



Pachyonychia Congenita Project

Fighting for a cure. Connecting & helping patients. Empowering research. Partnering with industry.

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2020 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 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:

Fighting for a Cure. Connecting & Helping Patients. Empowering Research. Partnering with Industry.

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 2020 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 1454 patients in the IPCRR at the end of 2020 with 1037 of those being genetically confirmed with PC.

- 118 patients contacted PC Project for the first time
- 64 individuals received genetic testing results

NOTE: COVID-19 touched all of our lives in some way and during the uncertain time, PC Project continued to carry on it's mission. Some of PC Project's biggest annual events were canceled in 2020. PC Project will always be good global citizens and put the safety and health of our PC and broader communities first. However, PC did hear some good from the pandemic, as PCers didn't have to commute to work, school etc and not wear appropriate shoes helped many PC feet to do better.

PATIENT SUPPORT MEETINGS

Roissy, France. The scheduled in person PC Patient Support Meeting 2020 was cancelled due to the COVID-19 pandemic.

Virtual PC Town Hall Meetings – On March 19, 2020, PC Project held the first-ever PC digital town hall meeting right after a 5.7 magnitude earthquake shook PC Project headquarters in Utah. The meeting gave an overview of PC and PC Project, the burden of living with PC, and shared some of the exciting developments that have been happening, including the VALO trial, current research efforts, and more. This was a free web meeting that lasted 45 minutes and 67 PCers registered to attend. One PC patient commented on the meeting, "Thank you for all you do on our behalf. I was moved to tears a number of times."

On November 20, 2020, again to connect with the PC community during the pandemic, PC Project held a second PC town hall meeting to update patients and other stakeholders on the activities of PC Project during the past months of the pandemic. Over 73 PCers attended.

Virtual Meeting for PC Teens.- On November 21, 2020, 24 PC teens from all over the world gathered virtually to discuss a teenager's life with PC, how they cope, and what

their hopes and dreams are for the future. Four teenagers with PC presented and all participated in the discussion.

PC PROJECT PUBLICATIONS

PC NewsBrief. Each month PC Project sent out its monthly newsletter, the PC News Brief, to over 2000 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

Scottsdale, AZ. The annual IPCC Symposium, scheduled for May 2020 was cancelled due to COVID-19. However, PC Project still had a presence at the Society for Investigative Dermatology Meeting. (See below.)

MEETINGS ATTENDED IN 2020 FOR EDUCATING AND PROMOTING PC

Rare Disease Week

PC Project took part in Rare Disease Week in Washington, DC February 25-28, 2020, joining more than 800 advocates to barnstorm Capitol Hill in support of greater funding for rare diseases. PC Project representatives met with members of congress and their staff in the House and Senate on Pachyonychia Congenita. A PC poster about the burden of Pachyonychia Congenita was shared with attendees.

Society of Investigative Dermatology Annual Meeting

The Society for Investigative Dermatology (SID) Annual Meeting was held virtually this year. Included were presentations from two young scientists who used deidentified data from the International PC Research Registry (IPCRR) to study specific symptoms about PC.

1. Novel Distinctions in the Profiles, Impact, and Management of Nail Disease in Pachyonychia Congenita Subtypes Presenting: Albert Wu, MS, New York Medical College—Mentor: Sheri Lipner, MD, PhD, Weill Cornell Medical Center

2. Neurovascular Structures on Feet in Pachyonychia Congenita Presenting: Xiang Li Tan, MBBS, BSc(Hons), Queen Mary University of London Mentor & Session Chair: Edel O'Toole, MD, PhD, FRCPI, FRCP, Queen Mary University of London

PC Project and IPCC members are keen to encourage young scientists and doctors to be involved in PC Project activities and research projects.

Watch the recording at [https://www.pachyonychia.org/townhall/ PC Teen Meeting](https://www.pachyonychia.org/townhall/PC%20Teen%20Meeting)— AADA Virtual Legislative Conference - PC Project participated in the American Academy of Dermatology Association's Virtual Legislative Conference in September, and talked one-on-one with representatives of the US Congress and Senate about the important issues facing those who suffer from rare diseases like PC. Global Genes Virtual Summit – PC Project attended and was reminded that the number one recommendation for attracting researchers and drug developers is to have a patient registry.

PeDRA Annual Meeting – PC Project had a virtual booth and two posters in collaboration with Palvella, at the Pediatric Dermatology Research Alliance Annual Conference. Because patients continue to join the registry as adults, having a presence and raising PC awareness among clinicians who can potentially make the earliest diagnoses of PC is important for PC Project.

