Pachyonychia Congenita (PC) is an ultra-rare, genetic, autosomal dominant skin disorder. PC is caused by a mutation in any one of five keratin genes: KRT6A, KRT6B, KRT6C, KRT16, KRT17. Over 118 specific mutations have now been identified. The gene and mutation affect the condition for each PC patient.

THE MOST COMMON FEATURES OF PC INCLUDE:

1. **Painful calluses and blisters** on the soles of the feet (focal plantar hyperkeratosis). Pain is one of the distinct characteristics of PC. Blisters are found under the callus in PC patients. Calluses may also form on the palms of the hands (palmar hyperkeratosis).
2. **Thickened Nails** (hypertrophic nail dystrophy) although not all nails are affected in all patients with PC.
3. **Cysts** of various types (including steatocystoma and pilosebaceous cysts). In some forms of PC, this is the most dominant, painful and problematic characteristic.
4. **Follicular hyperkeratosis** (FHK or bumps around hairs at friction sites such as waist, hips, knees, elbows). Most common in children and lessens after teenage years.
5. **Leukokeratosis of the oral mucosa** (white film on tongue and inside cheeks). This is not painful but is often misdiagnosed as thrush or as leukoplakia.
6. **Neurovascular Structures in Calluses** (painful blood vessels or nerve endings). These can grow in the calluses and make trimming difficult and walking extra painful.
7. **Deep itch** under, around, or in the calluses. Like the painful calluses, this deep itching can interfere with sleep and make the feet feel uncomfortable and irritable.

ABOUT PC PROJECT
PC Project was founded in 2003 as a 501(c)3 public charity in the USA. PC Project staff work together with medical professionals, scientists, PC patients, friends and family members to make a difference for those suffering with Pachyonychia Congenita. PC Project makes effective use of the limited budget to serve patients in over 60 countries around the world and to facilitate research.

MISSION STATEMENT:

PC Project is dedicated to finding effective treatments and a cure for Pachyonychia Congenita, a painful, debilitating skin disorder, through helping and connecting patients, empowering research, and partnering with industry.

VISION:

A day when PC sufferers will live without excruciating pain, isolation, and embarrassment.

VALUES:

♥ Hope – We hope for a future with treatments that minimize pain, increase mobility, and eventually cure PC.
♥ Love – We show our love by caring for and supporting all members of the PC community.
♥ Empower – We empower research and we empower patients to become their own advocates to successfully navigate living with this painful, rare disease.
♥ Collaborate – We collaborate with physicians, scientists, industry, and patients across the world to advance research and drug development for meaningful treatments and ultimately a cure for PC

MOTTO:

♥ Love, it’s in everything we do.
♥ PC Project: It’s all about love.

SLOGAN:


To find effective treatments for those suffering from Pachyonychia Congenita, PC Project actively sponsors two major efforts:

1. The International Pachyonychia Congenita Research Registry (IPCRR).
   • Free genetic testing for those diagnosed with PC or similar disorders.
   • Annual Patient Support Meetings and other patient support services.
2. The International Pachyonychia Congenita Consortium (IPCC).
• Research grants, clinical studies and clinical trials.
• Annual Scientific meetings.
• Publications of PC data and research.

SUMMARY OF 2021 PROGRAMS AND SERVICES

INTERNATIONAL PACHYONYCHIA CONGENTIA RESEARCH REGISTRY (IPCRR)

The IPCRR patient registry is the key to all patient services. Through the registry, each patient has an opportunity to contribute data about their condition and to receive important services. Isolation is a major burden for those with rare diseases and through the IPCRR, patients can connect with other patients and specialists who understand PC. Those in the IPCRR are offered free genetic testing. The testing is performed using a saliva collection kit provided by PC Project at no cost to patients. Physician consultations, support by PC advocates, assistance with applications for disability or work accommodations and other services are provided for those in the IPCRR.

