YEAR END—Thank you so much to all who donated in 2012. We will prepare a formal 'annual report' and accounting, but in this PC News Brief we wanted to express out gratitude for the growth in funding which is allowing us to provide services to patients as well as fund patient meetings and offer research support. We appreciate each donation and every effort made to increase PC awareness and funding.

We share here a few highlights from special events in 2012.

Donations in lieu of gifts. Two PC families (Block/Bramer and Misiano/Nikiteas families) made donations in lieu of holiday gifts.

Good neighbors. Roseann and Mike McGrath made a special effort to share the year end donation cards with friends and neighbors. One neighbor sent a donation and when we called to say thank you he said “You’ll never know how wonderful they are. They worry about it. They care for me. They talk about PC Project and I wanted to send a donation to help out.”

Bike Ride. Dr. Philip David Gard, his wife Mary, and friends raised funds for PC Project by taking part in the Beaune Challenge in France held September 27-30. They raised over $1,500.00.

The Netherlands All Year Effort. Elise van der Laan has been working all year with her husband Mark on behalf of their son Ian and all PC patients to really make a difference. Elise wrote about some of their fundraisers:

Sponsored walk. Ian’s school held a sponsored walk to help PC Project and a small project in Indonesia. The children walked an amount of €5262.80 (abt $5,999.52 US) for each group!!!!

Wedding. Mark’s boss donated the collections of the church at her wedding to PC Project. In total this was: €212,65 (about $282.82 US)

Sponsor marathon. Each year in Eindhoven there is a yearly marathon in which a couple of friends participate. They raised €545,00 (about $724.85 US).

Store Donation. The vegetable shop "De Pompoen" where the van der Laan’s live sold banana boxes for €1.00 euro. They raised €65,00 (about $86.45 US)

In closing Elise says: “In total we raised €6,145.45 and over the year we have raised €21,705.45!! (about $28,868.25 US). What wonderful people there still are! With love,” Mark, Elise en Ian van der Laan.

PS Christmas Stable Roderweg is still running; I will send later.

WE AGREE! WONDERFUL PEOPLE!

Good News——PC Project has received a full $2-for-$1 match for all funds donated for 2012. This is a good start to a solid foundation to move forward to fund additional research and continue to provide all services free to every patient.

Thanks to all PCers who sent cards and good wishes to Prof. Irwin McLean to wish him a Happy 50th. Many happy birthday cards were received. Thank you.
**CAPSTONE STUDENTS PROJECT MAKING PROGRESS**

In mid-December, Mary and Janice Schwartz went to BYU to attend the end-of-semester CAPSTONE team presentations. There are about 32 different projects at the university (i.e. improving surgery equipment, fuel-efficient cars, faster trains and more).

We were very interested to see the number of people who came to see the “PC Shoe” project. There was a lot of interest and discussion from students, professors and advisors for this particular project. The team did a wonderful job and their presentation was excellent.

It was fascinating to see how this group of very bright students are figuring out the complexities of PC and working towards ideas that might alleviate pain from walking. They’re looking at different ways to alleviate pressure/pain through braces, supports or special insoles as well as unique ways to cool the feet. They have a lot of great ideas and some prototypes under development. We appreciate the dedication of these outstanding students.

**Thanks** again to all our PC volunteers who shared your experience with these students. We could not do this without you! A further thank you to the 135 PCers who responded so quickly to the supplemental 4-question survey on insoles. And, a thank you to those who helped the students view PC patients walking either in person or by sending your videos. The response from our PC community is always so amazing to us and the students. Thank you, PCers!

**NAIL REMOVAL SURVEY**

PC Project is gathering information for physicians interested in PC patients’ experiences with nail removal. We are contacting patients in the IPCCR who have reported one or more nails removed. Did the nail(s) grow back? Were they pleased with the results? Were there problems? Good results? Which procedures were used? Very little is really known about results of nail removal for PC patients. It is important that we learn what causes failure or success and if there is a technique or surgical procedure that is most effective and successful. As always, every patient’s experience and information has great value in this rare, rare disease. If you have not taken the survey and have had a nail or nails removed, please contact info@pachyonychia.org.

**SURVEY FOR PARENTS OF CHILDREN WITH SPECIAL NEEDS**

Parents of children with PC may be interested in participating in a university-sponsored research survey aimed at learning more about the experience of parents in advocating for their special needs children. The survey is being conducted by researchers at California State University, East Bay, and San Francisco State University. PC Project is not involved in the study but we wanted to pass on information about this opportunity. If you are interested in learning more about the survey and participating, go to: [http://www.surveymonkey.com/s/Spclneedsadvocacy](http://www.surveymonkey.com/s/Spclneedsadvocacy).

**2013 PATIENT SUPPORT MEETING SANTA CRUZ, CALIFORNIA USA JUNE 20-22, 2013**

We are so pleased with the early registrations for this meeting. Visit [www.pachyonychia.org](http://www.pachyonychia.org) to register. The meeting will be held at the lovely Chaminade Resort & Spa. Optional activities on Saturday include tours of TransDerm, Inc, (our biotech partner) and a chance to support the Second Annual ThickSkin Duathlon to raise PC Awareness and funds for PC research.

**PCER VOTED #1 RARE DISEASE PATIENT IN FRANCE.** Thanks for voting for our dear Sylvie Cierpucha who won this award. We hope to have an English translation of this article to post with the original on Facebook. Congratulations!

**COMING IN 2013-NEW WEBSITE**

We are developing a new website to better serve patient needs. Share any ideas or suggestions with us at info@pachyonychia.org.
NEW PUBLICATIONS—A new article titled Best Treatment Practices for Pachyonychia Congenita appears in the Journal of the European Academy of Dermatology and Venereology. JEADV is a leading dermatology journal published by the European Academy of Dermatology and Venereology. It is available on the PC Website under Bibliography. Simply put 2013 in the year search and quickly find the article.

This will be the first time any treatment information has been published in a ‘peer-reviewed’ journal for physicians treating PC patients. It will have a major impact in increasing understanding of PC. As explained in Yahoo Answers, this type of information is accepted by professionals because “A peer-reviewed journal ensures that the articles contained within it are checked by experts in the field to make sure the information conveyed by each article is accurate and up-to-date, and to make sure the methods or theories employed by each author are appropriate and correctly applied. "Peer reviewed" means the article has been read, critiqued, sent back for rewrite, and then given final approval by a group of recognized scholars in that particular field of study. This is done without any of the reviewers knowing who the author of the article is, so that preferential or prejudicial treatment is made unlikely.”

A second article entitled Pachyonychia Congenita Project: A Partnership of Patient and Medical Professional is in the Journal of Dermatology Nurses Jan/Feb issue and is available on the PC website under Bibliography.

HOW CAN PATIENTS USE THESE NEW ARTICLES? A major goal of PC Project is to continue to successfully publish ‘peer-reviewed’ articles. It is the most effective thing we can do to help PC patient care.

We encourage you to read the articles and send in any questions. We’ll provide answers in future PC News Brief issues so that we, as a patient population, can increase our understanding of PC.

Most important: Print a copy of these articles and provide these to your physicians, dentists and other medical professionals. You are a powerful tool in helping educate medical professionals about PC.

Remember, there are over 7000 rare diseases and no physician can know about each of those. Physicians usually disregard information in brochures and pamphlets. However, physicians really appreciate journal articles like these. Please print and share these articles.

STEPS TO PUBLICATION—the Best Practices article has taken great effort and we appreciate each person who has made this possible.

1. In May 2010, about 50 members of the International PC Consortium (IPCC) met to discuss how to improve PC patient care. They worked to outline questions for a survey of ‘best practices’ currently available to PC patients.
2. PC Project staff developed the online survey and circulated it to those in the patient registry. 125 patients responded
3. 25 physicians also responded and a future publication will seek additional physician input and comparative analysis between physician experience and patient experience.
4. To ensure the responses applied to PC (not other disorders) only responses those in the patient registry with genetically confirmed PC were included in the final data.
5. The data underwent statistical analysis using a variety of methods because of the small sample size.
6. Ilan Goldberg, dermatologist in Tel Aviv, became interested and worked to prepare the manuscript.
7. The information was presented in May 2011 at the annual IPCC meeting and was then prepared for submission.
8. The article underwent ‘peer-review’ with changes and corrections in format, questions regarding methods, etc. and was then approved.
9. The final article was sent for publication in December 2012 and now appears in print.

Thank you PC Patients in the registry! Without you we could make no progress at all. Thank you for the 125 who responded to this survey. We hope you are pleased with the result.
**NEW PC PROJECT WEBSITE**—We are so excited about the new PC Project website. It will be rolled out before the June Patient Support Meeting. We wanted to give you a sneak peak so you’ll see the direction we are heading.

In the section “Read My Story”, we will be asking for both adult and children to be featured on our website and share their PC Story in text or video. We want to show real, wonderful people dealing with the effects of PC! We will have 3-4 rotate on the main page, then keep updating and replacing and adding those stories to the ‘patient-community’ to supplement Jan’s Corner information which ended Dec 2012.

**ANNUAL IPCC MEETING**

**Park City, Utah**

**February 14-17, 2013**

This important scientific meeting is essential to move our PC research objectives forward to clinic. We thought you might like to see a few of the nearly 50 of the world’s scientific leaders who will be attending to focus on PC research. A meeting report will be published in March.

Agarwala, Manoj K. - India
Baker, Carl - NIH/NIAMS
Coulombe, Pierre A. - Johns Hopkins
Faver, Inacio R. - Brazil
Hansen, C. David - University of Utah
Kaspar, Roger L. - TransDerm, Lane, E. Birgitte - Singapore
Lv, Yongmei - China
McLean, W. H. Irwin - Dundee, Scotland
Milestone, Leonard - Yale University
O'Toole, Edel - London, UK
Rice, Robert H. - Univ of CA, Davis
Roop, Dennis R. - University of CO
Smith, Frances J.D. - Dundee, Scotland, Sprecher, Eli - Israel
Teng, Joyce M. - Stanford University
Terry, Sharon F. - Genetic Alliance
van Steensel, Maurice - The Netherlands

**2013 PATIENT SUPPORT MEETING**

**Santa Cruz, California USA**

**June 20-22, 2013**

REGISTER www.pachyonychia.org

We are thrilled with those already registered for this important patient meeting. The website includes a link to the Chaminade Resort & Spa as well as a link to the scholarship application form. In addition to the excellent program and exchange in the PSM, there will be optional activities on Saturday with our biotech partner and a chance to support the Second Annual ThickSkin Duathlon to raise PC Awareness and funds for PC research.

