16th Annual International Pachyonychia Congenita Consortium (IPCC) Symposium

May 7-8, 2019

just prior to the SID Annual meeting in Chicago, Illinois at the Hilton Chicago

Please register at www.surveygizmo.com/s3/4783588/2019IPCC

The registration fee is waived with pre-registration; sessions & meals included.

**SCHEDULE**

**Tuesday, May 7**
12 pm  Lunch and welcome
12:30-5:00 pm  Presentations
6:00 pm  Meet for offsite dinner cruise

**Wednesday, May 8**
7:30 am  Breakfast
8:30-12:30 pm  Presentations
12:30 pm  Lunch

**INVITED SPEAKERS AND ATTENDEES**

Alain A. Hovnanian  
Albert A. Bravo  
Alex Hinbest  
Braham Shroot  
C. David Hansen  
Christopher Bunick  
David A. Giljohann  
David Kelsell  
Dennis R. Roop  
E. Birgitte Lane  
Edel A. O’Toole  
James Rittle  
John D. Doux  
Joyce M. Teng  
Liat Samuelov  
Mark P. de Souza  
Maria Morasso  
Michael Conneely  
Michael J. Caterina  
Michael J. Polydefkis  
Minh Ho  
Pierre A. Coulombe  
Rame Yousif  
Robyn P. Hickerson  
Roger L. Kaspar  
Thomas M. Magin  
Tracy L. Funk  
Vivien Chua  
Vu Van Quang  
Wesley Kaupinen
Spring is here and it is nice to wake up at 5:45 am in London to brightness and a new day. In this newsletter, we put the spotlight on Dr Hansen, a University of Utah dermatologist, who has dedicated a lot of time to genetic skin disorders and PC. Maria Morasso and Olivier Duverger from the NIH explain about their interesting work on keratin variants and teeth and what that might mean for our patients. In the USA, doctors and patients are about to start a clinical trial of topical rapamycin for PC. Over here in Europe, we are waiting for Brexit, but are hopeful a clinical trial of topical rapamycin will happen here soon too. We look forward to seeing as many of you as possible at the IPCC meeting in Chicago.

**IPCC Spotlight: C. David Hansen, MD**

*University of Utah Dermatology. PC Project Board Member and International PC Research Registry PI*

Following our success with this oral “retinoid” we began to study a cousin medication, now called Acitretin, in the treatment of psoriasis. This proved to be helpful in a small number of patients but not as dramatic as the initial experience with the genetic skin disorders. We also participated in the early studies of “Accutane” for the treatment of severe cystic acne – again with striking success in a condition that had been very difficult to manage.

My exposure to genetic skin diseases and the remarkable response we found in this select group of conditions encouraged my interest in genetic keratinizing disorders. In 2004, I participated in the first PC symposium involving many of the scientists with whom we continue to work with at PC Project. I was delighted at that time to meet several individuals with Pachyonychia Congenita for the first time. My hope was that we could find a similar medication that would reverse some of the challenging skin changes found in PC.

Since that symposium I have been privileged to continue to associate with PC Project, helping with over 200 patient consultations, patient support meetings and sharing consultations with incredible scientists who are pushing the frontiers of therapy in Pachyonychia Congenita. For me this has opened a vision of the potential for diagnosis and management of PC along with other genetic conditions that involve changes in the way the skin functions. One of the great accomplishments of PC Project was to establish an international registry where we could document the specific mutations in the PC genes and establish the physical findings and challenges faced with this rare skin condition. Using the data from the registry, that was willingly provided by so many PC patients, we were able to publish articles helping doctors throughout the world to better understand and manage this difficult condition. Thanks to all the patients who participated in the questionnaire and support meetings – it has allowed us to make significant strides in understanding the potential for effective treatments.
At home I am married and have raised four children, one of whom is also a dermatologist at the University of Utah. As we continue to work together, I see great potential to modify the skin changes that produce the calluses, pain and other problems found in PC. This keeps me excited about continuing my association with PC Project – I see great things coming.