There were 1629 patients in the IPCRR at the end of 2021 with 1067 of those being genetically confirmed with PC. The following statistics were noted for the IPCRR in 2021:

- 127 saliva kits were sent for genetic testing
- 93 individuals received genetic testing results

PC Project Awarded Grant

The Sorenson Legacy Foundation awarded PC Project a $30,000 grant for the continued building and maintaining of the International PC Research Registry. Thanks to the patients who wrote letters of support about the impact the registry and the ability to have a genetically confirmed diagnosis have been on your lives.

PATIENT SUPPORT MEETING

Virtual PC Patient Support Meeting – “Joy in the Journey” was the theme for the Virtual PC Patient Support Meeting held on November 20, 2021. We laughed, we cried, we learned. What a blessing to meet with so many PC patients on Saturday, November 20, 2021 for our Virtual PC Patient Support Meeting!

Over 126 people joined the Zoom meeting, and that's not counting those who were watching with spouses and other family members. This was just a small portion of the wonderful PC family, which includes dedicated scientists, doctors, and biopharma partners. We love them all!

PC PROJECT PUBLICATIONS

PC NewsBrief. Each month PC Project sends out its monthly newsletter, the PC NewsBrief, to over 1000 recipients. The newsletter contains articles about meetings,
clinical studies and trials, photos of PC Patients, updates on PC Project and tips for patients and family members who care for someone with Pachyonychia Congenita.

**IPCC Newsletter.** Dr. Edel O’Toole serves as the editor for this publication. All members of the International Pachyonychia Congenita Consortium (IPCC) receive the quarterly published IPCC newsletter. The newsletter includes updates on clinical studies and trials, recent publications, genetic testing information, annual meeting information and updates on the International Pachyonychia Congenita Research Registry (IPCRR)

**INTERNATIONAL PC CONSORTIUM (IPCC)**

The IPCC connects physicians and scientists with an interest in keratin disorders who agree to work collaboratively in areas that relate to progress for PC research and therapies. There are several hundred members of the IPCC and about 50 who are actively exchanging and assisting with research.

**IPCC ANNUAL SYMPOSIUM**

**IPCC Virtual Symposium.** The 17th annual symposium for the IPCC Innovations & Transformations was held on June 28-29, 2021. This was the first virtual gathering of doctors, scientists, and pharmaceutical representatives who listened to presentations about PC-related research and engaged in discussions on how to move the work forward. Professors Eli Sprecher and Edel O’Toole co-chaired the meeting which featured 20 speakers. Over 100 people registered and on each day of the symposium, approximately 78 professionals attended. One presenter told PC Project that she had more people listen to her talk at the IPCC Symposium than her talk at the American Academy of Dermatology annual meeting!

The co-chairs and the PC Medical and Scientific Advisory Board were thrilled at the attendance, the engagement, and more importantly, the new research that was presented. We are grateful that there is still so much interest in PC in the scientific and medical community. Not only did PC Project’s key collaborators participate in the meeting, but the virtual format also allowed many new people to register whom PC Project is excited to welcome to the International PC Consortium.

The symposium was held in a Zoom meeting style (not webinar style) so attendees could interact, discuss, and make personal connections. Seeing long-term friends as well as new faces was a delight for all. The following presentations were given during the recent IPCC Symposium based on new information gleaned from de-identified IPCRR Data:

- Structural modeling guided understanding of genotype-phenotype correlation in PC Joyce Teng, MD, PhD, and Christopher Bunick, MD, PhD, Stanford University and Yale University
- Revisiting pachyonychia congenita: a case cohort study in 815 patients Liat Samuelov, MD, Tel Aviv Medical Center
Heart Prevalence and characterisation of itch in PC Lloyd Steele, Academic Clinical Fellow in Dermatology at Barts Health NHS Trust, London

♥ Patient-reported quality of life differentials in PC management Albert G. Wu, MD Candidate, New York Medical College and Shari Lipner, MD, PhD, Weill Cornell Medicine, Department of Dermatology

♥ Co-existence of PC and hidradenitis suppurativa: more than a coincidence. Mor Pavlovsky, MD, Tel Aviv Medical Center

All of those presentations were recently or are in the process of being published in medical and scientific journals. In the quest to find effective treatments, scientists and drug developers are using the registry data to learn more about PC, to advance PC research, and to develop therapeutics that may help PC and other rare skin diseases.

