



Pachyonychia Congenita Project

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

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2016 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 100 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 2016 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 1730 patients in the IPCRR at the end of 2016 with 746 of those being genetically confirmed with PC. The following statistics were noted for the IPCRR in 2016:

- 122 patients contacted PC Project for the first time
- 87 saliva kits were sent for genetic testing
- 21 mouth swab kits were sent for confirming genetic testing
- 108 individuals received genetic testing results

PATIENT SUPPORT MEETINGS

Edinburgh, Scotland. PC Project held its annual Patient Support Meeting October 28-30, 2016 at the Edinburgh Capital Hotel in Edinburgh Scotland. This meeting was co-sponsored by PC Project and Professor Irwin McLean's laboratory at University of Dundee. There were 75 attendees including 32 PC Patients. PC Project awarded over £5,000 in scholarships. Many PC patients were able to experience their first Patient Support Meeting. Family members, physicians and scientists also participated in the meeting. The theme of the meeting was "*PC: The Power of You!*"

Attendees listened to presentations and participated in panels and discussion groups during the two-day event. These presentations were made by PC Project staff, scientists and physicians with topics covering PC research around the world, pain, genetics, characteristics of PC, patient adaption and fundraising. These presentations allowed attendees to receive support and the latest information on Pachyonychia Congenita from experts in PC. The patients were given the opportunity to participate in a sweat study and foot imaging during the meeting.

Panels and discussion groups were led by PC patients on employment issues with PC, managing pain, and parenting of PC kids. A special group for children with PC fun and PC focused on issues important to that age group. Also, individual discussion groups for each of the PC types and teens were held. These breakout groups and panel discussions allowed patients to lead and share their expertise with one another and at the same time have the expertise of medical experts available in the discussions.

Madrid, Spain. In addition to the regular annual patient meeting, PC Project held a one day Patient Support Meeting on October 22, 2016 at the NH Hotel Nacional and CIEMAT in Madrid Spain. There were 34 attendees including 10 PC Patients. A small group for the six children attending included activities to help them understand PC and become “PC Superheroes.” The theme was the same as the Edinburgh meeting: “*PC El Poder de Ti*” or “*The Power of You.*” Presentations were given on genetics, research and endpoints and sessions included physician questions and answers, mutation group discussions and a care discussion. Patients were able to see the CIEMAT laboratory of Fernando Larcher and Marcel del Rio, scientists who are part of the International Pachyonychia Congenita Consortium (IPCC).

PC PROJECT PUBLICATIONS

PC NewsBrief. Each month PC Project sends out its monthly newsletter, the PC NewsBrief, to over 600 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 the column ‘The Keratin Corner’ written by Dr. Emily Warshaur, 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 Scottsdale, Arizona May 10-11, 2016 with the theme “*Overcoming Welcoming Trials....*” A group of over 30 scientists and physicians were in attendance. Presentations included PC Genetics, Genodermatoses, Keratin mutation vs pathogenesis in PC, Stem cells in sweat glands, Initial report on PC pain study and clinical exam findings, Nrf2 in PC-associated palmoplantar keratoderma, The Role of miRNAs in PC, EB research, Cell-to-cell adhesion, Hydrolase inhibition, Histological features of the nail plate in PC, PC teeth study, FlexPad delivery of botulinum toxin, Properties of human keratins using x-ray crystallography, Clinical endpoints for pain, Neuroanatomy in PC patients, Topical sirolimus for Olmsted Syndrome, Proposed Clinical trials for PC, Proposed clinical trial using botulinum toxin

for PC- laser assisted drug delivery, Nail removal as a PC treatment, and Current research at the Institute of Medical Biology, Singapore.

Discussion was held throughout the meeting and goals were made to move PC Research forward. After the meeting, PC Project's Medical and Scientific Advisory Board met over a working lunch to filter what was presented in order to plan for future clinical trials.

IPCC GENETICS TEAM

PC Project is fortunate to work with our IPCC Genetics Team members to guide genetic testing and help with 'unresolved cases'. During the monthly call 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.