**2012 FINANCIAL REPORT**—We’d like you to know how your donations are used and are providing this ‘quick financial overview’ for 2012 of program expenses for research and patient support. When complete, the 2012 audit and our 2012 990 tax form will be available on the website.

**Contributions & Fundraising** $123,131 (before match*)
**Research & Patient Support Expenses** $169,807

Including Clinical Trials/Studies, Physician Consultations, Genetic Testing, Patient Support Meetings

*Matching Funds covered the unmet Research & Patient Support Expenses and all additional program expenses and operating expenses for PC Project.
2013 Patient Support Meeting
Santa Clara, California
June 20-22, 2013
This is the 12th Annual PC Patient Support Meeting! We believe these meetings are extremely valuable — for patients to connect and learn from one another and for physicians and scientists to meet and spend time with a number of PC patients. The meetings have had an enormous impact on research progress and on individual lives.

We need your help so that we can best plan the program. Please asap

1. REGISTER for the meeting.
   (a) If this is your first meeting, the meeting fee is automatically waived. You can apply for scholarship funding for hotel, travel expenses and family members fee.
   (b) If this is not your first meeting, you can apply for scholarship help for the meeting fee, hotel or travel costs.

2. REGISTER at the hotel.
   (a) The hotel charges (other than incidentals in your own room) are covered in the meeting fee and will be paid either by that fee or by scholarship funding this year.
   (b) There will be no charge to your credit card for registering but you need to register and give your card to hold a room.

3. APPLY for any needed scholarship funding. Pay what you can yourself so we can help as many as possible—but don’t not come because of financial needs!

2013 PC Awareness Day—June
Choose your date (any day in June) and plan your 2013 event. PCers around the world will again ‘join together’ to hold events in their own communities to
(a) raise PC awareness
(b) raise funds
(c) empower and strengthen one another as we join together.

PC Awareness Day in 2012 was amazing. We have to have more events this year. All who held an event have reported a great sense of accomplishment. PC is an ultra rare disorder, but we can work together no matter where we live to be part of the PC movement. Please let us know what you are planning and how we can be of help.

LeCoeur au Pied Donation

We just received a 7000€ check (about $9,150 USD) from our wonderful partner organization in France, LeCoeur au Pied. Led by Sylvie Cierpucha, LeCoeur au Pied has consistently participated with PC Project. Sylvie has located and registered in the Int’l PC Research Registry more than 60 PC patients. She helps each one complete the IPCRR forms and photos required so that each patient can receive their genetic testing information.

The check included a €2000 donation from Solhand, a French charity working on behalf of rare diseases.

€4000 of the donation was from an event organized by Nathalie Kilchoer, a PCer living in Switzerland. She and her husband are professors of fitness and indoor biking (spinning). In November 2011 they organized the first marathon to benefit PC. It worked so well that they repeated it in November 2012.

Sylvie Cierpucha attended the event and writes “…it was great to see all these people ride to the beat/rhythm of the music, with a smile. There was 6 hours of non-stop marathon riding and 150 people cycled for 1 hour minimum. One of these people cycled 6 hours.” You can see all the details and pictures at www.leglebemarathon.ch
Graduating Seniors
Over the last week, we’ve heard from 3 PCers who are graduating this spring (from high school/secondary school). Each one has a story to tell and has accomplished a lot!

WANTED: The May 2013 issue of PC News will feature all PCers who are graduating. Please send a photo and a little bit about your plans, awards you may have won, an essay you wrote for university, or anything you’d like to submit.

Report of 10th Annual International PC Symposium
On February 14-17, 2013, more than 50 physicians and researchers met in Park City to present the current status of PC research and to outline plans to move forward toward clinical studies with treatments for those with PC. More than 80% of those who participated in 2004 are still active in the IPCC. A formal ‘meeting report’ will be published in one of the scientific journals.

Mouse Models for PC. Mouse models are essential for research on PC. Mouse models showing phenotype (callus/blisters) on paws are now available for treatment.

Assessment Tools for Studies—Patient Volunteers Needed
The group agreed on the need to develop excellent measurement tools to report effectiveness of drugs being tested. WANTED: Patients to try out the assessment measures and provide feedback as to their effectiveness. Thanks to those who reported on the PC Standing Test.

Clinical Studies. Microarray work with patient biopsies is revealing the relationship between various keratins with the hope of finding new approaches for treatment.

Overview of PC: What we have learned. The introductory lecture showed all we have learned since 2004 about PC through the participation in the IPCRR of hundreds of PC patients. Thank You!

PC Cyst Study Continuing
Many thanks to the 12 PC patients who have donated cyst samples for this project. If you are having a cyst removed, please contact us.
25 PCers Registered for 2013

We are looking forward to the PC Patient Support Meeting which will be held in Santa Cruz, CA June 20-22, 2013. We have heard from many other PCers indicating you want to come and we urge you to register if you plan to attend this 12th Annual PC Patient Support Meeting. We look forward to meeting many new patients and greeting our dear friends from previous meetings.

Please call if you have questions.

1. REGISTER for the meeting.
   (a) If this is your first meeting, the meeting fee is automatically waived. You can apply for scholarship funding for travel expenses and family member fees as needed.
   (b) If this is not your first meeting, you can apply for scholarship help for the meeting fee (which includes hotel) and travel costs.

2. REGISTER at the hotel.
   The hotel charges (other than incidentals in your own room) are covered in the meeting fee and will be paid either by that fee or by scholarship funding this year. There will be no charge to your credit card for registering but you must reserve a room.

3. APPLY for scholarship funds.
   Pay what you can yourself so we can help as many as possible—but don’t not come because of financial needs! We are waiting to allow everyone time to apply — but the deadline is May 1, 2013.

MEETING SCHEDULE

Thursday, June 20
- 1pm to 3pm Registration
- 3:30pm Opening Session
- 6:30pm Dinner

Friday, June 21
- 7:30am Breakfast
- 9:00am Session
- 12:00 noon Lunch
- 1:30pm Session
- 6:30pm Dinner

Saturday, June 22 - 7:30am Breakfast and you don’t want to miss the PC Awareness Event — you will help us host this special event. On Saturday morning, TransDerm will host tours. All events will end about noon on Saturday so patients can travel home.

SATURDAY, JUNE 22, 2013

Registration 7:30 - 8:30 AM ★ Duathlon 8:30 AM ★ Bike-only event 9:00 AM

For information, to donate or to register, go to www.TransDermInc.com or email Andrea.Burton@TransDermInc.com

-worldwide pachyonychia (pak-é-ó-nik) congenita awareness day-

-run bike run thickskin santa cruz, california off-road duathlon

-help us raise funds to help those suffering from this rare and debilitating skin disease which causes painful blisters and calluses on the soles. With a rare disease, patients may often feel isolated and frequently there is little or no hope because of limited research and resources. you can make a difference by participating in and supporting the 2nd annual thickskin duathlon.

100% of proceeds go to PC Project, a 501(c)(3) public charity working to “find a cure for PC” — and all proceeds will be matched $1 for $1 by an event sponsor so your contributions will be tripled and will really make a difference.

PC patients will be in Santa Cruz at the time of the thickskin duathlon for the 2013 patient support meeting. TransDerm, a local biotech company, will again host the Duathlon to raise awareness and funding for this cause.

kids activities - face painting - art projects
live music & raffle prizes

-kids activities - face painting - art projects
live music & raffle prizes

2386 East Heritage Way, Ste B, Salt Lake City, UT 84109 · www.pachyonychia.org · Phone 877-628-7300 · Email: info@pachyonychia.org
**RESULTS: BYU CAPSTONE.** The PC Shoe team gave an excellent presentation at the concluding event which featured numerous mechanical engineering and health projects. Their poster is included below.

The orthotic brace available from Toad Medical (www.toadmedical.com) reduces pressure by 33%. With an extra two-layer foam cushion, the pressure is reduced by 77%. The cost of the brace including the orthotics fittings is about $6400 (USD). We do not know whether insurance will/will not cover these costs.

A very important finding after all the testing was done, is that the Vasyli Armstrong II insole (www.vasylimedical.com) at a cost of about $50 (USD) also reduces pressure by about 30% *not shown in poster*. This is a much better pressure reduction than any of the other insoles recommended by PC patients in the insole survey. If you use the Vasyli Armstrong II, we will welcome your feedback. We will try to get some of this product to test for PC patients.

**THANK YOU** to the twenty PC patients who recently helped with a 10-day standing pain test to help us in development of tools (and the longer process of evaluating and validating tools). It is an important part of the progress we are making towards clinical studies. How to measure improvement is a challenge which the US FDA (and their counterparts in each country) requires us to meet. We will continue to need volunteers to assist us to gather 'real life' information - not just guessing what will happen if… Once again, thank you!

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**BYU CAPSTONE**

**Background:** Pachyonychia Congenital (PC) is a rare genetic disorder that leads to excessive callusing and blistering on the sole of the foot. These calluses and blisters cause intense pain when standing and walking.

**Objective:** Create a device for PC patients that relieves some of the pain experienced during standing and walking.

**Solution:** An orthotic brace combined with a foam support transfers weight from the sole of the foot to the lower leg. This reduces pain by lowering pressure peaks on the foot.

**Results:** The brace alone reduces pressure peaks by 33% compared to a normal shoe. The brace combined with foam cushions reduces pressure peaks by 77%.

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2386 East Heritage Way, Ste B, Salt Lake City, UT 84109 · www.pachyonychia.org · Phone 877-628-7300 · Email: info@pachyonychia.org
Thank you to PC Patients for Attending Atlantic Derm Conference April 13, 2013

Sean Dempsey, James Andrade and Amir Ataee attended the Atlantic Dermatology Meeting in Washington, DC and represented the PC community.

Here are some of their comments about the meeting:
- The meeting started at 7:30am and ended at 11:15am.
- Before the meeting, they served us a light breakfast.
- About 600 doctors visited us and got to see PC in real time!!
- There were 58 patient located on two floors.
- Our rooms were next to each other and the doctors got to see three different PC mutations one after another.
- About 10% of the doctors were very enthusiastic about PC and asked a lot of questions.
- Some knew about PC Project and others were very impressed about the brochures and about how organized we are. We gave out hundreds of the specially prepared brochures.
- Most of the questions were about how painful PC is and how we care for it.
- Some had suggestions, but there was not anything new for us.
- After the meeting, there were lunch boxes for us to take away.

