



# Pachyonychia Congenita Project

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

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## 2017 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 110 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.

### 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 and family members to make a difference for those suffering with Pachyonychia Congenita. PC Project makes effective use of the limited budget to accomplish all possible for those with PC who live in the USA and in over 60 countries around the world.

### 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 2017 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 1867 patients in the IPCRR at the end of 2017 with 792 of those being genetically confirmed with PC. The following statistics were noted for the IPCRR in 2017:

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

### PATIENT SUPPORT MEETING SALT LAKE CITY, UTAH

PC Project held its annual Patient Support Meeting, June 15-17 at the R&L Hotel in downtown Salt Lake City, UT. There were 89 attendees including 36 PC patients. The theme of the meeting was PC: The Power of You. The presentations and panel discussions covered a vast array of topics relevant to those living with PC including news about ongoing research into treatments for PC, PC pain, care tips and day-to-day life with PC. One of the highlights of the meeting was the focus group discussion held on Saturday morning led by James Valentine and Robyn Hickerson. This intense and often emotional discussion gave PCers the chance to share in great detail the ways that PC impacts their lives. The information gathered and stories shared will help to gain recognition of PC by the FDA, and to lead to future clinical studies. A children's program coincided with the main meeting filled with games, discussions, laboratory experiments and a PC Kids Discussion led by Janice Schwartz.

### 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.** All members of the International Pachyonychia Congenita Consortium (IPCC) receive the quarterly published IPCC News Brief. 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

The IPCC Annual Symposium was held in Portland, Oregon April 25-26, 2017. The theme was "New Horizons in Keratoderma Research." In the audience of over 35 scientists and physicians, there were physicians and scientists who have continuously worked on PC over many years. In addition, we welcomed new physicians and scientists who focus on different keratoderma research to join the IPCC meeting to help expand our horizon and reach new heights of research and discovery. Presentations included Horizons in PC research, Broadening our horizons to tackle the problem of keratoderma, The clinical horizon – similarities and differences between PC and other PPKs, The molecular horizon – the genes and proteins involved in PC and PPKs, Translational horizons, Mouse models of PC and PPK, Cellular reprogramming and gene editing therapy in genodermatology, Topical Rapamycin-Update on PC Project, Palvella Therapeutic's collaboration to rapidly advance towards the next clinical study, Small molecular approaches to treating pathogenic keratin aggregation, Scanning the PC pain and itch horizons, Pain in PC and other PPKs: Clinical and Basic Science insights, From inflammation to therapy: novel insights from cell biology, How does Palmoplantar epidermis know that it is palmoplantar?, and a Toward new horizons-brainstorming session. The discussion during brainstorming session included Pain in PC, Therapeutic tractability of PPKs, Drug repurposing in PPKs, Oligonucleotide therapeutics for PPKs and the next meeting. Many discussions and collaborating came from the meeting.

### IPCC GENETICS TEAM

PC Project met with its Genetics Team once a month in order to guide genetic testing and help with 'unresolved cases'. During the monthly web meeting, cases were 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.

### IPCC GENETICS TEAM MEMBERS

Philip David Gard, MD

C. David Hansen, MD

Edel A. O'Toole, MD, PhD, FRCPI, FRCP

Frances J.D. Smith, PhD (Chair)  
Eli Sprecher, MD, PhD

### IPCC STEERING COMMITTEE

The Steering Committee conducted several conference calls as well as monthly webmeetings throughout the year to discuss clinical trials and issues governing PC Project goals and actions relating to research.

#### **IPCC Steering Committee Members:**

Philip David Gard, MD

C. David Hansen, MD

Edel A. O'Toole, MD, PhD, FRCPI, FRCP

Frances J.D. Smith, PhD

Eli Sprecher, MD, PhD (Chair)

### PC PROJECT KEY ACCOMPLISHMENTS IN 2017

#### TOPICAL SIROLIMUS

Palvella, continued to partner with PC Project in preparation for a major clinical trial with a topical Sirolimus (first developed by TransDerm). Pavella worked with James Valentine who lead a focus group-oriented patient discussion at the 2017 PC Patient Support Meeting in Salt Lake City, Utah. Palvella continued raising funds for a clinical trial and consulted with PC Project's Medical and Scientific Advisory Board. During the fall of 2017, PC patients completed an endpoint survey to help Palvella gain a better understanding of clinical endpoints and outcome measures in order to design the clinical trial.

#### ACTIVITY TRACKER AND PC PAIN APP

The fourth and final phase of the Activity Tracker and PC Pain App Study concluded at the end of January 2017. Twelve PC patients and 12 matched normal control subjects wore a Withings Activite Pop Tracker 24 hours a day. This Tracker measured steps taken each day between the PC patients and the control group. Participants also answered two questions on an APP each day about their PC Pain: 1) What was the highest plantar pain in the last 24 hours? 2) What was the average plantar pain in the last 24 hours?