On a clinical side, registry data is literally changing what is known about PC. Factual information prevents doctors from prescribing treatments that are ineffective or harmful to patients. And with more publications about PC in high impact medical journals, physicians will better be able to recognize PC and clinically diagnose their patients so those with PC don’t have to live for decades without a proper diagnosis. Thank you for participating in the IPCRR. Together we are making a difference!

IPCC GENETICS TEAM AND IPCC STEERING COMMITTEE

PC Project’s MSAB Meeting – February 12, 2021 members of PC Project’s Medical and Scientific Advisory Board (MSAB) met under the leadership of Prof. Eli Sprecher to discuss research priorities and advise PC Project on how to best move PC-related research forward. Wes Kaupinen, CEO of Palvella and Braham Shroot, CSO of Palvella, joined the meeting to present data about the VALO clinical trial to the MSAB.

Research Agenda started One of PC Project’s high-priority strategic goals this year is the development and dissemination of a PC Research Agenda (RA). The RA will be developed over the next 6-10 months with input from key thought leaders in our field. Dr. Helaine Resnick is coordinating the efforts with Drs. Eli Sprecher and Edel O’Toole serving as the project co-chairs and leading the various writers of each research topic.

Definition of a Research Agenda

A research agenda articulates a set of research questions or objectives that have been identified as high priority in a specific field of study. For organizations that focus on specific diseases, research agendas often include a heterogenous group of topics that cover a wide variety of issues.

These topics may include:

♥ The genetic basis of disease
♥ Identifying signaling abnormalities that may offer promise for drug development
♥ Identification and validation of biomarkers that inform on diagnosis and/or disease progression
Improved understanding of disease phenotypes and the implication of these phenotypes for treatment
Research on care planning, care coordination, continuity of care, and optimizing patient engagement in their own care
Identifying how technology can be harnessed to enhance patient education and outcomes
Determining how to maximize physical activity and other favorable behaviors in the PC setting
Understanding and addressing mental health outcomes for PC patients and their families

The heterogeneity of research areas that are highlighted in a RA should reflect the breadth of issues that impact patients and the clinicians who care for them. Topics will include a mix of high-priority objectives that can be reasonably met in a 5-year time frame as well as goals that may require a longer time horizon to achieve.

PC Project meets with its Genetics Team once a month via web meetings in order to guide genetic testing, help with ‘unresolved cases’ and review cases who join the International PC Research Registry (IPCRR). During the monthly web meeting, cases are reviewed to try to establish a genetic testing target. If the target is not Pachyonychia Congenita, every effort is made to find a resource for testing for the patient. The members of our Genetics Team volunteer their time and are vital to the mission of PC Project. Once cases are reviewed, the committee then discusses and advises PC Project concerning goals and other actions concerning research, patients and various subject in which PC Project needs guidance.

IPCC Genetics and Steering Committee Members include:
Philip David Gard, MD
C. David Hansen, MD
Edel A. O'Toole, MD, PhD, FRCPI, FRCP
Eli Sprecher, MD, PhD
Alain Hovnanian, MD, PhD

**PC PROJECT KEY ACCOMPLISHMENTS IN 2021**

**PARTNERED WITH PALVELLA FOR PHASE 2/3 CLINICAL TRIAL**

VALO Study for K17/K6c recruited for VALO phase 3b clinical study in Jan 2021

Thanks for the tremendous support and interest this community has had in the VALO Phase 2/3 clinical trial, sponsored by Palvella Therapeutics, to evaluate the safety and effectiveness of the 3.9% rapamycin gel.