PC Project is eager to sponsor educational outreach events which include multiple PC patients who are prepared with publications to represent the PC community.

Congratulations Graduates!

We are aware of a number of outstanding students who are graduating soon. We hope to include news of these students and their achievements. We think they are great examples of the way PCers succeed. Their stories will encourage younger PCers and parents with PC kids.

We’ve heard Tara Ataee, Alexis Baker and Nicky Smith are heading for college in the Fall. We’re waiting pictures and details to share.

We know many others are graduating — and we send Congratulations to each of you. Please let us hear from you and we’ll share as received.

Utah Sterling Scholar Competition Winners

Computer Technology
Samuel David Schwartz
Cottonwood High School

Parents: David and Janice Schwartz

The Sterling Scholars are the “best in state” in Utah in 15 categories. Sam will attend Utah State University in Logan, Utah. He has received several scholarships in addition to the Sterling Scholar award (which includes an automatic scholarship to Utah universities).

For several years during high school, Sam has worked as a programmer for the firm that provides Worker’s Compensation insurance for the State of Utah. He’ll continue working this summer and work remotely once school begins. We’re so happy for you, Sam!

Patient Support Meeting

There are 39 PCers (and 37 others) now registered for the meeting which will be held in Santa Cruz on June 20-22. If you haven’t reserved your room and registered, please contact us asap. The PSM are held every other year in the US. We don’t want anyone to miss out who hopes to attend, but the time is growing short. Register now!

Scholarship Awards

PC Project was able to award scholarships to all applicants in the US for the Santa Cruz PSM. The awards will be presented at the meeting to Catana Abundis, Jessica Jenkins-Smith, Stephen Jiang, Gladys Eileen Lusk, Charity Oswald Cook, and Janie Youhas.

The Xtreme Barefoot Charity Challenge

Inspired by Tom Baker and his young son Timothy, who both suffer from PC, Steven Macey is currently undertaking this effort. This entails Steven walking/cycling barefoot for 350 miles in an attempt to raise awareness of, and funds for, the PC Project. On his challenge Steven says, “Some people think I’m crazy for doing this but really I’m only going to suffer a little discomfort for a limited period, whereas PC sufferers have to endure constant pain on a daily basis. What is crazy is that people still have to suffer like this!!!” To follow Steven’s progress through the challenge, visit https://www.facebook.com/Xtremebarefootchallenge where you can find out about his battles with Billy the blood blister, his campaign to rid streets of those annoying little sharp stones, and his encounter with a spear. Support this cause and donate for PC research!
A Special Report for PC Awareness Around the World 2013

By Julie Peconi, Social Media Co-ordinator

Last year on June 2nd, PCers around the world participated in the first ever PC Awareness Day. The financial benefits were amazing, with a total of $80,883 raised for PC research and patient support! With the PC Project $2-for-$1 match, the grand total raised was $240,000! The personal benefits were just as positive, with many PCers reporting feelings of empowerment, community and control. And this year, we’re doing it all again: June 2013 is PC Awareness Around the World month!!

We invite every PC family as well as friends of PCers to host a local event to: (a) raise awareness of Pachyonychia Congenita and (b) raise funds for research, patient support and clinical trials. It’s easy to become involved and we welcome all events. No event is too small and every single activity helps. Getting involved is easy:

1. CHOOSE Your Project! This event can be a bake, trunk, yard or garage sale; a bike ride; a talent show; a walk; a run; a dinner with friends. The possibilities are endless. And whether your project raises $1 or $1000, you will be joining with other PCers around the world to raise PC awareness. Some of the events from last year included: a mountain bike race, family fun days, pizza parties, donation tins in local restaurants and letters to families and friends explaining PC. One woman wrote a PC related post on her facebook page every day for a week! A simple and effective way to raise awareness!

2. REGISTER your event with the PC Project. Send an email to info@pachyonychia.org and if possible post your event on our facebook page (Pachyonychia Congenita (PC) Awareness Around the World). This helps and encourages others who may be wondering how to get involved. We will advertise the events through our website and other social media outlets and can provide PC flyers for you and help you contact your local news outlets.

3. REPORT your success! When you forward the funds raised at your event, please also send a report and photos to tell us what you did. This will help others who may want to use your ideas in the future. Our sponsor will again match $2-for-$1 on the money you send from your events so that your efforts will bring three times the amount earned.

We’ve already had reports of several great events planned for PC Awareness in June and look forward to reporting more. The many events around the world (large and small) create a Pachyonychia Congenita news story which will enable us to meet the goal of public awareness for PC. Every contribution helps in linking up the PC community, raising funds for research and support, and gets us closer to our end goal: a cure for PC.

We appreciate all your support of the PC Project and look forward to hearing your news!

NEWS FLASH –
We plan to launch the amazing new PC website by June 1st in time for PC Awareness 2013!
EVERYONE IS IMPORTANT!
Please join in PC Awareness 2013. We need every family to do something to raise awareness and funds! Before PC Project, most patients felt isolated, as though they (or their family) were the only ones with PC. Now we are a community and moving forward together — but we are still few in number. Everyone is needed or we will fail.

It may not seem like much, but please let us know anything you do — anything at all. Give out the website address to all your mailing list friends. Post on Facebook or other social media (and ‘like’ us on Facebook). Have a yard sale, a dinner, a party, a cookout. Do something that spreads information about PC — and let us know about it. If you can also raise funds (every penny really counts in our efforts!) that’s great. We hope to have more than 60 events this year. Please do not let us down. Send pictures if you can. Tell us what you are doing by email or by posting on the PC Events Facebook page. You really do count! Here are a few of the early events already completed:

GUESS HOW MANY?
A family in Southwest Wales held some fundraising activities at their son's school. Their son did a “guess how many gumbrops are in the jar” and earned £32! The family also sold craft bits as part of their new craft venture, Cinnamon & Timbit, and sold £57. They were able to speak to many parents and teachers about PC.

2ND ANNUAL GARAGE SALE
The McGrath, Filoso & Sands families held their 2nd annual garage sale as their PC Awareness Kick-off over Memorial Day weekend. Despite stormy, cold and very windy weather at the beach, they were able to raise almost $300 during the 2-day garage/yard sale.

2ND ANNUAL PC BAKE SALE
In Wisconsin a family again held their PC Awareness Bake Sale in connection with a local mountain bike race. They reported they had “a great response again this year and raised $730 with donations and sales at the bake sale at the mountain bike race.”

PC REGISTRY IS ONLINE!
UPDATE YOUR IPCRR DATA
One of the most exciting and important features of the new website is that the International PC Research Registry forms can now be completed online.

If you have completed the IPCRR forms in the past, we invite you to update your information. Having information updated over time will provide (for the first time ever!) a “life history” view of Pachyonychia Congenita. This is something that is usually required as a starting point for researchers, but which has not been possible before. You can update all or part of your questionnaire easily online. We’ll be contacting you and explaining more about this in the future.
It is especially important for parents of children with PC to update the information at least annually. This will provide, for the first time ever, documentation on how PC changes from birth to adulthood. The feature will provide valuable information from patients of all ages who contribute by updating their information.

**GENETIC TEST RESULTS**

We first met Rebecca Rhodes in 2005. It has taken nearly 8 years of effort to find the specific mutation and disorder for this one patient. Because there are many conditions that “mimic” PC, we urge patients to participate in the IPCR and find their exact condition and mutation. Treatments for one gene or disorder will almost certainly not be effective for a different gene or condition. When something “looks like PC,” the genetic testing is essential to identify the actual mutation and condition involved.

Rebecca’s condition is not Pachyonychia Congenita — and is not a keratin disorder at all, but a mutation in TRPV3 gene — a completely different mechanism. See the PC website IPCR data for more details on all the conditions misdiagnosed as PC. Many of these conditions are even rarer than PC and most have no patient support group working on their behalf.

Since the breakthrough discovery for Rebecca, 3 other ‘unsolved’ cases have now been identified in this gene. The McLean/Smith lab working in partnership with PC Project continues to lead the way. They don’t give up! They work to find answers for patients.

**40 PC PATIENTS HEADING TO PATIENT SUPPORT MEETING IN SANTA CRUZ JUNE 20-22**

We are eager to welcome 40 PCers as well as family members to a wonderful PC PSM in Santa Cruz, California. Hosted by our biotech partner, TransDerm, the meeting will end with the highly successful Thick Skin Duathlon. This is a major fundraising event for PC research and PC support.

These PSM events help patients to better understand the basics of PC, both what is known and what is yet to be discovered. It is an opportunity for physicians to learn from PC patients and for patients to share with each other. Each meeting we have opportunities to gather data that moves us forward towards the next clinical studies.

We are grateful for each patient who will attend the 2013 meeting. We are also grateful for those who have donated to PC Project through the year to make scholarship funding available to many of those unable to attend without the financial assistance.

With PC everyone is needed and together we do make a difference!

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**REBECCA RHODES: I AM STRONG AND DEDICATED**

I am strong and dedicated.

I wonder if I will ever walk. I hear people bully me. I see people stand up for me. I want to be “normal”.

I am strong and dedicated.

I pretend that I can handle everything. I feel alone. I touch my painful feet. I wonder if I will ever have pretty feet. I cry because I want to belong.

I am strong and dedicated.

I understand things happen for a reason. I say God put me in this situation for a reason. I dream for a cure. I try to become an inspiration. I hope to be pain free.

I am strong and dedicated.

A poem by Rebecca Rhodes (for her Literature class)

Rebecca Rhodes was recently selected as one of two upcoming Juniors from each high school to participate in the Youth Leadership Douglas program. Participants in this program will broaden their knowledge of local government, business and civic activities. Rebecca took Honors classes and also was on the Yearbook staff. She had 34 days of absence this past school year, due to her condition. However she has done extremely well academically. Rebecca competes on a Power Wheelchair Soccer team and just completed her 3rd season. Rebecca has also competed in the National American Miss Pageant for 5 years. She has been in the Top 10 Finalists, Top Model Photo Shoot-1st place winner, Spokes model-1st runner up and Spirit of America-1st place winner. The award she is most proud of (she has won this 3 times) is the Miss Personality Award. This award is voted on by the contestants who they feel is the friendliest, most helpful and most fun to be around. There are over 150 girls who compete in her age division! She was invited to the Music City Invitational in Nashville, TN. This past December she auditioned in front of talent agents and casting directors from across the country. She auditioned for modeling and commercials. She was asked to sign on with DAN Talent Agency in Nashville, TN. who now represent her. Rebecca has attended Camp Horizon in Millville, PA sponsored by the American Dermatological Association and Camp Wonder in Livermore, CA sponsored by the Children's Skin Disease Foundation. She is now a Junior Camp Counselor for both camps.
PC AWARENESS AROUND THE WORLD—June 2013 was an exciting month for PC. We hope you have shared the link for the new website with family, friends and co-workers. The website is a great asset for PC!