The study began in Feb 2016 and the final phase ended at the end of Jan 2017. Each phase lasted at least four weeks during each season of the year. The purpose of this study was to develop validated baseline data for use in future clinical trials designed to reduce pain for PC patients by gathering a record of daily pain and activity levels for patients with Pachyonychia Congenita (PC) and normal controls matched by gender/age/location during the four different seasons of the year. The study was analyzed and showed a statistical difference between the steps walked each day by the PC patients and the control subject.

#### GIVING TUESDAY

On November 28, 2017 PC Project participated for the second time in the Giving Tuesday fundraising event. This event is recognized as a day of giving back after Black Friday and Cyber

Monday. During this event PC Project raised almost \$100,000 which was matched by an anonymous donor. Social media images were created by PC Project for followers on Facebook and Twitter to share with their friends and family. These images helped share the message of what it is like to live with Pachyonychia Congenita and how PC Project is trying to help patients suffering from this rare disease. This was the most successful fundraising effort PC Project has held.

#### PC AWARENESS MONTH

During the month of June 2017, PC Project encouraged our worldwide community to participate in PC Awareness Month. Many funds were donated, but just as important as the funds was the increase in awareness of PC. Events included a Wiggle Spring Saddle Sportive bike riding event, a RideLondon 100 to raise awareness for PC, a yard sale for a granddaughter with PC, new monthly donors, sharing the PC story with others and a birthday/anniversary party where donations to PC Project were given in lieu of gifts.

#### WORLD CONGRESS OF PEDIATRIC DERMATOLOGY

PC Project was represented in the Patient Village at the World Congress of Pediatric Dermatology in Chicago, Illinois, July 6-9, 2017. Dermatologists visited the PC Project booth, glad for the assistance of PC Project in helping their patients. Not all clinicians were aware of PC Project. These experiences bring awareness across the globe to doctors who can in turn reach their patients and introduce them to the support of PC Project.

#### OTHER MEETINGS PC PROJECT REPRESENTATIVES ATTENDED IN 2017 FOR EDUCATING AND PROMOTING PC AND PC PROJECT

Rare Disease Day  
Society for Investigative Dermatology Annual Meeting  
European Dermatology Meeting

#### RESEARCH ARTICLES PUBLISHED

During 2017, PC Project and IPCC Members collaborated in publishing numerous research articles in leading journals including:

Title: Mutations in POGlut1 in Galli–Galli/Dowling– Degos disease

Journal: Br J Dermatol.

Authors: N.J. Wilson, C. Cole, K. Kroboth, W.N. Hunter, J.A. Mann, W.H. McLean, K. Lang Kerland, H. Beltraminelli, R.A. Sabroe, N. Tiffin, G.J. Sobey, L. Borradori, E. Simpson, F.J. Smith

Volume: 176, Issue: 1, Pages: 270-274

Title: Keratin 6b variant p.Gly499Ser reported in delayed-onset pachyonychia congenita is a non-pathogenic polymorphism

Journal: J Dermatol.

Authors: F.J.D. Smith, W.H.I. McLean

Volume: 44, Issue: 12, Pages: e312

Title: Report of the 13th Annual International Pachyonychia Congenita Consortium Symposium

Journal: Br J Dermatol.

Authors: L. Rittie, R.L. Kaspar, E. Sprecher and F.J.D. Smith

Volume: 176, Issue: 5, Pages: 1144-1147

Title: Proteomic profiling of Pachyonychia congenita plantar callus

Journal: J Proteomics.

Authors: Robert H. Rice, Blythe P. Durbin-Johnson, Michelle Salemi, Mary E. Schwartz, David M. Roche, Brett S. Phinney

Volume: 165, Pages: 132-137

Title: RNA-based therapies for genodermatoses.

Journal: Exp Dermatol.

Authors: Olivier Bornert, Patricia Peking, Jeroen Bremer, Ulrich Koller, Peter C. van den Akker, Annemieke Aartsma-Rus, Anna M. G. Pasmooij, Eva M. Murauer, Alexander Nyström

Volume: 26, Issue: 1, Pages: 3-10

Title: Pachyonychia Congenita in a Toddler

Journal: Plast Reconstr Surg Glob Open.

Authors: M Mandelbaum, JW Chao, GF Rogers

Volume: 5, Issue: 5, Pages: e1325

Title: First Report of Pachyonychia Congenita Type PC-K6a in the Romanian Population

Journal: Maedica (Buchar).

Authors: Anca CHIRIAC, Cristina RUSU, Alina MURGU, Anca E CHIRIAC, Neil J WILSON, Frances J D SMITH

Volume: 12, Issue: 2, Pages: 123-126

Title: Mutations in desmoglein 1 cause diverse inherited palmoplantar keratoderma phenotypes: implications for genetic screening

Journal: Br J Dermatol.