**WHAT ARE EPITHELIAL KERATINS DOING IN TEETH?**

*By: Dr. Olivier Duverger and Dr. Maria I. Morasso*

Concurrent with epidermal differentiation, during embryogenesis there is development of ectodermal appendages such as hair and teeth. Previously, the Morasso group showed that the epithelial hair keratin K75 is expressed in developing teeth and is an essential organic component of human mineralized tooth enamel.

The group recently published their research in PLoS Genetics (2018) and JID (2019) showing that K6a, K6b, K6c, K16 and K17, epithelial keratins that are mutated in patients with Pachyonychia Congenita (PC), are also produced in developing teeth and are essential organic components of the mineralized tooth enamel.

The expression of these keratins in dental tissues had not been described before, and dental manifestations in PC, a cutaneous disorder characterized by nail dystrophy and painful palmoplantar keratoderma, had not been reported. In these studies, using human genetic and intraoral examination data, the Morasso group identified several missense polymorphisms in the genes encoding K6a, K6b and K6c that lead to increased susceptibility to cavities, which supports a function of these keratins in the resistance to tooth decay (Duverger et al., PLoS Genetics, 2018).

Interestingly, their findings on K16 and K17 suggest a distinct function for these two keratins that exhibit a different distribution in the enamel when compared to the K6 family and seem to have a role in shock absorption and protection against cracking (Duverger et al., J. Invest. Dermatol., 2019).

These results raise numerous questions about the potential functions of these keratins besides intermediate filament components and provide a novel understanding of the genetics of susceptibility to tooth decay and other enamel defects. Furthermore, besides determining novel clinical features of PC, it has broad implications for personalized prevention risk assessment and dental care for patients with PC.

**References:**


**RECENT PUBLICATIONS**


**WHY PC PATIENTS HIDE THEIR PC?**

PC patients were asked the following question on a private PC Facebook chat group:

*Why do PC patients so often hide their symptoms or even the fact that they have PC?*

Katie: My daughter is only 11-years old and hides it as others don’t understand. She is always in pain but gets sick of telling people what’s wrong etc. I think it’s more to do with others not judging.

Ramon: Mostly, to avoid the long conversation: “Yes, my whole life. No, not contagious at all. Yes, it hurts. Yes, I've been to a doctor.” and the most annoying one: "Yes, I've tried that home remedy already."

Lacey: Judgement. My whole life I've been judged. People thinking I'm contagious from the time I was a toddler and just wanted to play with the other kids but their parents wouldn't let them, to even now just handing money to a cashier and getting a dirty look because my hands are different. I hide my disorder because the world is ignorant to what they don't understand or care to even try to understand before judging.

Malgosia: Looking through my life I see a couple of reasons. First, the disease is rare and not typical, and people don’t understand what we really have. I usually say that I have problems with walking and standing. For some people it’s enough, some ask for more details, even doctors don’t want to know more. Second, usually it's not visible, and people don’t believe that "healthy looking" people struggle. Third, shame to ask for help. I have to force myself to not overdo, and in my country, I don’t want to speak, to not have problems with work and study. It's sad but the discrimination of disabled people, forces them to behave as normal to have a good education and job.
Tom: First, until a year ago, I thought I was the only person in the world that had this issue. I’ve seen what seems like a thousand doctors that just stared at me and shook their head. So because of that I “hid” my condition because even I didn’t understand. Second, I’ve dealt with the pain and if I told someone my feet hurt, they’d go into how they have a bunion or a blister from tight shoes etc., and tell me how to get rid of it. I’ve dealt with this so long, telling people I hurt, to me, sounded like I’m complaining...and I don’t want people to look at me like someone that just complains about everything.

Jason: I was recently bullied at work by someone who told me to go to a doctor for my “damned dirty nails”.

Laura: It’s embarrassing and ugly. I think when people see other disabilities, they’re more common so more accepted. I definitely don’t feel “pretty” or “womanly” with them. And that affects my confidence and self-esteem.

Marion: It is very hard on children - our son went through merciless teasing and bullying growing up when other kids saw his feet.

Nykole: About 8 years ago, I went to get my hair cut. The lady was combing my hair and said “You need to get this taken care of!” She threw the comb in the trash in front of me and didn’t even tell me she was not going to cut my hair. I sat in that seat for what seemed like hours with her and another stylist she called over. They were standing there glaring at me in disgust because my scalp had cysts on it. It was such an embarrassing and awkward moment.