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	Edel A. O'Toole, MD, PhD, FRCPI, FRCP
C. David Hansen, MD	Frances J.D. Smith, PhD
Roger L. Kaspar, PhD	Eli Sprecher, MD, PhD (Chair)
W. H. Irwin McLean, PhD	

PC PROJECT KEY ACCOMPLISHMENTS IN 2016

ACTIVITY TRACKER AND PAIN APP

PC Project created a pain app to help patients track their highest level of plantar pain each day. This app was part of a WIRB approved study combining the pain app with the Withings Active Pop activity tracker. The purpose of the 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 during 2016. The 30 participants had to wear the activity tracker 24 hours a day and enter the pain app once a day. The patients were diligent and wore the tracker even when it did not match their outfits. A

substantial difference in pain was measured and lessened activity in PCers compared to the controls.

TOPICAL SIROLIMUS

Palvella is a new pharma company with a goal to go after rare disease neglected by pharmaceutical companies. An agreement was made to take over topical sirolimus (developed by TransDerm) to try and get it to patients.

WEBSITE

The PC Website was updated to make it mobile friendly. The site is now a word press website. On-campus interns from Brigham Young University translated pages of the website into French, Korean, Portuguese and Spanish.

TOOTH STUDY

The National Institute of Health is conducting an on-going study on PC Teeth. During the year PC Patients were asked to donate baby teeth, molars that are pulled, teeth that are extracted for braces or any other teeth extracted from a PC Patient. The purpose of this study is to see if a mutation in the Keratin gene KRT75 affects the enamel structure of PC Patients teeth.

JERRY SEINFELD

On January 14, 2016 Jerry Seinfeld performed in Salt Lake City, UT. He donated the proceeds of his show, \$160,000, to PC Project. This amount was matched by an anonymous donor.

GIVING TUESDAY

On November 29, 2016 PC Project participated for the first 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 over \$30,000 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 one of the most successful fundraising efforts PC Project has held.

GOLF TOURNAMENT

Our annual PC Project Golf Tournament was held on August 13, 2016 on the Crater Springs Golf Course at the Homestead Resort in Midway, Utah. There were 121 golfers who enjoyed 18 holes of golf, lunch, and a silent auction and raffle. Members of our Board of Trustees, International PC Consortium (IPCC) and of our PC Project community were in attendance. Over \$8,200 was raised by this event. The event raised also increased awareness of Pachyonychia Congenita among golfers who learned about PC for the first time.

PATIENT ADVOCATE TRAINING

PC Project held a US Patient Advocate Training May 2016 in connection with the 2016 IPCC meeting. Eight PC patients teamed up with eight IPCC members for a four-hour training. The in-person trainings were preceded by five webinar training meetings.

In Oct 2016, PC Project held a similar Foreign Patient Advocate Training in connection with the 2016 Patient Support Meeting in Edinburgh. Advocate training was funded by PC Project and by a \$4,800 Global Genes RARE Patient Impact Grant award.

The PC Advocate Team now consists of 18 members who either have PC or who have a child with PC. PC Advocates will be able to represent PC Project at meetings, government offices, educational outreach efforts and fundraising functions. This training also educated advocates to provide support to other PC patients and their family members.

GRUNENTHAL PATIENT DAY

PC Project was invited to again attend the Grunenthal Pharmaceuticals Patient Day on June 1, 2016 in New York City. Grunenthal Pharmaceuticals is one of the largest pharmaceutical companies in the world and focuses on pain. Mary Schwartz and Janice Schwartz presented on PC and living with PC. That evening, six PC patients were invited to a Patient reception at the Friar Club in Manhattan. Dr. Michael Polydefkis met with these patients and conducted pain tests that were later published.

PC AWARENESS MONTH

During the month of June 2016, PC Project encouraged our worldwide community to participate in PC Awareness Month. There was a good response to this request and funds for PC Project were raised by a Fire Walk, PC t-shirt sales, Cans-for-a-Cause, garage sales, cupcake sales and bike club rides. Many funds were donated, but just as important as the funds is the increase in awareness of PC generated by the events.