YEAR ROUND AWARENESS—Eileen Lusk called with a great idea. She said she is starting now to think about projects for PC Awareness. It takes time to set things up and she wants to do several things throughout the year and not just wait until June 2014 to start. We think this is a fantastic idea — you can participate in events at any time. Research is on-going and funds are always welcome. Each June, we will have a special celebration of PC Awareness, but what you do year round is very, very special. Thanks!

We listed several events last month and here are a few more highlights:

BAREFOOT CHALLENGE—Inspired by Tom Baker and his young son Timothy, who both suffer from PC, Steven Macey is currently undertaking ‘The Xtreme Barefoot Charity Challenge’. This entails Steven walking/cycling barefoot for 350 miles in an attempt to raise awareness of, and funds for, the PC Project.

On his challenge Steven says, “Some people think I’m crazy for doing this but really I’m only going to suffer a little discomfort for a limited period, whereas PC sufferers have to endure constant pain on a daily basis. What is crazy is that people still have to suffer like this!!”

To follow Steven’s progress through the challenge, you can visit https://www.facebook.com/Xtremebarefootchallenge where you can donate — and find out about his battles with Billy the blood blister, his campaign to rid streets of those annoying little sharp stones and his encounter with a spear.

EMPLOYER MATCH—Lisa Noe an employee at JPMorgan Chase set up a regular donation which her employer matches. This doubles, then triples the amount donated!

COFFEE MORNING IN UK—Jeanette Howell asked “where would you like the money to be sent” that she raised in the morning coffee event she held.

FAMILY DONATIONS—I wanted to do “something” for June Awareness month, so I really stepped out of my comfort zone and asked my mother, father, and older sister to make a donation, and I believe they were quite generous! My older sister is a hospital pharmacist in New Mexico, and I asked her to forward the website link to all her medical friends and hopefully they will continue forwarding to their friends! Yay, I did something!

MARATHON—Gina and Jason Defebaugh wrote “I wanted to let you know you should be receiving a check in the mail soon. We sold a new plastic shoe storage box (all the girls in the office like their shoes) and will fill with sweets. I will charge for guessing the number of sweets in the shoe box. She raised $100 for PC! (and what a great way to let others know about her own PC!)

RUMMAGE SALE. On June 8th, Janie Youhas put together a rummage Sale and offered some white fudge with the PC Logo attached, which made for a great "approach" in talking about PC with all those who came to the sale). “I even made me a special "PC Awareness Day" shirt to wear! I wasn't going to let anyone get past me!!! I thought it turned out pretty good, considering it was kind of last minute. Anyway, I was able to make a little over $200.00. I am also counting on friends and family members whom I have talked with, to make their donations as well, via check or online. Sooooo, PC Project... the money is on the way.”
BEAUNE CHALLENGE—Phil and our son Chris have the K6c mutation of PC and we feel we have benefitted so much from PC Project and the Patient Support Meetings in Edinburgh, that Phil and I decided to do a 500 mile charity bike ride in France to raise money for PC Project. We signed up to Challenge Adventure Charities ride from Caen in Normandy to Beaune in Burgundy, in a team of four with 2 friends last September with the aim of raising £1000, £500 for PC Project, and £500 for the Challenge Adventure Charities’s own charities Cancer Research UK and British Heart Foundation.

We started from the D-day landing beaches in Normandy, crossing Pegasus Bridge, then were to head down the Loire to Orleans, across to Vichy and then onto Beaune in Burgundy. We aimed to ride in pairs, each doing 250 miles in 3 days. However things did not go according to plan, as Phil crashed on the first day, resulting in 3 ½ hours in Orleans Accident and Emergency Department. Despite lots of bruises and 11 stitches, he still managed to ride next day, doing an equal share of the ride, though we had to change our plan of each cycling 250 miles and instead each rode 135 miles over 3 days. Only later did we find that Phil had in fact chipped a 3cm piece of bone off his thigh bone!

The ride took us through lovely French countryside, some of it very hilly, undaunted by rain on the first and last day, and we arrived at Chateau de Mersault in Beaune in glorious sunshine, to celebrate with the other 316 cyclists who took part.

Thanks to many people’s generosity we were really pleased to raise £2400, £1200 has been sent to PC Project Mary Gard, UK, June 2013.

EVENTS IN FRANCE—Sylvie Cierpucha and friends made and sold porcupines to raise money and had a nice article in the local newspaper about PC and Le Coeur au pied (the French group that supports PC Project).

Beatrice Wannamacher wrote that she held a fundraiser book fair for PCAwareness 2013. “And I’ve decided to talk about what Steven Macey is doing for us in the local newspaper article they’re about to publish. I’m going to make a special box to collect money especially for Steven Macey’s Barefoot Challenge. I’m deeply touched and am very grateful for his effort for 2013 PC Awareness Day. Let’s hope other people here will do so too.”
University of Dundee, Scotland — this is one of the leading research universities in the world. In June 2013, PC Project was recognized at the University Graduation ceremony with an Honorary Doctorate degree awarded to PC Project Director, Mary Schwartz.

As a complete surprise to Mary, five PC patients — representing each of the PC types (PC-K6a, PC-K6b, PC-K6c, PC-K16 and PC-K17) — were invited to Dundee and recognized at the university graduation events.

New Whole Exome Screening at Dundee

At the time of graduation, a new facility was opened at the McLean/Smith lab and the visiting PC patients were guests at the lab opening. This new unit will provide whole exome screening for PC samples to help identify

Front row: Steve Appleton, Mary Schwartz, Birgitte Lane, Frances Smith and Suzanne Barrall. Back row: Melanie Febrer (head of genetic sequencing lab section), Paul Bowden (a visiting scientist from Cardiff, Wales) and Neil Wilson (who runs all of the PC genetic tests).

At the McLean/Smith lab, Frances Smith (one of the scientists who first discovered the PC genes) shows trays used in genetic screening to Sam and Tania Ryland, Mary and Phil Gard and James Wark.
2013 Patient Support Meeting—Santa Cruz
Hosted by TransDerm, the opening day included a time for each patient to tell one great thing about themselves. In that session, Holly Evans (PC Project Assistant Director) and Janice Schwartz (Patient Advocate), focused on some of the features now available on the newly launched PC website. Friday was the day for formal meeting sessions. The morning focused on scientific and research information. The afternoon included group discussions.

Delivery Methods Tested—As part of the meeting, IRB approval was obtained so that patients could try out the microneedles now produced under standards for human trial. Three delivery options were evaluated (1) dissolvable microneedles, the Tri-M laser and a cream. Although not everyone was able to test these, the findings are very important as we continue to move forward to clinical trials.

New Clinical Trials for PC—Roger Kaspar announced that initial meetings have been held with the FDA for two upcoming clinical trials:
1. sdTD101. An improved, targeted siRNA. The purpose of the trial is to prove (a) safety (b) effectiveness to stop PC and (c) patient-friendly (pain free) delivery.
2. Topical rapamycin. There is a two patient off-label study now underway. If approved by the FDA, the clinical trial will next enroll 20 patients by the end of 2013.

As trials are successful, we will move forward to make treatments available to all with confirmed PC. The key is a knowledge of each PC gene and mutation. A number of other studies are being conducted now in basic lab research, in animal studies and in single patient efforts. Our goals are clear — to benefit each person that has PC.
40 PCers Gather in Santa Cruz—Old friends and new friends joined together to learn and share at the 2013 PSM.

Holly Evans, Asst Director at PC Project had a bright smile for everyone!

At Registration...

One of the group discussions.

The Kids — a ton of fun!!

Our teens—six great men!

Group discussions.

Friday Night on the Patio — Smores and More!
On Saturday morning, those attending the 2013 PSM were invited to join with many from the Santa Cruz community to participate in a major fundraising event for PC.

Hosted by TransDerm (our biotech partner), the 2nd Annual Thick Skin Duathlon had more than 75 participants in the Run-Bike-Run events and more than 150 attendees. The event center featured a band, facepainting, treats, a raffle, and more. With the $2-for-$1 match, close to $100,000 will be available for PC research, clinical studies and patient support efforts. Together we make a difference.
One of the goals of PC Project is to assist every patient to:
(a) find a local physician that can provide basic care and 
(b) develop a good relationship with that physician over time.

Most PC patients understand that PC is so very rare, that their local physician will not have experience with PC.

**Tips for successful patient/physician relationships**

It is wise for PC patients to look for a physician who is someone: they like, they feel comfortable talking with, and who cares about them. A physician such as this will learn what they need about PC to best assist the patient. PC Project can and has connected physicians not experienced with PC to physicians who are experienced with the specifics of PC. Our experienced doctors can answer questions the local doctor may have and help them gain a deeper understanding of this ultra rare disease.

Presently there is no treatment or a cure for PC, but the team of doctors working with PC Project has a knowledge of the various types of PC, the challenges a PC patient has and the type of care that may help a patient.

For example, if a patient has a nail infection or an infected blister, a physician can help with those general health needs, without knowing a lot about PC. However, with a strong relationship, quicker access to the needed medicine may be possible. At other times, special knowledge is needed. If a patient has keratin plaque on vocal chords or a baby is having pain when sucking, a medical expert who knows PC can be a great resource to help the local physician.

**FACT:** Patients can help medical care providers by sharing copies of the best, most correct, and most current articles now available on the PC website. Patients should print copies and share. If unsure which articles to share, please contact us as we’re glad to send copies to patients or directly to their physician.

**SET A GOAL**—If patients don’t have a good physician relationship, we encourage them to set a goal to find a good local physician. Then plan over time, to develop a strong, successful relationship with that physician using PC Project resources.

