



# Pachyonychia Congenita Project

*Fighting for a cure. Connecting & helping patients. Empowering research.*

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## 2019 ANNUAL REPORT FOR PACHYONYCHIA CONGENITA PROJECT

### ABOUT PACHYONYCHIA CONGENITA

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 116 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:

Fighting for a cure. Connecting and Helping Patients. Empowering research.

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 2019 PROGRAMS AND SERVICES

### INTERNATIONAL PACHYONYCHIA CONGENITA 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 1343 patients in the IPCRR at the end of 2019 with 977 of those being genetically confirmed with PC. The following statistics were noted for the IPCRR in 2019:

- 137 patients contacted PC Project for the first time
- 133 saliva kits were sent for genetic testing
- 112 individuals received genetic testing results

### PATIENT SUPPORT MEETING

**Boston, MA, USA.** PC Patient Support Meeting 2019 The 18th Annual Pachyonychia Congenita Patient Support Meeting (PSM) was held June 20-22, 2019 in Boston, MA. Sixty-three PC patients, along with their loved ones, clinicians, scientists and drug developers spent a day and a half learning from one another about how to best live life with PC. A big thank you to our PC advocates and other volunteers who helped with registration, gave presentations, and led group discussions, including teen and children's discussions. Some program highlights included having patients group according to their affected gene. Patients who wished to could show visiting clinicians

their feet and other PC symptoms. This educated physicians about PC in a profound and easy way. Other program discussions and topics included PC research, clinical trials, PC pain, the social and emotional impacts of PC, being a loved one of a PCer, taking control of our health, how to help children and teenagers navigate life with PC, and being stronger than PC.

### 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

PC Project hosted an impressive group of approximately 60 scientists, clinicians and drug developers from around the world who presented and collaborated on PC related research at the International PC Consortium (IPCC) Symposium in Chicago, May 7-8, 2019. With 18 speakers and even more interested researchers in attendance, PC Project is humbled to have this group on its team. As one key researcher said, "This is a special group and it's a privilege to be part of it." After the IPCC Symposium, the PC Medical and Scientific Advisory Board, a smaller group that guides PC Project, met to discuss projects, goals and next steps for PC research. Following that meeting, PC Project had a table at the larger Society of Investigative Dermatology Meeting.

### IPCC GENETICS TEAM AND IPCC STEERING COMMITTEE

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 2019**

### **PARTNERED WITH PALVELLA FOR NEARLY FULL ENROLLMENT FOR PHASE 2/3 CLINICAL TRIAL**

PC Project and Palvella continued to partner in 2019 to recruit and enroll PC patients in the Phase 2/3 study evaluating PTX-022 (novel, high strength topical rapamycin, optimized for dermal targeting) for the treatment of PC.

In January, Palvella invited all clinical trial coordinators and vendors who would play key roles in the study to Salt Lake City for a study kick off retreat. PC Project representatives were invited to educate about PC and PC Project before the trial was launched. Official recruitment efforts began in April 2019.

By the end of 2019, the study was on track to have enrollment close by the end of February 2020. In December 2019, some PC patients had already entered Phase 3 of the study. Interest from the PC community continued to remain strong with more than 75 patients having entered the study as of mid-December, with nine clinical study sites actively enrolling. The trial saw intense engagement and collaboration from all clinical study investigators, PC Project and PC patients.

Some of the requirements for participation included:

- Must live in the United States (and later in the year, opened to Canada)
- Must be at least 18 years of age or older
- Have a clinical diagnosis of PC, genetically confirmed to involve any of three keratin genes KRT6A, KRT6B, or KRT16
- Have not participated in a clinical research study in the past sixty days
- On a daily basis during the study, wear an activity monitor and answer questions on a smartphone-based app. Participants must be, in the opinion of the study doctor, able to understand the study, cooperate with the study procedures and willing to return to the clinic for all of the required visits.

PC Project spent considerable time and resources to help recruit patients, provide genetic testing and genetic testing reports, coordinate with the trial sites, and collaborate with Palvella team members for successful clinical trial recruitment and enrollment.