IPCC GENETICS TEAM AND IPCC STEERING COMMITTEE

PC Project meet with its Genetics Team once a month via web meetings to guide genetic testing, help with 'unresolved cases' and review cases of patients who join the International PC Research Registry (IPCRR). The members of our Genetics Team volunteer their time and are vital to the mission of PC Project. Once registry cases are reviewed, the committee then discusses and advises PC Project concerning goals and other actions concerning research, patients, and various subjects in which PC Project needs guidance.

IPCC Genetics and Steering Committee Members include:

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 2020

PARTNERED WITH PALVELLA FOR PHASE 2/3 CLINICAL TRIAL

PC Project and Palvella continued to partner in 2020 to fully 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 February Palvella's Board came to Utah to talk directly with PC Project representatives. This gave PC Project an opportunity to answer questions, share

accomplishments of our patient organization, and help these professionals better understand the burden of living with PC.

In March 2020, Palvella in a press released announced the completion of enrollment for the study. Wes Kaupinen, President and Chief Executive Officer of Palvella stated, “The unwavering commitment of the clinical investigators, study coordinators and our partners at PC Project to achieve full enrollment of the VALO study has brought us all one step closer towards achieving this objective. We look forward to reporting top-line study results in the fourth quarter of 2020.”

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 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.

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 to raise funding for the PC mission. In 2020, the PC Project launched the #Worst2First4PC Campaign. The PC community answered the following questions: "What is the Worst thing about PC?" And, "What is the First thing you'll do when there is a cure?" Patients and caregivers all over the world participated and shared their powerful stories and dreams of what they wish they could do without the pain of PC. Over 512 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.

RESEARCH ARTICLES PUBLISHED

The March 2020 Rare Disease issue of the British Journal of Dermatology contained numerous articles on Pachyonychia Congenita. This strong emphasis on PC in an accredited journal was the result of collaborative efforts of members of the International PC Consortium that are comprised of scientists and physicians worldwide who work together to advance PC related research. A number of the articles were made possible because of the information provided by PC patients who are part of the powerful International PC Research Registry.

Articles published about PC during 2020 included the following:

- ♥ Pavlovsky M, Peled A, Samuelov L, Malki L, Malovitski K, Assaf S, Mohamad J, Meijers O, Eskin-Schwartz M, Sarig O, Sprecher E. Molecular epidemiology of pachyonychia congenita in the Israeli population. *Clin Exp Dermatol*. 2021 Jun;46(4):663-668. doi: 10.1111/ced.14509. Epub 2020 Dec 20. PMID: 33190296.
- ♥ Mathews J, Hansen CD, Chandrashekar L. Homozygous dominant missense mutation in Keratin 6b leading to severe pachyonychia congenita. *Clin Exp Dermatol*. 2021 Mar;46(2):410-412. doi: 10.1111/ced.14494. Epub 2020 Dec 10. PMID: 33301203.
- ♥ Liu J, Zhong W, Yu B, Lin Z, Zheng Y, Hu X. Generalized bullae in a young girl with KRT6A-related pachyonychia congenita. *Pediatr Dermatol*. 2020 Sep;37(5):974-976. doi: 10.1111/pde.14285. Epub 2020 Jul 14. PMID: 32662074.