Authors: M.L. Lovgren, M.A. McAleer, A.D. Irvine, N.J. Wilson, S. Tavadia, M.E. Schwartz, C. Cole, A. Sandilands, F.J.D. Smith and M. Zamiri

Volume: 176, Issue: 5, Pages: 1345-1350

Title: Pachyonychia Congenita: Brief Appraisal of History and Current Classification

Journal: Indian Dermatol Online J.

Authors: NK Kansal

Volume: 8, Issue: 4, Pages: 287

Title: The x-ray crystal structure of the keratin 1–keratin 10 helix 2B heterodimer reveals molecular surface properties and biochemical insights into human skin disease

Journal: J Invest Dermatol.

Authors: Christopher G. Bunick, Leonard M. Milstone

Volume: 137, Issue: 1, Pages: 142-150

Title: Cutaneous Cysts with Nail Dystrophy in a Young Female: A Classical Association

Journal: Indian J Dermatol.

Authors: Romana Ghosh, Kingshuk Chatterjee, Jayanta Kumar Barua, and Anupam Roy

Volume: 62, Issue: 6, Pages: 661-664

Title: Early severe pachyonychia congenita subtype PC-K6a with a novel mutation in the KRT6A gene

Journal: J Eur Acad Dermatol Venereol.

Authors: F Cammarata-Scalisi, K Natsuga, E Toyonaga, W Nishie, H Shimizu, A Avendano, G Da Silva, E Bellacchio, M Callea

Volume: 31, Issue: 2, Pages: e94-e96

Title: Chronic pain in Pachyonychia Congenita: evidence for neuropathic origin

Journal: Br J Dermatol.

Authors: S Brill, E Sprecher, FJD Smith, N Geva, H Gruener, H Nahman-Averbuch, R Defrin

Abstract:

Title: Keratin 17 Mutations in Four Families from India with Pachyonychia Congenita

Journal: Indian J Dermatol.

Authors: Manoj Agarwala, Pankaj Salphale, Dincy Peter, Neil J Wilson, Susanne Pulimood, Mary E Schwartz, and Frances J D Smith

Volume: 62, Issue: 4, Pages: 422-426

Title: Nail removal in pachyonychia congenita: Patient-reported survey outcomes

Journal: J Am Acad Dermatol

Authors: CMC DeKlotz, ME Schwartz, LM Milstone

Volume: 76, Issue: 5, Pages: 990-992

Title: Proteomic profiling of Pachyonychia congenita plantar callus

Journal: J Proteomics

Authors: Robert H. Rice, Blythe P. Durbin-Johnson, Michelle Salemi, Mary E. Schwartz, David M. Rocke, Brett S. Phinney

Volume: 165, Pages: 132-137

Title: A novel KRT6A mutation in a case of pachyonychia congenita from India

Journal: Indian Journal of Dermatology

Authors: Anup Kumar Tiwary, Neil J. Wilson, Mary E. Schwartz, Frances J. D. Smith

Volume: 83, Issue: 1

## PC PROJECT BOARD OF TRUSTEES

Board of Trustee Members at the end of the year 2017 were:

Janice N. Schwartz, Chair

Jack Padovano, Vice-Chair

Barbara Feinstein, Secretary

C. David Hansen, MD, Medical Advisor  
Jason Hunter, Treasurer

Board of Trustee meetings were held on June 14, September 29 and December 18 in 2017.

### PC PROJECT STAFF

Irwin McLean, Chief Executive Officer, Chief Scientific Officer  
Holly A. Evans, Patient Support Officer  
Frances J.D. Smith, Chief Geneticist  
Joanne Udy, Bookkeeper

### 2017 INCOME AND EXPENSE REPORT FROM 990 TAX RETURN

<b>Total 2017 Income</b>	<b>\$ 258,292</b>	[Page 9, Line 12a]
Contributions	\$ 199,950	[Page 9, Line 1f]
Fundraising Events		[Page 9, Line 1c \$0 plus Line 8c \$0]
Investment Income	\$ 34,420	[Page 9, Line 3]
Investment Loss	\$ 19,864	[Page 9, Line 7da]
<b>2017 Total Expenses</b>	<b>\$ 322,403</b>	
Program Expenses	\$ 273,845	[Page 10, Line 25, Col B]
General Expenses	\$ 35,750	[Page 10, Line 25, Col C]
Fundraising Expenses	\$ 12,808	[Page 10, Line 25, Col D]
<b>Expenses over/under income</b>	<b>\$ -64,111</b>	
<b>Net Assets 2017 Total</b>	<b>\$ 1,423,056</b>	[Page 1, Line 22]

### DONATED SERVICES AND VOLUNTEERS

In 2017 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 Hours

#### DONATED SERVICES

##### Physicians and Scientists

IPCR patient consultations	70
IPCC Genetics Team & Steering Meeting	51
IPCC Meeting	400
Patient Support Meeting	100
Program services & events	30
Program services (ED salary)	7 months