### PC LOVE BUILDERS CAMPAIGN

During the month of April 2019, PC Project encouraged its worldwide community to become part of the PC LOVE BUILDERS, a group of monthly donors who help sustain the work of PC Project. 12 new monthly donors joined to offer consistent support to the mission of PC Project, bringing our total to 60 monthly donors.

### PC AWARENESS MONTH

During the month of June 2019, PC Project launched the campaign, “Together, We Are Stronger Than PC” for PC Awareness Month. The focus was on the fact that while PC patients may feel isolated and sometimes discouraged while living with this rare, painful disease, together, as a PC community, “We are stronger than PC.”

Questions patients were asked to consider that month were:

- How can we be, and stay, strong in the face of PC?
- Why should I share my PC story?
- Am I ready to talk about it?
- Why does my involvement matter?
- Why should I give?
- How are we stronger than PC?

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

### NEW PC SYMPTOMS ANALYZED

Two issues many PC patients deal with that aren't typically associated with PC are deep itching and neurovascular-like structures in the calluses. As new patients join the registry and share their experiences, PC Project is ever-learning about PC and how it affects patients.

Because of this anecdotal evidence, in October 2019, PC Project surveyed its genetically confirmed patient community with an IRB approved registry addendum. With 350 responses, 69% of patients reported they experience deep itching, an itch that is under the calluses that is difficult to reach. Furthermore, 62% of patients reported having neurovascular-like structures. In truth, what they are exactly is not known. What is known is they significantly increase pain and make it difficult for patients to trim their calluses.

These two symptoms of PC are not typically talked about in PC discussions but are clearly a part of life for a significant portion of the PC population. Data from the series of questions about these issues are now being studied and will be published.

Thanks to all patients who participated in the questionnaire addendum to help researchers broaden their understanding of PC.

### GIVING TUESDAY

Celebrated on the Tuesday following the US Thanksgiving and entering its eighth 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 “Stronger Than PC” was conducted via email and social media worldwide before and on December 3, 2019. Over 340 donors gave to PC Project. All donations for Giving Tuesday through the end of the year were matched 2-to-1 by an anonymous donor.

## MEETINGS ATTENDED IN 2019 FOR LEARNING AND PROMOTING PC

### **Society of Investigative Dermatology Annual Meeting**

PC Project hosted a display table to share information about PC with scientists attending the SID meeting. PC Project was already in Chicago for the Annual IPCC Symposium and stayed an extra day for networking purposes.

### **European Society for Dermatological Research (ESDR)**

French PC patient, Marie Jose Billeau, and her daughter, Alice, represented Pachyonychia Congenita and our French PC group, Le Coeur Au Pied, at the European Society for Dermatological Research (ESDR) annual meeting in Bordeaux, France on September 19-20, 2019. Marie and Alice shared materials about PC in French and in English with scientists from around the world and met with members of PC Project’s Medical and Scientific Advisory Board (MSAB).

In addition, they received the contact information for new researchers who are interested in being connected to PC Project. Note: Le Coeur Au Pied is a group for French PCers which supports PC Project. The president is Sylvie Cierpucha. This group is exceptionally effective at patient recruitment for the IPCRR (patient registry), information sharing and fundraising for PC Project.

### **American Academy of Dermatology Annual Legislative Conference**

Parents of a PC patient, Barbara Feinstein and Aaron Klein represented PC Project at the American Academy of Dermatology’s Annual Legislative Conference, held September 8-10, 2019 in Washington, DC. The meeting brought together more than 200 dermatologists and representatives of patient advocacy organizations to lobby Congress on issues affecting dermatology and patients. In addition to raising awareness of pachyonychia congenita among Members of Congress, doctors and patient groups, Barbara and Aaron also pressed legislators, including Representative Jamie Raskin (D-MD) to prioritize funding for rare diseases like PC.

**PeDRA Annual Meeting** – November PC Project participated at the PeDRA (Pediatric Dermatology Research Alliance) Annual Conference in Chicago, November 14-16, 2019. PC advocate and patient, Jim Rittle, attended the patient track, along with his daughter, Kaelyn.