Seeing a new doctor every time a patient has a need or going to the emergency room when there is a crisis can be devastating. Working to find someone who knows the patient, who can respond and help when there is an immediate need or a special circumstance will take time — but is very worth the effort.

We’d like to hear your stories about good physician relationships. Let us know how you found the doctor and how you have been able to develop the relationship so you receive the care you need.

**USING THE PC WEBSITE**

The new PC Website was launched June 1 to kick-off PC Awareness 2013. We are eager to hear your comments and have you participate on the site.

Tips on using the site:

1. The PC website is state of the art and does not work well with older versions of browsers so we urge you to update your browser. The site works best with Google Chrome or Firefox. Some features do not work well with Internet Explorer.

2. There is a search feature for the entire site. Type any word in the search box at the bottom and it will find all references to that word on the website. EXCEPTION: published research articles have a separate search and will not be found with the site search.

3. We welcome patient stories and patient photos. We are ready to add new main page stories (when you submit your photo for these, take the photo against a white background).
4. Together we can help to emphasize the challenges of PC. If it seems PC has little or no affect on life, it is hard to convince others that research and funding is needed. Your stories and experiences make a difference. THANK YOU for sharing them!!!

5. Please share the website with others. We welcome your comments and suggestions to continue to improve the website.

**WEB MEETINGS — A NEW WAY TO CONNECT FOR PC**

PC Project will sponsor a series of web meetings to help build the PC community and create more opportunities for exchange in addition to the formal Patient Support Meetings.

On July 28, the first PC-K17 community planning meeting was held. Some joined by phone, others by computer and others had their computer with webcams so that they could ‘meet’ on screen. There were 7 participants and it was awesome to see the connections across the group.

The group decided to hold monthly web meetings where topics of specific interest can be discussed. The link for the next meeting will be sent to all PC-K17 adult patients in the IPCRR.

The agenda for the PC-K17 meetings will be as follows:
- 10 minutes - intro by PC Project
- 15 minutes - specific topic discussion
- 30 minutes - patient discussion without PC Project (Notes on care suggestions will given to PC Project and added to the PC Wiki)

If you would like to form a PC web meeting community (for example PC Parents, PC-K6a, PC-K16, PC Teens) please let us know. We will set up the first planning meeting with you and let your community plan how often, the day/time, agenda, etc.

**PC-K6A PATIENTS RESPOND**

In preparing for the various clinical studies, there are many, many steps, over months of time with a large number of physicians and scientists involved. PC Project is often asked for information or opinions on how to set up the protocols (what to measure, how to measure, etc.)

For example, a question recently came up about how frequently PC patients trim their feet. An email was sent out to all PC-K6a patients in the USA (due to time zone needs) asking the question — and had more than 50 responses immediately. That was spectacular!

A table was put together very quickly showing the responses — with new responses added as received. The information was very well received and made a real difference in what will be required of patients in one of the upcoming studies. THANK YOU! PS — other groups will be surveyed in upcoming weeks …

**MICRONEEDLE TESTING**

Because hypodermic needle injection into affected skin is unbearably painful, a great deal of effort continues to be put into developing other pain-free delivery methods.

At the recent Patient Support Meeting the first microneedles produced by TransDerm (our biotech partner) under quality standards for human use were tested. Additional testing has now been completed with 2 PC patients and a ‘normal control’ patient. They applied the microneedles (without any drug product) to plantar, palm and arm every day for 19 days.

The patients reported there is no pain with the application — only a very slight prickly sensation. The photos show there was no redness, irritation, swelling, or erythema at all. This was very good news.

Microneedle strip (about actual size). Needles are the small square

Below the strip pressed on the palm (stays for 5 minutes). The purple dots (gentian blue) mark where to apply the strip so that it was placed in the same spot each day

After daily application for 19 days — no irritation or problems!
June Memories

Mary Schwartz, Frances Smith, and Dr. Leonard M. Milstone, head a discussion at our Santa Cruz Patient Support Meeting.

Patients in France made pigs, hedgehogs and mice with old books and sold them as part of our June fundraising events.

A few members of our PC family enjoying Friday Night on the Patio — S'mores and More at our Santa Cruz Patient Support Meeting.

Bob McLean enjoying the view from the bike portion of the TransDerm Duathlon.

The van der Lann family sold items at several different markets to raise funds during PC awareness month in June.
PHYSICIANS & PC PATIENTS: SUCCESS STORIES
Thanks to Carol Friedman who shared with us memories of her childhood podiatrist: “About every four months or so my mother would make an appointment for me with Dr. Curtis on one of the weekends I went to visit her. He always had time to see me. He would grind down the toenails on the big toes just enough so they didn’t press into the tops of the shoes. He always gave a quick foot massage.

I think any podiatrist that sees a child as more than a patient with PC will help that child emotionally. I remember how kind he and his brother were in making me feel special. One thing they did is tell me how much they liked my freckles.”

We’d like to help every child (and every adult!) with PC to be treated by a doctor/friend. Please share your stories and help us make a plan on how to effectively identify these types of physicians.

DISABILITY CLASSIFICATIONS
Many with PC are contacting us for assistance with disability requests. It may be helpful to understand the different types of disabilities and the requirements for each. The rules for these things are different in every country and within each state or division within each country. These are general guidelines only:

1. Vehicle placards which give a person permission to park in a ‘handicapped’ or restricted zone. Many PCers find these very helpful and we have had good success in supporting and winning approval for these applications for PC patients.
2. Disability adjustments made by schools or employers. PC Project can provide letters of support which have usually been effective in getting options for PC patients to have options. These might be to have a stool instead of standing or to sit/stand/participate depending on their pain level at the time. If you need some special adaptations at school or work, PC Project can provide supporting documentation.
3. Disability payments which provide supplement money to a disabled person to help with childcare or other living expenses. These types of approval are much more difficult.

- PC is not on the list of diseases which automatically qualify for disability payments.
- In most cases, the review is done in the local office by someone who will not know anything about PC at all. This may be a doctor, nurse or staff person and they will make the final decision.

- Three keys are (1) be sure to gather all supporting information (genetic testing results, etc.) before you apply and (2) be sure to make a friend of the reviewer and (3) PC Project will speak with the reviewer if there is an opportunity to do that.
- We have no data that supports the position that someone with PC is disabled to the point that they cannot work at all. We have lots of data supporting the pain involved in walking or standing as well as the complications of cysts in lifestyle.

SCIENE NOTES 2013
Under Thick Skin
Paul Gabrielson
This article on PC was written by a student at Univ of CA—Santa Crug and features several patients and provides a good understanding of some types of PC. The article is only available online so we have attached a .pdf file to this Newsletter. NOTE: This article is for you, your friends, possibly teachers or employers. It is not a research article designed for physicians or medical experts.

Patient Support Meetings. Start saving now so you won’t miss out 2014—Edinburgh, Scotland 2015—USA (Please send your suggestions for where you’d like this meeting.)
HOW ARE BIOPSIES USED? WHY THEY ARE COLLECTED?
The attached recent article from UCSC talks about biopsies and the experience of one patient. We thought it might be a good time to pay tribute to the dozens of patients who have donated biopsies.

Some biopsies are taken from hip or other non-affected areas and are very simple, somewhat routine and have little pain involved. This type of biopsy can be used for creating ‘cell lines’ which can be used in a laboratory for testing new types of treatments. For example, PC cells lines are used in ‘screening’ of drugs to see what ones may affect PC. Two of the drugs that have gone forward to clinical studies were discovered in this way. These cell lines are critical for seeing if a drug will/will not affect a particular type of PC, so that patients are not treated with something that cannot possibly benefit them. These cell lines last for a long time for research and are referred to as ‘immortalized cell lines”

Another type of biopsy is taken from an affected area—usually the sole of the foot. Sometimes biopsies are taken from an affected and an unaffected area of the same patient. These biopsies can be painful although we have several patients who have found these to be very tolerable when administered in a specific manner by one of the dermatologists working with PC Project. These biopsies are used for microarray studies to understand exactly the mechanisms of the mutations. Several important discoveries have been uncovered through these biopsies such as the role of keratin in transmitting pain apart from the nerves or the increase in other keratin genes in affected skin (providing completely new targets for treatment).

We are so grateful for those who donate biopsies. We will never ask for biopsies without a valid and specific purpose for research we believe will be beneficial to all.

PC AWARENESS 2013
Thanks to everyone for the many events held in 2013—from bake sales, to garage sales, to plastic donation boxes at stores, restaurants or at work. Each patient is important to PC Project and together we can make a difference for PC research. We hope 2014 will see even more neighborhood events. We are a small community but we can be a power for good for PC research and awareness.

Xtreme Barefoot Challenge 2013
We appreciate so much the efforts of Steven Macey, a friend of PCers Tom and Timmy Baker (and wife/mother Julie Peconi) in Wales. The total raised from the Extreme Barefoot Challenge was £1800 (or $2,797.74 USD). For the blog (now closed) and more information see http://xtremebarefootchallenge.blogspot.com/

3rd Annual PC Charity Golf Tournament
We are very grateful the weather held strong on August 24 and we had a gorgeous morning at Crater Lakes Golf Course in Midway, Utah for the 3rd Annual Charity Golf Tournament for Pachyonychia Congenita. (A huge thunder storm struck the area shortly after the luncheon ended). There were 128 golfers and dozens of sponsors! More than $10,000 was raised for PC research.

EXERCISE
Exercise and sports activities can be a challenge for PCers. A few years ago Helaine Alessio, PhD made a video of exercises designed for those with PC. This is available on the PC website.

Recently, the PC Patient Chat on Facebook had a wonderful string of comments from those who have found great ways to include exercise. Some have reported biking, swimming or using machines at the gym that don’t require pressure from the feet. We think this is a valuable conversation and appreciate each Facebook post. If you are not part of the PC Facebook Chat, we invite you to join. The Facebook Chat is a benefit provided to patients who have joined the PC registry. (Join on the PC website).

We understand that Google translate will translate pages on Facebook as well as on the PC website. Although not 100% perfect translation, this is a good tool to use when needed.

FACEBOOK GUIDELINES
We recently learned that as a Patient Advocacy Group, we need to have guidelines posted on Facebook and Facebook Chat. With the help of several organizations and several PC patients, these have been written and posted. Please review and give us any feedback.
**Clinical Trial Progress**

(1) Topical Rapamycin for PC

Roger Kaspar, CEO of TransDerm, Inc. (Santa Cruz, CA) reports that their Investigational New Drug (IND) application has been filed with the FDA for use of topical rapamycin in Pachyonychia Congenita patients. Kaspar indicated that initial animal studies and a small off-label trial have shown excellent results. The clinical trial will be held under the direction of Joyce Teng, MD, (Stanford University) with a planned enrollment of 15 patients. The trial will run for six months and may begin before the end of 2013 if FDA approval is received by early October.