- ♥ Steen K, Chen D, Wang F, Majumdar R, Chen S, Kumar S, Lombard DB, Weigert R, Zieman AG, Parent CA, Coulombe PA. A role for keratins in supporting mitochondrial organization and function in skin keratinocytes. *Mol Biol Cell*. 2020 May 15;31(11):1103-1111. doi: 10.1091/mbc.E19-10-0565. Epub 2020 Mar 26. PMID: 32213122; PMCID: PMC7353162.
- ♥ Stewart CL, Takeshita J, Hansen CD, Rubin AI. The histopathological features of the nail plate in pachyonychia congenita. *J Cutan Pathol*. 2020 Apr;47(4):357-362. doi: 10.1111/cup.13630. Epub 2020 Jan 9. PMID: 31845382.
- ♥ Steele L, O'Toole EA. Pachyonychia congenita, a paradigm for rare skin disorders. *Br J Dermatol*. 2020 Mar;182(3):521-522. doi: 10.1111/bjd.18817. PMID: 32107781.
- ♥ Mordaunt DA. Sharing (data) is caring for patients with pachyonychia congenita. *Br J Dermatol*. 2020 Mar;182(3):537. doi: 10.1111/bjd.18850. Epub 2020 Jan 20. PMID: 31960408.
- ♥ Youssefian L, Vahidnezhad H. Management of symptomatic mucosal involvement in paediatric pachyonychia congenita. *Br J Dermatol*. 2020 Mar;182(3):536-537. doi: 10.1111/bjd.18849. Epub 2020 Jan 20. PMID: 31957008.
- ♥ Thomas BR, Sahota A. Pachyonychia congenita and botulinum toxin. *Br J Dermatol*. 2020 Mar;182(3):531-532. doi: 10.1111/bjd.18784. Epub 2019 Dec 25. PMID: 31875943.
- ♥ Samuelov L, Smith FJD, Hansen CD, Sprecher E. Revisiting pachyonychia congenita: a case-cohort study of 815 patients. *Br J Dermatol*. 2020 Mar;182(3):738-746. doi: 10.1111/bjd.18794. Epub 2020 Jan 14. PMID: 31823354.
- ♥ Leube RE, Schwarz N. Current mysteries of pachyonychia congenita. *Br J Dermatol*. 2020 Mar;182(3):525-526. doi: 10.1111/bjd.18688. Epub 2019 Dec 8. PMID: 31814103.
- ♥ Goldberg I, Mashiah J, Kutz A, Derowe A, Warshauer E, Schwartz ME, Smith F, Sprecher E, Hansen CD. Symptomatic mucosal involvement in pachyonychia congenita: challenges in infants and young children. *Br J Dermatol*. 2020 Mar;182(3):708-713. doi: 10.1111/bjd.18742. Epub 2019 Dec 25. PMID: 31777952.
- ♥ Funk T, Hansen CD, Paller A, O'Toole EA. Update on pachyonychia congenita research. *Br J Dermatol*. 2020 Mar;182(3):788-789. doi: 10.1111/bjd.18630.

Epub 2019 Dec 13. PMID: 31648361.

- ♥ Vetter A, Magin TM. Old mitochondria accumulate in pachyonychia congenita. Br J Dermatol. 2020 Mar;182(3):529-530. doi: 10.1111/bjd.18465. Epub 2019 Sep 30. PMID: 31571193.
- ♥ 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. 2020 Mar;182(3):671-677. doi: 10.1111/bjd.18169. Epub 2019 Sep 8. PMID: 31127950.
- ♥ Zieman AG, Coulombe PA. Pathophysiology of pachyonychia congenita-associated palmoplantar keratoderma: new insights into skin epithelial homeostasis and avenues for treatment. Br J Dermatol. 2020 Mar;182(3):564-573. doi: 10.1111/bjd.18033. Epub 2019 Jul 24. PMID: 31021398; PMCID: PMC6814456.
- ♥ Lehmann SM, Leube RE, Schwarz N. Keratin 6a mutations lead to impaired mitochondrial quality control. Br J Dermatol. 2020 Mar;182(3):636-647. doi: 10.1111/bjd.18014. Epub 2019 Jul 21. PMID: 31004504.
- ♥ Zhang B, Sun L, Fu X, Yu G, Liu H, Zhang F. Mutation analysis of the KRT17 gene in steatocystoma multiplex and a brief literature review. Clin Exp Dermatol. 2020 Jan;45(1):132-134. doi: 10.1111/ced.14030. Epub 2019 Sep 17. PMID: 31237972.

2020 INCOME AND EXPENSE REPORT FROM 990 TAX RETURN

Total 2020 Income	\$ 641,236	[Page 9, Line 12a]
Contributions	\$ 541,574	[Page 9, Line 1f]
Grants	\$ 15,600	[Page 9, Line 1e]
Fundraising Events	\$ 0	[Page 9, Line 1c \$0 plus Line 8c \$0]
Investment Income	\$ 71,463	[Page 9, Line 3]
Investment Gain/Loss	\$ 12,381	[Page 9, Line 7da]
Other	\$ 218	[Page 9, Line 11aa]
2020 Total Expenses	\$ 189,324	[Page 10, Line 25, Col A]
Program Expenses	\$ 148,762	[Page 10, Line 25, Col B]
General Expenses	\$ 29,193	[Page 10, Line 25, Col C]
Fundraising Expenses	\$ 11,369	[Page 10, Line 25, Col D]
Expenses over/under income	\$ 451,912	[Page 1, Line 19, Current year]
Net Assets 2020 Total	\$2,735,430	[Page 1, Line 22, Current year]

DONATED SERVICES AND VOLUNTEERS

In 2020 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.

	Total
DONATED SERVICES	2484 hours =
<i>Estimated Fair Market Value</i>	<i>\$176,200.00</i>
Physicians, Scientists and Volunteers	Hours
IPCRR patient consultations	5
IPCC Genetics Team & Steering Meeting	123
IPCC Meeting	0
Patient Support Meeting	0
Program services & events	276
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 2020 were held February 21, May 22, September 18, and November 13.