Janice Schwartz, from PC Project, spoke on how the Externally-led Patient Focused Drug Development Meeting with FDA has benefitted PC Project. This gave PC Project an excellent platform to share with all attendees the strength of the registry and the

commitment of PC patients and their families to finding treatments for PC. Janice also participated on a panel with other patient advocate leaders.

PC Project presented a poster and had a PC display table. These encouraged networking and provided opportunities to discuss PC with many clinicians, researchers and representatives of drug companies. The work to educate others about PC will always be a priority for PC Project.

### RESEARCH ARTICLES PUBLISHED

During 2019, PC Project and IPCC Members collaborated in publishing numerous research articles (<https://www.pachyonychia.org/research-articles/>) in leading journals including:

- ♥ Samuelov L, Smith FJD, Hansen CD, Sprecher E. *Revisiting pachyonychia congenita: a case-cohort study of 815 patients*. Br J Dermatol. 2019 Dec 10.
- ♥ Leube RE, Schwarz N. *Current mysteries of pachyonychia congenita*. Br J Dermatol. 2019 Dec 8. doi: 10.1111/bjd.18688.
- ♥ Goldberg I, Mashiah J, Kutz A, Derowe A, Warshauer E, Schwartz ME, Smith F, Sprecher E, Hansen CD. *Symptomatic mucosal involvement in pachyonychia congenita: the challenges in infants and young children*. Br J Dermatol. 2019 Nov 28.
- ♥ Funk T, Hansen CD, Paller A, O'Toole EA. *Update on Pachyonychia Congenita Research*. Br J Dermatol. 2019 Oct 24.
- ♥ Mohamad J, Samuelov L, Ben-Amitai D, Malchin N, Sarig O, Sprecher E. *PLACK syndrome shows remarkable phenotypic homogeneity*. Clin Exp Dermatol. 2019 Jan 17.
- ♥ Wright JT, Fete M, Schneider H, Zinser M, Koster MI, Clarke AJ, Hadj-Rabia S, Tadini G, Pagnan N, Visinoni AF, Bergendal B, Abbott B, Fete T, Stanford C, Butcher C, D'Souza RN, Sybert VP, Morasso MI. *Ectodermal dysplasias: Classification and organization by phenotype, genotype and molecular pathway*. Am J Med Genet A. 2019 Jan 31.
- ♥ Zieman AG, Poll BG, Ma J, Coulombe PA. *Altered keratinocyte differentiation is an early driver of keratin mutation-based palmoplantar keratoderma*. Hum Mol Genet. 2019 Jul 1;28(13):2255-2270.
- ♥ Koren A, Sprecher E, Reider E, Artzi O. *A treatment protocol for botulinum toxin injections in the treatment of pachyonychia congenita-associated keratoderma*. Br J Dermatol. 2019 May 25.