(2) Targeted siRNA

A second clinical trial is also planned for sdTD101 (an improved version of the drug used in the successful 2007 clinical trial). Orphan Drug status has been granted for sdTD101 in both the USA and the EU.

Because injections by hypodermic needles were unbearable in the earlier trial, a new delivery system has been developed using dissolvable microneedles or PADs. The drug, sdTD101, targets a specific mutation—K6aN171K. There are only 17 patients in the world with this mutation.

If the trial proves safety and efficacy, the technology developed will be available not only for the other mutations found within PC patients, but for many other disorders which require delivery of large molecules such as siRNA.

**Webmeetings for PC-K17**

Although the mutations that cause PC-K17 are known, a great deal more needs to be learned before treatments can be designed. Much of the research focus is on plantar pain. To focus on cysts, more information is needed. These webmeetings are a start to enable patients to talk together and help us to plan the best way forward for research on this type of PC.

The meetings are currently scheduled for the fourth Wednesday each month at 10:15am MDT (or MST when the time changes). The next meeting will be October 24, 2013 at 10:15am MDT.

**Webmeetings for Others**

We’d love to host a series of webmeetings where patients can meet and discuss specifics about PC research, ask questions and participate with each other and with PC Project in discovering information about PC that can provide helpful data that may lead to treatments.

What webmeeting groups would you like to see us host?
- Group for parents of kids with PC?
- Group for teens (13-19)?
- Group for kids (8 to 12)?
- Group for specific PC types?
- We have many recorded presentations by physicians and scientists. Would you like to have a ‘podcast’ of some of these and then have a discussion about the topic?
- Would you like us to arrange a time when a PC ‘expert’ physician or scientist could be on a meeting and lead a discussion with patients?

Please let us know your ideas and thoughts. Send email to info@pachyonychia.org or through the Connect With Us button on the website.

**PC Website Update**

The PC Website has been up for about 3 months and this week we are going to spend time to update a number of areas.

1. **Feature Stories.** We need many more PC stories. If you haven’t shared your story, or provided a white background photo, please do that asap. We’ll be changing out the front page during September to keep it fresh and rotate the stories. All stories will be available in the main story section.

2. **Published Research Articles.** These are the articles to share with your physicians and medical professionals. Not lay articles! We are so grateful that PC continues to have many published articles. We will continue to add comments and feature the best of these articles. Print and take a copy of one of the featured research articles to each doctor visit.

3. **PC Wiki.** One of the things we most want to do and catch up on is the PC Wiki where we hope to share all community input for tips, techniques. If you have information to add, please send email to info@pachyonychia.org or through the Connect With Us button on the website.

4. **FAQs.** Do you have questions you’d like answered on the website? Please don’t hesitate to suggest these to us. We appreciate all your suggestions.
A biotech startup battling a rare, disfiguring disease prepares for its defining test. Paul Gabrielsen cuts to the quick.

Illustrated by Alex Babakitis and Christina DiPaci.

Esteban Abarca and I wait in a dermatology clinic in Santa Cruz, California. We’re there to donate biopsies of the skin and upper layers of flesh from our heels. Scientists will study the 3-millimeter-wide punch-outs — half the diameter of a pencil — to examine how his severely damaged nerve endings differ from my healthy ones. We both know it will hurt. But Abarca is sweating. It will hurt him more than either of us imagine.

Abarca, 32, has a short crew cut and a well-trimmed goatee. He works as a truck driver in Oakland. Nine years ago, he found out why his feet hurt so intensely. He’d thought his thick yellow calluses and scorching pain were just “bad feet.” But after visits to the right doctors and a genetic test, he heard the rare, tongue-twisting diagnosis: pachyonychia congenita (pak-ee-o-NEE-kee-a kon-GEN-ih-ta), or PC.

PC is not life-threatening but that’s little comfort for the 1,200 patients (one in 6 million people) worldwide. Caused by the smallest of DNA mutations, PC can mean shaving calluses with a razor blade and trimming fingernails with a power tool. Patients sometimes crawl rather than walk. The disease disfigures feet, hands, and nails. For now, there is no treatment.

But a decade ago, shortly before Abarca’s life-changing diagnosis, a genealogist in Salt Lake City resolved to do something for PC patients. Her activism inspired biochemists in Santa Cruz to launch a company dedicated to treating the disease. Now that company, TransDerm, prepares for clinical trials that could bring PC patients back to their feet. Their treatment silences the genetic mutation responsible for the disease. It’s injected via microneedles — thinner than a hair and short enough to barely pierce the skin. A preliminary human trial five years ago showed enough promise to merit continued funding from the National Institutes of Health (NIH).

If TransDerm succeeds, millions with other skin disorders may also benefit from their technology. But that’s a far-off dream for the small company. The ongoing pain for PC patients, in contrast, is very real. They watch the company’s progress with anxious anticipation. It’s their best hope.

Roots of the disease

German dermatologists first named PC in 1906, describing the case of “E.C.,” a 15-year-old girl with thick fingernails and toenails. “They cannot be cut with a scissors,” the dermatologists wrote. “The father has to trim them with a hammer and chisel.” The disease’s name, “pachyonychia,” is Greek for “thick nails.” Over the years, frustrated doctors tried radiation...
and thyroid medications, among other treatments, with no success.

In 1994, scientists in Scotland identified a key gene responsible for the disease. PC is caused by a point mutation, a change in a fundamental unit of DNA. The mutation may occur in any of five genes encoding keratin, a protein found in hair and skin. Keratin supports cells like a wooden frame supports a house. The mutated gene overwhelms the four normal genes and turns that frame into small fragments, weakening its structure, and leaving the skin vulnerable to damage. Even a little friction inflicts a wound, leaving an exquisitely sensitive callus. (See sidebar: Profiles in Pain.)

PC affects the keratin found in nails, palms, and soles. Not all PC patients have the same mutation. One specific mutation, called K6a N171K, is shared by only 14 known patients worldwide.

In 2001 Mary Schwartz, a Salt Lake City genealogist, read in Reader's Digest about efforts to cure a rare liver disorder in a 13-year-old boy. Schwartz pondered the heroics of the researcher in the article and thought of her daughter-in-law and two grandsons, all afflicted with PC. She decided to act.

It seemed simple in her mind: Keep researchers funded until they found a cure. "It's like the cure existed, like gold, and you went out and found it," Schwartz says. "I was wrong on every point."

In 2003 Schwartz founded the non-profit PC Project. With no scientific background (her only degree, she says, is as a grandma — a "GMa"), she organized a conference the next year in Park City, Utah, and called for scientists who could offer plans for clinical treatments.

Santa Cruz biochemist Roger Kaspar attended as an invited scientist on behalf of his employer, Somagenics. A tall man with dark wavy hair and a narrow face, Kaspar had taught biochemistry at Brigham Young University before coming to California's central coast.

Kaspar first presented his company's technology, then mentioned a new and more potent approach that could halt PC at a genetic level. Intrigued, Schwartz began a detailed dialogue with him. Kaspar told Schwartz that funding a series of academic grants probably would not lead to a treatment. Researchers and students work on many different projects and constantly seek more funding, he said. Employees, though, could sustain a focused effort.

"I said, 'If you want to start a company and the goals line up with yours for the next few years then, yeah, I might be interested,'" Kaspar recalls. In 2005, with initial angel funding, TransDerm opened its doors with Kaspar as CEO.

At first, Kaspar wondered whether he was making a mistake. But he's reminded why he made the choice whenever he meets patients. "You realize these people are depending on you," he says.

Breaking into stubborn skin

Today, TransDerm has seven employees, with offices less than a mile from a monarch butterfly sanctuary overlooking Monterey Bay.

Kaspar's first challenge was to quash the mutated keratin gene. Genes build keratin by sending single strands of genetic material, called messenger RNA, to protein-building areas of the cell. TransDerm's approach, known as RNA interference (RNAi), chops the mutated-gene-RNA in half with targeted synthetic RNA. This prevents the cell from forming defective keratin. Other unmutated keratin genes are then free to build strong cell-supporting filaments.

By 2006 Kaspar's team had a precise RNAi inhibitor, designated TD101. Two years later, the team began a clinical trial approved by the U.S. Food and Drug Administration. A single patient (out of six known at the time with TD101's target mutation) received an injection into each foot twice a week for 17 weeks. The right foot got the drug, while the left got a placebo. Neither the patient nor the physician knew until later which foot received which injection. As the trial progressed, the right foot's calluses visibly shrank. On day 98, a dime-sized piece of the treated callus fell off at the injection site. Healthy skin grew underneath.

"We have every reason to believe, but cannot prove, that the mechanism of the clinical effect was through RNA interference," the team wrote. Proof would have required a biopsy of the injection site, compromising the rest of the study.

TransDerm scientists supported their conclusion, both before and after the study, with lab experiments using cultured human cells engineered to produce either a red or green fluorescent protein. An RNAi inhibitor knocked out only the red genes. The RNAi approach appeared to be working.
But the injections of TD101 caused incredible pain in the patient’s sensitive feet. I witnessed this hypersensitivity during my foot biopsy with Esteban Abarca. He and I sat in adjacent exam rooms. My anesthesia injection hurt: a long, deep pinprick followed by burning lidocaine. As Kaspar teased me about the pain, we heard a sudden shout from the other room. “I can’t do it,” Abarca gasped. “I can’t go through with it.” For him the injection felt like a fiery, piercing stab, more intense than anyone had anticipated.

In 2009, Kaspar and his team began searching for a more “patient-friendly” way to deliver their drug to diseased cells. RNAi delivery is the technology’s stiffest challenge, says molecular biologist Steven Dowdy of the University of California, San Diego. Large RNA molecules don’t enter cells easily, he says. “Here’s this gift that can target every single gene in the body,” Dowdy says, “and the joke is that you can’t deliver it inside a cell.”

Kaspar is on “the right track,” Dowdy believes, by using inhibitors designed to overcome some of the cell’s barriers. Still, RNAi is inefficient, he says, and must be delivered precisely and frequently.