The following are some important things about this investigational drug and the trial:

- We are still on the pathway for a potential drug approval for this treatment.
♥ The VALO trials (the combined phase 2/3 and the extension study) are the farthest a treatment specifically for PC has ever gone on the path towards FDA/regulatory approval. This is amazing progress since no PC treatment was even being considered when PC Project was first started.

♥ Palvella and PC Project are working closely together on the design and implementation of the next clinical study in this journey. Patients in the VALO extension study needed to get off drug and begin to “wash out” in the event they are needed again for another trial. The extension study patients who are now phasing out of that study and getting off the drug may be understandably disappointed. Our hearts go out to each one of you. Please know you are part of a bigger picture and all your data and experiences from that study are helping to guide the next steps.

♥ The Palvella team, having participated in several meetings in Europe and the US since 2016, is acutely aware of the pain and struggles each patient faces daily and is working as fast as they can to get this next trial ready. At the same time, they will be as thoughtful as possible so that the study is designed and implemented in a way that will maximize the possibility that it will support a potential approval.

♥ The data from the previous VALO clinical trials have been meticulously gathered, analyzed, and learned from in order to prepare for future clinical trials for PC. You can find a summary of the top line VALO study results on Palvella’s website (www.Palvellatx.com) under press releases.

♥ The information of every patient who participated in any way in previous VALO studies has been needed (including the information of those who were screened out at various points in the trial) and has been extremely critical for every step in this process. Patients in the trial have performed an incredible service on behalf of the entire PC community, including their demonstration to the medical and scientific world that PC patients are willing to participate in clinical trials for treatments.

♥ Developing a drug is time consuming and extensive and almost always requires conducting more than one clinical trial. As part of this journey, as noted above, Palvella intends to run another study to further evaluate the effectiveness of this drug. This is a normal, expected process on the path to drug approval.

♥ We will advise you as soon as we know when enrollment for this next study will begin. Currently, we anticipate that adult patients with K6a, K6b, K6c, and K16 in the US and the UK with a genetically confirmed diagnosis of PC will be invited to participate. If you live in either of those countries and think you might be interested in participating, you will need to have a genetic testing report to confirm your PC. Please contact us at info@pachyonychia.org if you need a copy of your genetic testing report, or if you’ve never received a genetic diagnosis, please join the registry.

Our partners at Palvella Therapeutics are actively preparing for a phase 3 clinical trial to continue the evaluation of topical PTX-022 (Qtorin 3.9% rapamycin). The study will be held in the continental US and the UK. Patients with a genetic mutation in K6a, K6b,
K6c, or K16 willing to participate in the trial will be needed. Stay tuned for more information in the coming days.

Seeking PCers for Clinical trial – Phase 3 clinical trial US and UK.

**PC AWARENESS MONTH**

During the month of June 2021, PC Project launched the campaign, “#WeAreUltra!” for PC Awareness Month. The focus was on the fact that while PC patients may feel isolated and sometimes discouraged while living with this ultra-rare, painful disease, together, as a PC community, we needed to celebrate our ultras including our ultra-spectacular network of supporters and professionals who are ultra-committed, ultra-kind, and ultra-generous.

PCers were asked to take a photo of themselves, or something that represents you or where you are from. Send the image with a few words of encouragement for the PC community. Or finish the sentence. “PCers are ultra…” or “The PC community is ultra…” Encouraged to share their messages with social media community.

Ultra posts were published in the patient News Brief and on social media.

**GIVING TUESDAY**

Celebrated on the Tuesday following the US Thanksgiving and entering its ninth year, #GivingTuesday is a global day of charitable giving fueled by the power of social media. For the past few years, PC Project has participated in Giving Tuesday and have successfully raised money to help fund our mission of finding a cure for PC. This year, the PC awareness and fundraising campaign #PCunselfie was conducted via email and social media worldwide. Over 457 donors gave to PC Project in 2021. All donations for Giving Tuesday through the end of the year were matched 2-to-1 by an anonymous donor.

