory Board and Board of Trustees continue to sacrifice time, energy and resources to support PC Project and its mission.

A mother of a PC patient assisted PC Project staff in translating and speaking with a mother of a PC baby who doesn’t speak English. This baby is a spontaneous case and the new parents needed support and sound care advice.

A PC advocate translated important documents for disability status from English, into her native language for another patient.

PC patients continue to support and encourage one another the PC Facebook Chat private group. The level of kindness and love shown in that group is heartwarming.

On Valentine’s Day, supporters donated to PC Project because of a social media meme. In addition, 62 PC Love Builders continue to donate monthly.

It was an exciting time in human genetics as DNA-based technologies were changing. The switch from the laborious week long Southern Blotting method (to map genes using Somatic Cell Hybrid cell lines and also to identify DNA polymorphisms) to the two hour or less polymerase chain reaction (PCR). was truly game changing. This PCR technology led quite quickly to its use in studying microsatellite polymorphisms (for family-based linkage studies) and then to automated fluorescent systems for genotyping and gene sequencing. Since then, I have always kept a lookout for new emerging technologies to speed up and expand research capabilities. For example, using SNP arrays, we homed in on ABCA12 as the cause of the skin disease Harlequin Ichthyosis and, since the arrival of high throughput sequencing, we have identified many other disease genes.

During my PhD, I also formed a longstanding collaboration with Professor Irene Leigh performing genetic linkage studies on familial palmoplantar keratodermas (PPKs) which then...
kick-started my research career in genetic skin disorders and keratinocyte cell biology. One aspect that particularly cemented my long term interest in rare skin disease was that some PPKs were associated with syndromic disorders. Using our genetic approaches in these PPK syndromes, we were able to not only identify genes associated with PPK but also with other conditions. These include GJB2 mutations as the major cause of genetic hearing loss (published in Nature), desmoplakin mutations with cardiomyopathy and, more recently, iRhom2 mutations and oesophageal cancer. Over the years with the relatively ease of high throughput sequencing for disease gene identification and genetic diagnosis, my groups research time has shifted more towards cell biology, biochemistry, signaling and model systems to understand disease mechanisms. For example, we have shown iRhom2 to regulate epidermal thickening and also be a key player in modulating the cytoskeletal stress response including keratin 16 and 17. These two keratins are defective in many cases of PC.

Unlike many non-clinical academic scientists, I have not had many postdoctoral positions or even worked abroad. My biggest move was moving from the Peak District to South Mimms where I did my PhD. I thought this village hamlet was close to London until I tried to get to Covent Garden one Sunday. One bus every two hours and then train plus tube. I think it would have been quicker to get there from Manchester. My next big move after my PhD was crossing the M25 ring road to Whitechapel in the East End of London for a brief (9 month) postdoctoral fellowship with Irene Leigh and then I re-crossed the M25 out of London to work for SmithKline Beecham (now GlaxoSmithkline) at Harlow. After a spell of learning bioinformatics and drug discovery in the pharmaceutical industry (11 months), I rejoined the Centre for Cutaneous Research at Barts and The London School of Medicine and Dentistry, Queen Mary University of London as a senior lecturer to build an independent research team working on human skin genetics and keratinocyte biology. A few years later, I was made Professor of Human Molecular Genetics at the age of 36 and have stayed there ever since.

Some of my proudest work moments include being awarded the Chanel-CERIES award for skin research in 2016 and the other was being on the board of the European Society of Dermatological Research (ESDR). I am leaving the ESDR board later this year after 8 years (longest serving board member I think) and I was the first non-clinical ESDR president (2018-2019) in its 49th year.

Research into skin diseases like PC is important and the collaborative environment generated by PC Project brings researchers from academia and industry together with the patients to understand the PPKs and identify potential therapeutic approaches. I am delighted to be a new member of the Medical and Scientific Advisory Board of PC Project.

Recent Publications

pachyonychia.org/research-articles/

Special PC BJD edition March 2020
onlinelibrary.wiley.com/doi/10.1111/bjd.18817


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**PC TOWN HALL MEETING**

On Thursday, March 19 at 5:30pm PT (6:30pm MT, 7:30pm CT, 8:30pm ET), PC Project will host a town hall style webinar. This first-ever town hall meeting for the PC community will give an overview about PC, the burden of living with PC, and all the exciting developments that have been happening at PC Project, i.e. VALO trial, current research efforts, etc.

Anyone interested is invited to register for the free meeting: 
[pcproject.townhall.sgizmo.com/s3/](pcproject.townhall.sgizmo.com/s3/)

This web meeting will last approximately 45 minutes. You can join by computer, smart phone or tablet or you can join the listen-only mode by calling from any telephone.

**PC UNCOVERED: DID YOU KNOW?**

Many PCers report that they sleep with their feet outside of the bed covers, often with their feet hanging off the side of the bed so that nothing touches their feet.

“Otherwise the feet start sweating and the next day morning pain increases significantly.”

“I can’t rest the sides of my feet on the mattress as it’s too painful.”

“If my feet are somehow not over the edge, I’ll wake up because of the burning.”

“I always sleep with my feet off the bed and outside of the sheets. The slightest friction hurts or annoys me.”

“The pressure of the blanket on my feet is too much. My feet hurt and make it hard to sleep and sometimes my feet start hurting in the middle of the night and wake me up.”

“Last night I was up multiple times, tossing and turning, trying to prevent my feet from touching anything. Every time I moved I was in horrible pain.”
The International Pachyonychia Congenita Research Registry was established primarily for two reasons:

1. To gather accurate data about PC. For example, the word pachyonychia means thick nails. Because of the registry, we now know that not only do some PC mutations NOT have nail dystrophy, but the most prevalent symptom of PC is painful plantar keratoderma.

2. To assemble a group of genetically tested patients available for clinical studies.

More basic data about the registry can be found online at [pachyonychia.org/pc-data/](http://pachyonychia.org/pc-data/)

If you know patients who may have PC, please encourage them to join the registry and be part of a supportive, global PC community: [registry.pachyonychia.org/s3/IPCR](http://registry.pachyonychia.org/s3/IPCR)

If you have research ideas, questions or need to request registry data, please contact PC Project.

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International PC Research Registry (IPCR)

Location of 977 PC Patients in 52 countries as of Jan 2020

All are genetically confirmed with Pachyonychia Congenita and have Questions, Photos & Notes on file in the IPCR.

Demographics of 977 individuals with genetically confirmed PC

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<th>Patients in 45 other countries</th>
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IPCR PC Mutations Jan 2020

List of PC Mutations and Percentage of PC Genes for those in the IPCRR who are genetically confirmed as Pachyonychia Congenita

115 mutations — 977 individuals in 517 families

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K6a

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K6b

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K6c

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