After exploring myriad delivery options, Kaspar’s team turned to an elegant concept: microneedles.

Inspired by thistles

Microneedles puncture only the top layer of skin, producing little pain. They’re not new, Kaspar says. The first microneedle-delivered flu vaccines arrived in pharmacies two years ago. But TransDerm’s manufacturing method is unique.

The man who makes the needles, Tycho Speaker, is a chemist and a tinkerer. His office is littered with tools, soldering equipment, and curled tubes of polymer gel. His expressive hands and eyebrows help him tell his story.

Speaker was working in his yard one day when he ran into a thistle. “I looked down and thought, ‘Those are microneedles,’” he says. He and his daughter plucked a few thistles, then pressed the tiny spines into clay to make a mold. But Speaker found that pouring a thick polymer into a narrow mold was tricky. “It got really burdensome, really quickly,” he says. Sticky stringers of goo kept pulling off his polymer-covered fingers.

Speaker was frustrated, until he looked at the tapered stringers closely. “I put a hair dryer to it, cut it off, and poked myself. That was the first microneedle.”

Today, Speaker makes grids of microneedles (which TransDerm calls protrusion arrays) by spreading a polymer on a flat microscope slide. He puts a block of pins onto the slide and slowly draws the block away while blowing hot air over the rapidly drying needles. A finished array, with 25 needles per square centimeter, feels “like a cat’s tongue,” Speaker says.

He goes to a microscope and focuses on the Lincoln Memorial on the back of a penny. Abraham Lincoln, he says, is about a millimeter tall. He replaces the penny with a protrusion array loaded with fluorescent dyes. The polymer cones glisten, filled with alternating greens and blues, and fade into the out-of-focus distance. Each needle is between 400 and 600 microns long — half as tall as President Lincoln.

Speaker then sticks the array into his hand between his thumb and forefinger. “When they poke you in the skin, they don’t go that deep,” he says. “The skin deforms so much that they only poke you in the 150-200 micron range. Pain
Filled with medicine, microneedles pierce the skin's outermost layer, the stratum corneum (left), and penetrate to the stratum spinosum. The needle tips dissolve (center), releasing a drug that diffuses into skin cells. Healthy genes then produce the skin's proteins properly (right).

Illustration: Christina DiPaci

Caring for orphans

Even though microneedles may hold promise for PC patients, NIH small business grant committees — which largely fund the company — want to see broader impacts.

Kaspar's first application stated that TransDerm's goal was to make RNA therapeutics for pachyonychia congenita. "The gist of the critiques was, 'We don't believe any self-respecting company would do this because there aren't enough people in the world to justify that,'" Kaspar says. "We didn't get funded."

So, he resubmitted the application with new wording. The company hopes to treat genetic-based skin disorders, he wrote, and the lessons learned from this disease could apply to a wide range of disorders. "That grant got high scores and was funded," Kaspar says.

Many of these genetic skin disorders are rare. Epidermolysis bullosa, which causes skin to blister at the slightest friction, affects one in 100,000 people. Other disorders are more common. Keratosis pilaris affects nearly half of all adults, forming red bumps on the upper arms.

The FDA designates treatments for rare diseases as "orphan drugs." Incentives, such as FDA fee waivers and seven years of competition-free marketing, encourage pharmaceutical companies to invest in diseases with fewer than 200,000 patients. These large companies, Kaspar says, jump into markets where no current drug exists. Their investment sometimes pays off. The second-most profitable drug, Rituxan, was developed for rare cancers, but then found widespread use as a treatment for rheumatoid arthritis. Others aren't so lucky. Even when companies successfully develop a drug, many small firms fold due to lack of funding, Kaspar says, leaving their patients without a treatment yet again.

"We don't ever expect to make money off of drugs for PC," he says, noting that TD101's potential patient pool is tiny. "We're more interested in helping people."

This summer, ten years after the first Park City conference organized by Mary Schwartz, TransDerm will file an Investigational New Drug application with the FDA. If it's approved, further clinical trials of a next-generation TD101 could begin this year. Eventually, TransDerm and its partners plan to develop additional RNAi inhibitors, one for each PC-affected gene. This summer's application is the first step on a long road.

During my biopsy, I felt nothing when the doctor plunged the punch into my left heel twice. He plopped the samples into vials of yellow fixative, and reminded me that the anesthesia would soon wear off.

The next day, I hopped on one foot for 300 yards to my office. With each day I hopped less. After three weeks, I'd fully healed. But I'll remember the twinges that caused me to question every step, and Abarca's acute anguish. I'm walking again, but his pain doesn't ebb or ease. At least not yet.

Sidebar: Profiles in Pain

Roseann McGrath lives near Philadelphia. She was diagnosed with pachyonychia congenita at age 4. The pain, she says, is constant. Wearing socks, or getting her feet wet, is unbearable. When you walk on top of it, you get these blowtorch burning sensations," she says. Most patients use over-the-counter pain medications and stay off their feet as much as possible. But McGrath, now 46, uses a cane or wheelchair only at home, never at work. "This is a part of our lives we usually try to hide," she says.
As a teenager McGrath heard that half of the children born to PC parents inherit the disease. She chose to never have kids of her own. “Living with something so painful and so excruciating, I felt it would have been selfish to pass it along to someone else,” she says.

Eight years ago, she met another PC patient for the first time at a support meeting organized by the PC Project. It was exhilarating, she says, and almost overpowering. “This feeling of being so alone and feeling like such a freak, that nobody really understands what this is and who we are, is now negated.”

New patients continue to enter the PC “family.” One of the newest, a three-year-old in Wisconsin named Allison, is just starting to develop calluses. She doesn’t have much pain yet, so her parents encourage her to be active while she can.

Shortly after Allison’s diagnosis, her family contacted the PC Project, which helped them connect with doctors and fellow patients. Allison hasn’t even started kindergarten, but she already has met other people like her. She, and the patients to come, will never have to know the same isolation McGrath felt.

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passions as a wildlife illustrator and as a student of the natural world.

Alex Babakitis web site

Christina DiPaci

B.F.A. (illustration and communication design) Parsons School of Design
Internships: Kew Gardens (London), National Herbarium of South Africa

For most of my life, I have been training and developing my skills as an artist. Fascinated by the natural world, I constantly sought out inspiration from nature. I had not considered the field of scientific illustration until an artist residency brought me to a biological research station in Peru and I began focusing on work that connected science and art. After earning my B.F.A., I immersed myself in the world of botany, gardening in the day and illustrating at night. I am eager to employ my skills in my internships and new career.

Christina DiPaci web site
UNITY IS FUNDAMENTAL
Imagine, you and your family have planned a vacation. For months you’ve planned and anticipated this time together. The morning of the trip you each get into separate cars. Your maps are different, you have no cell phones or other devices with which to communicate. Will you each arrive at your destination? How will you help each other if you get lost?

Much like a family, those with a rare disease like PC must have a common goal and join together in order to succeed in developing effective treatments. We need to be moving together and heading in the same direction. The International PC Research Registry (IPCRR) unites us in ‘one car.’ Patients are no longer alone when meeting with a doctor. There are now dozens of publications available on PC because of more than 500 genetically confirmed PCers who have joined the registry and provided valuable information.

The IPCRR makes the difference for PC research. We are grateful for everyone in the IPCRR — but we need every patient young or old in the IPCRR and there is more to do for those who have registered.

Join If You Haven’t Yet Joined
Are you or a family member one of the nearly 700 people who have contacted PC Project but never filled in your piece of the puzzle? Your piece is as important as any piece of the puzzle. Please help us continue to complete the PC puzzle—fill out your forms today!

Numbers do make a difference. Most of the research focuses on PC-K6a because there are more patients with that gene than any other. Does it matter whether each and every family member is in the IPCRR? Absolutely yes.

NEW! NEW! NEW! Update Your IPCRR Information Every Year!
Our online software for the IPCRR now allows you to update your information.

This allows us to collect PC information over time — the type of information many scientists and physicians are seeking. This type of data collection is called a longitudinal or life history study and gathers information for the same patients over a period of time which provides insight and observations not otherwise possible.

Longitudinal studies usually cost from $50,000 to $200,000 or more. Now you can take an active part in creating the PC longitudinal study just by updating your information—on your birthday, on a holiday or any day that you choose each year.

You may also update your information more frequently if something changes for you. Please let us know if you have any questions. We plan to also begin sending reminders to those who have completed their forms more than one year ago.

Recruit PC Patients for the IPCRR
If you are in a non-English speaking country, post online in your own language and encourage patients to join the IPCRR. We applaud Le Coeur au Pied in France for their example in this regard. There are more patients from France in the IPCRR (64!) than in any other non-English speaking country. Therefore, several Patient...
Support Meetings have been held in France and a great deal of research focus is for the French patients.

**Report Any Treatments You Try**

We know many patients working with their own doctors are trying various treatments. Some of these have been tried by dozens of other patients and results are known (such as retinoids, urea creams, salicylic acid, etc.) However, other treatments may be new and be the exact breakthrough we are seeking, but will never be made available to other patients because with a ‘single patient study’ the results cannot be published.

The only way we can learn about these possibilities is through you—the patients trying these treatments. If you have used or are using a treatment, please let us know your experience and whether or not you feel the treatment was effective.

Here are a few treatments we are currently evaluating:

**Orthotics.** We know several patients who have reported good results from professionally prepared orthotics of the type that use at least two layers with a memory foam layer on top. If PC children had the benefit of special orthotics from a young age, would it reduce the damage and lessen the pain? Do you have experience with orthotics? Please let us know.

**Botulin Toxin** (Botox or Dysport brands). We know of six PC patients using this treatment. It is not currently approved in the USA for treating feet or hands. We need details on brand of toxin used, the amount, method of application and what anesthesia is required.

**Capsaicin.** We know of one patient who has had this treatment. If you have tried this treatment or are planning to do so, please let us know.

**Retinoids** (including acitretin with brand names like Neotigason). Dozens of patients have tried retinoid treatments. A study has been done on these which show the large majority of patients find the side effects not worth the small benefits. In some cases, pain increases. However, we do not know whether this treatment might be effective for cysts? If you have experienced any good effects from retinoids, please let us know.

PC Project continues to have many small on-going studies. For example, we have completed studies on statins, topical gabapentin, oral retinoids, nail removal, etc. Other studies are being planned. Also, progress is being made in regard to two clinical trials.