- ♥ Zieman AG, Coulombe PA. *Pathophysiology of pachyonychia congenita-associated palmoplantar keratoderma: New insight into skin epithelial homeostasis and avenues for treatment*. Br J Dermatol. 2019 Apr 25.
- ♥ Lehmann SM, Leube RE, Schwarz N. *Keratin 6a mutations lead to impaired mitochondrial quality control*. Br J Dermatol. 2019 Apr 20.
- ♥ Vetter A, Magin TM. *Old mitochondria accumulate in pachyonychia congenita*. Br J Dermatol. 2019 Sep 30.
- ♥ Theocharopoulos I, O'Toole EA. *Stopping pachyonychia congenita plantar pain with a statin?* Br J Dermatol. 2019 Sep;181(3):446-447.
- ♥ Daroach M, Dogra S, Bhattacharjee R, Tp A, Smith F, Mahajan R. *Pachyonychia congenita responding favorably to a combination of surgical and medical therapies*. Dermatol Ther. 2019 Jul 31:e13045.
- ♥ Gaucher S, Lwin SM, Titeux M, Abdul-Wahab A, Pironon N, Izmiryan A, Miskinyte S, Ganier C, Duchatelet S, Mellerio JE, Bourrat E, McGrath JA, Hovnanian A. *EBGene trial: Patient pre-selection outcomes for the European GENEGRAFT ex vivo phase I/II gene therapy trial for recessive dystrophic epidermolysis bullosa*. Br J Dermatol. 2019 Sep 26.
- ♥ Walker AL, Denis A, Bingham RP, Boulliot A, Edgar EV, Ferrie A, Holmes DS, Laroze A, Liddle J, Fouchet MH, Moquette A, Nassau P, Pearce AC, Polyakova O, Smith KJ, Thomas P, Thorpe JH, Trottet L, Wang Y, Hovnanian A. *Design and development of a series of borocycles as selective, covalent kallikrein 5 inhibitors*. Bioorg Med Chem Lett. 2019 Oct 15;29(20):126675.
- ♥ Elhaji Y, Hedlin C, Nath A, Price EL, Gallant C, Northgrave S, Hull PR. *AAGAB Mutations in 18 Canadian Families With Punctate Palmoplantar Keratoderma and a Possible Link to Cancer*. J Cutan Med Surg. 2019 Sep 16:1203475419878161.
- ♥ Temel ŞG, Karakaş B, Şeker Ü, Turkgenç B, Zorlu Ö, Sarıcaoğlu H, Oğur Ç, Kütük Ö, Kelsell DP, Yakıcıer MC. *A novel homozygous nonsense mutation in CAST associated with PLACK syndrome*. Cell Tissue Res. 2019 Aug 7.
- ♥ Koh R, Szeverényi I, Lee B, Denil SLIJ, Lim SYJ, Benny PA, Grasset N, Tan BK, Lane EB. *Oxygen-Mediated Control of the Keratinocyte Proliferation-Differentiation Axis*. J Invest Dermatol. 2019 Jul 5. pii: S0022-202X(19)31852-4.
- ♥ Lilly E, Strickler M, Milstone LM, Bunick CG. *Alterations in connexin 26 protein structure from lethal keratitis-ichthyosis-deafness syndrome mutations A88V and G45E*. J Dermatol Sci. 2019 Sep;95(3):119-122. doi: 10.1016/j.jdermsci.2019.07.002. Epub 2019 Jul 10.



- ♥ Atzmony L, Lim YH, Hamilton C, Leventhal JS, Wagner A, Paller AS, Choate KA. *Topical cholesterol/lovastatin for the treatment of porokeratosis: a pathogenesis-directed therapy.* J Am Acad Dermatol. 2019 Aug 23.

## 2019 INCOME AND EXPENSE REPORT FROM 990 TAX RETURN

<b>Total 2019 Income</b>	<b>\$ 470,023</b>	[Page 9, Line 12a]
Contributions	\$ 419,420	[Page 9, Line 1f]
Fundraising Events	\$ 0	[Page 9, Line 1c \$0 plus Line 8c \$0]
Investment Income	\$ 44,883	[Page 9, Line 3]
Investment Gain/Loss	\$ - 586	[Page 9, Line 7da]
<b>2019 Total Expenses</b>	<b>\$ 301,076</b>	[Page 10, Line 25, Col A]
Program Expenses	\$ 254,252	[Page 10, Line 25, Col B]
General Expenses	\$ 29,974	[Page 10, Line 25, Col C]
Fundraising Expenses	\$ 16,850	[Page 10, Line 25, Col D]
<b>Expenses over/under income</b>	<b>\$ 168,947</b>	[Page 1, Line 19, Current year]
<b>Net Assets 2019 Total</b>	<b>\$2,138,023</b>	[Page 1, Line 22, Current year]

## DONATED SERVICES AND VOLUNTEERS

In 2019 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.

	<b>Total</b>
DONATED SERVICES	2638 hours =
<i>Estimated Fair Market Value</i>	<i>\$190,900.00</i>
<b>Physicians, Scientists and Volunteers</b>	<b>Hours</b>
IPCRR patient consultations	17
IPCC Genetics Team & Steering Meeting	81
IPCC Meeting	69
Patient Support Meeting	100
Program services & events	297
Program services (ED salary)	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 2019 were held February 1, May 7, September 27, and November 25.