Claire: I have the thick nails on my hands and feet and have more cysts than I’m able to count. My experience at school made me embarrassed by it. I vividly remember being called elephant girl and the constant ‘eeww’ if people saw my nails. This still pains me nearly 30 years later. This is why I hide my nails with false nails and don’t wear certain clothes as I like to have my bumps and scars covered.

Suzanne: I think it’s an instinctive need to fit in, to be accepted. We have no control over other people only control over ourselves and how we deal with differences. For me, the patient support meetings are the only place I feel accepted. I’d never experienced this before. I had 40 years of feeling I didn’t belong. I don’t think I could describe the feeling I had. I was allowed to be who I am. I have moments of “stuff it, I’m not going to hide” but then just one thoughtless comment sends me right back to that “head-down, stay-low” mindset.

BOSTON PC PATIENT SUPPORT MEETING
JUNE 20-22, 2019

All interested clinicians and scientists are welcome to attend. This is an excellent opportunity to observe and learn first-hand from the PC patient community. If interested please contact PC Project at info@pachyonychia.org or see meeting and registration details here: https://www.pachyonychia.org/2019psm/
**PC Community Unites in Salt Lake City for Phase 2/3 Clinical Study Kickoff**

*By: Wes Kaupinen, CEO Palvella Therapeutics*

*Uplifting Kickoff Meeting held to discuss execution of study to evaluate Palvella Therapeutics’ Investigational Therapy for Pachyonychia Congenita*

On a majestic January weekend in Salt Lake City, members of the PC community converged for the kickoff of the Phase 2/3 clinical study that PC Project and Palvella Therapeutics have been building towards together the last two years. The study plans to evaluate the use of PTX-022, a novel, targeted formulation of rapamycin developed leveraging Palvella’s QTORIN™ technology, in pachyonychia congenita. This meeting in Salt Lake City marked the culmination of many years of work by PC Project, TransDerm, and Palvella Therapeutics to advance this program towards what will be the first-ever Phase 2/3 study in pachyonychia congenita.

Inspiration and passion abounded at the meeting from the outset, beginning with Janice Schwartz captivating the audience by describing the determined efforts of PC Project to extend their love and care to PC patients worldwide while concurrently partnering with physicians and scientists to advance meaningful potential therapies to PC patients. Jan eloquently reminded all in attendance, some of whom were new to PC, that PC patients are chronically debilitated for life, live in a constant state of mobility-limiting pain, and are without a single FDA-approved therapy. Following Janice’s presentation, several physicians and scientists including Dr. David Hansen (University of Utah), Dr. Joyce Teng (Stanford), Dr. Amy Paller (Northwestern), Dr. Sancy Leachman (Oregon Health and Sciences University), Dr. Tracy Funk (Oregon Health and Sciences University), Dr. Braham Shroot (Palvella Therapeutics), and James Valentine (Hyman, Phelps & McNamara) highlighted their work in PC, and more importantly, their underlying passion to strive towards improving the lives of PC patients.

The potential for the targeted delivery of rapamycin in pachyonychia congenita has its roots in the dedicated work of Dr. Roger Kaspar who utilized his background in gene expression to discover that the mutant keratin genes in PC could potentially be repressed through therapeutic intervention with rapamycin. Dr. Kaspar shared the story behind this original discovery more than a decade ago, as well as the work that immediately followed with Dr. Sancy Leachman conducting a study of oral rapamycin in pachyonychia congenita. Overall, while many key important themes emerged from the meeting, none were more powerful than “Love your PCer”, and meeting participants consistently offered a willingness throughout the meeting to deepen their commitment towards improving the lives of those affected by pachyonychia congenita.

If you have PC patients in your clinical practice that would be interested in participating in this future Phase 2/3 clinical study, please let us know at https://www.surveygizmo.com/s3/4854812/PCInterestSurveyPhase2-3

The clinical study plans to begin enrolling PC patients in the coming weeks, with clinical trial sites currently planned across the United States.