MEETINGS ATTENDED IN 2016 FOR LEARNING AND PROMOTING PC

Rare Disease Day
AADA CSD Development Day on the Hill
NORD Rare disease meeting
Grunenthal Meeting
Utah Life science Summit
UNA Meeting
Global Genes Patient Advocate Summit
Society for Investigative Dermatology Annual Meeting
European Dermatology Meeting
World Dermatology Conference

RESEARCH ARTICLES PUBLISHED

During 2016, PC Project and IPCC Members collaborated in publishing numerous research articles in leading journals including:

Peripheral neuropathic changes in pachyonychia congenita. Pan B, Byrnes K, Schwartz M, Hansen CD, Campbell CM, Krupiczkoj M, Caterina MJ, Polydefkis M. Pain. 2016 Dec;157(12):2843-2853.

Pachyonychia Congenita: New Classification and Diagnosis

Agarwala MK, Schwartz ME, Smith FJ. Indian J Dermatol. 2016 Sep-Oct;61(5):567. doi: 10.4103/0019-5154.190110. No abstract available.

Oxidative stress and dysfunctional NRF2 underlie pachyonychia congenita phenotypes. Kerns ML, Hakim JM, Lu RG, Guo Y, Berroth A, Kaspar RL, Coulombe PA. J Clin Invest. 2016 Jun 1;126(6):2356-66. doi: 10.1172/JCI84870. Epub 2016 May 16.

Chronic Foot Pain due to Pachyonychia Congenita in a Pediatric Patient: A Successful Management Strategy. Tariq S, Schmitz ML, Kanjia MK. A A Case Rep. 2016 May 15;6(10):305-7. doi: 10.1213

Realizing Our Potential in Biobanking: Disease Advocacy Organizations Enliven Translational Research. Edwards KA, Terry SF, Gold D, Horn EJ, Schwartz M, Stuart M, Vernon SD. Biopreserv Biobank. 2016 Aug;14(4):314-8. doi: 10.1089/bio.2015.0053. Epub 2016 Apr 8.

Imaging Functional Nucleic Acid Delivery to Skin. Kaspar RL, Hickerson RP, González-González E, Flores MA, Speaker TP, Rogers FA, Milstone LM, Contag CH. Methods Mol Biol. 2016;1372:1-24. doi: 10.1007/978-1-4939-3148-4_1.

Efficacy of botulinum toxin in pachyonychia congenita type 1: report of two new cases. González-Ramos J, Sendagorta-Cudós E, González-López G, Mayor-Ibarguren A, Feltes-Ochoa , Herranz-Pinto P. Dermatol Ther. 2016 Jan-Feb;29(1):32-6. doi: 10.1111/dth.12297. Epub 2015 Oct 7.

Can skin disease cause neuropathic pain? A study in pachyonychia congenita. Wallis T, Poole CD, Hoggart B. Clin Exp Dermatol. 2016 Jan;41(1):26-33. doi: 10.1111/ced.12723. Epub 2015 Sep 11.

Focal PPK secondary to a novel KRT6C mutation (Pachyonychia congenita-K6c). Wee JS, Smith FJ, Wilson NJ, O'Toole EA. J Eur Acad Dermatol Venereol. 2016 Aug;30(8):1415-6. doi: 10.1111/jdv.13259. Epub 2015 Aug 24.

Non-Invasive Intravital Imaging of siRNA-Mediated Mutant Keratin Gene Repression in Skin. Hickerson RP, Speaker TJ, Lara MF, González-González E, Flores MA, Contag CH, Kaspar RL. Mol Imaging Biol. 2016 Feb;18(1):34-42. doi: 10.1007/s11307-015-0875-z.

Isolated recessive nail dysplasia caused by FZD6 mutations: report of three families and review of the literature. Kasparis C, Reid D, Wilson NJ, Okur V, Cole C, Hansen CD, Bosse K, Betz RC, Khan M, Smith FJ. Clin Exp Dermatol. 2016 Dec;41(8):884-889. doi: 10.1111/ced.12934. Epub 2016 Oct 27. Review.