**MEETINGS ATTENDED IN 2021 FOR EDUCATING AND PROMOTING PC**

**Raising the Profile of PC**

PC Project participated in four conferences during September and October, educating the medical and scientific community about PC and encouraging new professionals to collaborate with the International Pachyonychia Congenita Consortium (IPCC).

**ESDR**—PC Project had a virtual booth at the annual European Society for Dermatological Research Meeting in September. Over 945 participants attended from 48 countries, including some key IPCC leaders.

**GLOBAL GENES**—This four day meeting was for rare disease patients, advocates, healthcare professionals, and researchers. The conference provided opportunities to connect and engage with others in the rare disease community and included more than
39 live sessions on the latest in rare disease innovations, best practices for advocating on an individual and organizational level, and actionable strategies.

**PEDRA**—This two day meeting with the Pediatric Dermatology Research Alliance focused on building bridges to develop collaborations with industry, patient advocacy groups, and basic and translational scientists.

PC Project had a digital booth and a scientific poster which was chosen to be featured for discussion. This poster (see below) using data from the registry, demonstrates that if a child does not have calluses on the bottoms of their feet by age 15, they most likely do not have PC. Because pediatric dermatologists may be the first to diagnose a young PC patient, correct information about PC is critical.

PC Project and PC was also the focus of a discussion in a genetics session. Pachyonychia Congenita was even an answer to one of the questions in the conferences game. Thanks to PC Advocate, Jim Rittle, for serving on the PeDRA Patient Advocacy Committee as PC Project’s representative.

**NIAMS COALITION OUTREACH AND EDUCATION**— At this meeting, PC Project shared a PC awareness poster (next page), only one of two about skin diseases. We hope to raise the profile of PC at NIAMS and the NIH and let them know this is a serious disease with unmet needs that has a supportive community. Special thanks to volunteer, Rutu Patel, and her team at Bond and Matter for helping PC Project with the posters for these meetings.

**RESEARCH ARTICLES PUBLISHED**

During 2021, PC Project and IPCC Members collaborated in publishing numerous research articles ([https://www.pachyonychia.org/research-articles/](https://www.pachyonychia.org/research-articles/)) in leading journals including a special PC edition of the March 2020 British Journal of Dermatology and the following:


2021 INCOME AND EXPENSE REPORT FROM 990 TAX RETURN

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<th>Description</th>
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<td>Contributions</td>
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<td>Investment Income</td>
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<td>Investment Gain/Loss</td>
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<td>Program Expenses</td>
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<td>Fundraising Expenses</td>
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<td><strong>Expenses over/under income</strong></td>
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<td><strong>Net Assets 2021 Total</strong></td>
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DONATED SERVICES AND VOLUNTEERS

In 2021 PC Project was greatly benefited by the help of volunteers. There were also many hours donated by physicians, scientists and professionals who provided their services and expertise to PC Project.

<table>
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<tr>
<th>Description</th>
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<td><strong>Total</strong></td>
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<td>DONATED SERVICES</td>
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<td>Estimated Fair Market Value</td>
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<td>Physicians, Scientists and Volunteers</td>
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<td>IPCC Genetics Team &amp; Steering Meeting</td>
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<td>IPCC Meeting</td>
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Patient Support Meeting  
Program services & events  
Program services (ED salary)  

28  
92  
2080

PC PROJECT STAFF
Janice Schwartz, Executive Director
Holly A. Evans, Patient Support Officer
Joanne Udy, Bookkeeper

PC PROJECT BOARD OF TRUSTEES
Board of Trustee Members at the end of the year were:
   Jack Padovano, Chair
   Barbara Feinstein, Secretary
   C. David Hansen, MD, Medical Advisor
   Kay Dee Holmes, Trustee, Board Attorney
   Jason Hunter, Treasurer
   James Rittle, Trustee
   Janice Schwartz, Trustee

Board of Trustee meetings in 2021 were held February 19, May 15, August 13, and November 5.