RESEARCH FUNDING AND LETTERS OF SUPPORT

Roger L. Kaspar, PhD with TransDerm also received a letter of support for his work on the National Institutes of Health SBIR Phase 2 proposal entitled, *Development of topical formulations for delivery of next generation mTOR inhibitors*. Sirolimus is the only mTOR inhibitor that has received attention for topical application use and effectiveness of topical formulations. siRNA - 2016 R21 Grant

Michael J. Polydefkis continued to receive support and a grant of \$16,200 for his study on neuroanatomy in PC to investigate neuropathic pain in PC patients.

2016 INCOME AND EXPENSE REPORT FROM 990 TAX RETURN

Total 2016 Income	\$ 743,859	[Page 9, Line 12a]
Contributions	\$ 713,560	[Page 9, Line 1f]
Fundraising Events	\$ 8,249	[Page 9, Line 1c \$5947 plus Line 8c \$2302]
Investment Income	\$ 25,645	[Page 9, Line 3]
Investment Loss	\$ -10,876	[Page 9, Line 7da]
2016 Total Expenses	\$ 442,775	
Program Expenses	\$ 387,156	[Page 10, Line 25, Col B]
General Expenses	\$ 39,551	[Page 10, Line 25, Col C]
Fundraising Expenses	\$ 16,068	[Page 10, Line 25, Col D]
Expenses over/under income	\$ 301, 084	

DONATED SERVICES AND VOLUNTEERS

In 2016 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. Generous discounts on genetic testing and on CPA services were received in 2016.

Total Value

DONATED SERVICES

Physicians and Scientists

IPCRR patient consultations	\$ 9,750.00
IPCRR special patient consultations	\$ 10,200.00
IPCC Genetics Team & Steering Meeting	\$ 36,000.00
IPCC Meeting	\$ 108,000.00
Patient Support Meeting	\$ 37,800.00
London Steering Committee Meeting	\$ 25,200.00
Program services (acting ED salary)	\$ 120,000.00

PROFESSIONAL SERVICES

Mantyla McReynolds (accounting)	\$ 4,400.00
GeneDx (genetic testing)	\$ 2,520.00
Fundraising Expertise	\$ 5,000.00
	\$ 355,550.00

PC PROJECT STAFF

Mary E. Schwartz, Acting Executive Director (volunteer)
Cindy Atha, Executive Director (September-December)
Holly A. Evans, Program Director
Frances J.D. Smith, Chief Scientific Officer
Joanne Udy, Bookkeeper

PC PROJECT BOARD OF TRUSTEES

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

Preston L. Cochrane, Chair
Barbara Feinstein, Fundraising Committee
C. David Hansen, MD, Medical Advisor
Jason Hunter, Treasurer
Roger L. Kaspar, PhD, Scientific Advisor
Jack Padovano, Fundraising Committee Chair, Patient Advocate
Janice N. Schwartz, Secretary, Patient Advocate
B. Jack Wixom, Fundraising Committee

Board of Trustee meetings were held on April 8, August 12 and December 9 in 2016.

The April 8, 2016 meeting was centered on the need for additional staff for PC Project. During the meeting Matt Morgan was hired as Office Manager and continuing search for Development Director, Outreach Director and Executive Director. The need for fundraising was discussed. A special presentation by Christine Sharer of Pathway Associated presented on how to effectively transition from a founding Executive Director to a new Executive Director.

Officers and Committee positions were reviewed during the August 12, 2016 meeting. The Board raised the Budget to \$225,000 to fund additional staff. Meeting focused on finding a new Executive Director, new Principle Investigator for IPCRR and current activities of PC Project.

At the December 9, 2016 board meeting, Jason Hunter joined as new treasurer. Shaw & Co was approved to be the new auditor. Need of fundraising personnel and strategy was discussed. Cindy Atha gave Executive Director Report. New computers and systems were requested.