**Upcoming Clinical Trial**

As of October 4, 2013, the FDA approved a trial of topical rapamycin for PC. We are now waiting for IRB approval at Stanford University. Also, the active drug product must be delivered from Pfizer to TranDerm and the topical formulation made. The trial will enroll 15 patients with confirmed PC-K6a for a six-month trial which will involve several in-person visits to Stanford University. PC Project will be supporting this study if no federal funding is available.

NOTE: Those in the IPCRR with genetics completed are eligible to enroll in PC clinical studies. Those with PC-K6a in the vicinity of Stanford University will be contacted for an opportunity to enroll.

Once the six-month trial is over, if it is successful and proves effective (as we hope!), we then have to find the way forward to make this available in other centers and to all PC-K6a patients.

**PC-K17 Web Meetings**

At the Philadelphia PSM, physicians recognized the need for more research on PC-K17 and we began these web meetings as the quickest way to capture patient experience.

For example, very little is known about cysts — and cysts are the major problem for those with PC-K17. Thanks to the open discussions about size, location, and nature of cysts, we have ideas for studies and areas of research that are needed. This is a great example of why the IPCRR is such an important part of what we do.

During the web meetings, we cover a general topic together, may review a presentation or have an expert join the meeting. We also allow a time when patients have a chance to go ‘offline’ to talk with one another on whatever topics they desire. It is not necessary to have a webcam or any video to participate in the meetings — that is up to each individual.
Just click the meeting link to view the meeting screen, call in to the toll free number and participate in the meeting.

We will continue to build a network of support and gather further information for research for PC-K17 patients. The next meeting (the fifth in this series) will be held October 30, 2013 at 10:15am MDT.

**OTHER WEB MEETINGS**
Would you like to have a web meeting with other PC patients? Let us know a topic you’d like to discuss, and a date and time you’d like to meet and we will do the rest. It’s a great way to share.

**TAKING ACTION**
We want to send a shout out to Janie Youhas for contacting the “The Dermatologist” and putting us in contact with their managing editor. We are in the process of writing a new article on PC for this journal. One way to help us move forward is to continually think of ways to increase awareness of Pachyonyica Congenita.

**PC SCIENTIFIC OFFICER**
PC Project has a job opening for a Scientific Officer (PhD or MD) to join our team. This person will oversee PC research projects and studies, facilitate the collaboration and coordination among scientists and physicians and participate in writing publications and grants.

**PC BABIES**
Over the last months, we have recognized a pattern in newborn babies with PC-K6a.

- Often treated for nail fungus
- Often diagnosed with thrush
- Hospitalized for failure to thrive

We believe the problem with feeding is not connected with the white leukokeratosis, but with the pain from ‘first bite syndrome.’

These babies thrive when parents receive guidance from other PC parents about using soft nipples and enlarging the hole so the formula is poured not sucked especially in the first 15-25 seconds. A physician has asked for information for a publication on these cases. Thank you for helping us!

**CYST STUDY**
Samples from the first 12 PC donors have now been analyzed and histopathology completed. It was a surprise that PC-K17 patients donated epidermal inclusion cysts and a PC-K16 patient donated a steatocystoma! Publications all associate steatocystomas with PC-K17 only. (See chart below.)

A group of specialists are now working to plan the next phase of the cyst study. We hope to collect additional samples and learn more about PC and cysts — information that will lead to better treatments for cysts.

### Cyst Study-First 12 Donors Summary

<table>
<thead>
<tr>
<th>IPCRR#</th>
<th>Gene</th>
<th>Mutation</th>
<th>Steatocystoma</th>
<th>Epidermal Inclusion</th>
<th>Pilus</th>
<th>vellous hair</th>
<th>Other samples</th>
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<tbody>
<tr>
<td>18</td>
<td>K6a</td>
<td>E428K</td>
<td>1</td>
<td>4</td>
<td></td>
<td></td>
<td>1 Unremarkable Skin</td>
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<tr>
<td>253</td>
<td>K6a</td>
<td>Q435X</td>
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<tr>
<td>7</td>
<td>K16</td>
<td>L132P</td>
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<tr>
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These words do not refer to types of cysts.
 
Pilosaceous is more of a clinical term not a pathologic diagnosis.
Pilosaceous cysts are usually inflammatory lesions that occur in relationship to acne and may cause the skin. The epidermal inclusion cyst is usually a "bump" under the skin and will become inflamed if it ruptures but is not primarily an inflammatory lesion. Unfortunately both terms are used interchangeably which creates confusion. Most of the cysts we are interested in will not be pilosaceous types.
**Clinical Trial Update**

Our hearts are full of hope as the Phase 1 clinical trial for topical rapamycin will enroll patients in the next 1-2 months.

While many things can be tried “off-label” by a physician for a single patient, to make treatments available to all patients, specific steps must be followed. This pathway has often been outlined with three parts:

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<th>Drug Discovery</th>
<th>Pre-Clinical</th>
<th>Clinical</th>
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**Drug Discovery.** This includes both developing new drug compounds as well as finding drugs that may be ‘re-purposed’ for PC. PC Project is working with researchers in both of these efforts.

**Pre-Clinical.** Before a drug can be used for patients, a great deal of preparation must be done using cells and animal models to test for safety — and to prove that the drug may be effective (have efficacy).

**Clinical.** This part of the pathway actually has many different parts. For example, first an application must be filed with the FDA (called IND for Investigational New Drug). This is true even if the drug is a re-purposed drug. Permission is then given to move forward to Phase 1 (safety) Phase 2 (safety and efficacy) and Phase 3 (then available for sale) clinical trials. In each of these sections, the FDA may require extensive additional testing such as additional animal toxicity studies which can cost $175,000 to over $1,000,000. We intend to involve PC patients in getting the message to the FDA of how much a treatment is needed.

After completing all the requirements, the drug development then moves to issues of licensing, manufacturing, payee (will insurance cover?) and ‘LAUNCH’ where the drug is available for sale and available to patients.

The typical time/cost for drug development is 10-12 years and over $1 billion in costs. PC Project is moving forward more quickly with less expense — but there are expenses.

**Topical Rapamycin Trial**

Originally this drug was thought to only be effective for PC-K6a. We have been advised that PC patients with painful keratoderma with PC-K6a, PC-K16 or PC-K6b are eligible for consideration for the trial. We have contacted patients 16 years of age and older for permission to release contact information.

If we have not contacted you and you would like your contact information released to our Stanford team for consideration for the clinical trial, please send an email to info@pachyonychia.org. This does not enroll you in the trial, but allows Stanford to contact you. We believe the patient contacts will begin in late December 2013 or early January 2014.

**A New Concern**

As the Topical Rapamycin clinical trial moves to enroll patients, we suddenly became aware of the problem that there is only enough drug for 15 patients for six months! We are very optimistic that topical rapamycin is going to be effective and reduce pain for patients without side effects — and then after six months there will be no more available for patients. So it is critical we find a way to solve this problem and (a) gain FDA approval to move more quickly and (b) have this drug manufactured and available.

**Marketing Effective Drugs**

What to do? We have never had anything effective so we have never had to even think about this before.

One solution would be for every individual patient to find a doctor, get a prescription and locate a formulating pharmacy to attempt to make the drug for them. But this is not the approach that has propelled the success of PC project this far! It is not the approach we want to take at PC Project. And, hopefully, it is not the approach any of you will want to take.

**Manufacturing.** We are approaching both Pfizer, our partner TransDerm and others to interest them in manufacturing topical rapamycin beyond this six month trial. There will be a cost to make the drug and companies must also make a profit to remain in business. We hope we are united as a PC community so that if we can interest pharma in manufacturing an effective product that reduces pain without side effects, we will be willing to pay the price and ensure a reasonable profit for the companies as well.

**Insurance.** We are also beginning our efforts to see that this drug will be
covered by insurance where possible and that there will be mechanisms in place to make the drug available to those without insurance. There are real costs for the drug that have to be sorted out.

**FDA.** The first request by TransDerm for ‘Fast Track’ was denied, but we will appeal this and will ask your help to tell the PC story. Also, we will request a ‘compassionate use’ designation to make the drug available while we move through the different phases before ‘Launch.’

### YEAR END FUNDING APPEAL

“Making Something Out of Nothing.”

is the theme for our 2013 fund drive.

The $2-for-$1 match is in place through the end of 2013.

Every donation makes a difference.

### A MONTH OF MEETINGS

PC Project attended three important meetings in October. Here are some highlights of each meeting:

**PeDRA**

"Amidst a growing sea of scientific work focused on skin disorders in adults, there is only a limited amount focused on children. In 2012, a group of pediatric dermatologists founded PeDRA, the Pediatric Dermatology Research Alliance, in hopes to better treat and cure dermatologic diseases in infants, children and adolescents. Their mission is to foster collaborative clinical, translational, and basic science research. The goal of this meeting was to gather the top leaders in pediatric dermatology research in one room to share, develop, and discuss new and innovative research to treat skin disorders." (Jean Pickford, F.I.R.S.T.)

The very first PeDRA conference was held in mid October with six patient advocacy groups and about 80 pediatric dermatologists attending. While each advocacy group was given a few minutes to introduce their organization and disorder, we were honored that PC Project (Mary Schwartz) was invited to give a formal 30 minute presentation on our patient registry. The presentation will be available to all members of PeDRA and will help to increase awareness of pachyonychia congenita and the patient registry.

"Throughout the meeting and informal discussions, it was easy to feel the passion of these physician/scientists. They are fueled by curiosity; relentless in their research efforts; and simply put – they get it. They understand how important it is to find better treatments and cures — and they really care." (Jean Pickford, F.I.R.S.T.)

From this meeting, we have pages of notes and dozens of follow-up contacts for additional research including plans for several additional PC studies for treatments that may be effective. This includes an opportunity to set up a comprehensive study on botulinum toxin injections (Botox or Dysport).

**Partnering For Cures**

PC Project received scholarships for Mary Schwartz and Roger Kaspar to attend the fifth Partnering for Cures meeting on November 3-5, 2013 in New York City, New York.

This dynamic meeting sponsored by Faster Cures (a Michael Milliken group) provided an opportunity to attend presentations and set up networking meetings. We were able to identify other disorders that may benefit from topical rapa and groups that may help us move this forward to ‘launch’ and market topical rapa as described on the front page. We also learned of new methods of collecting essential data using smart phones and other activity monitors to track steps, sleep and other factors which can prove the effectiveness of treatments (called endpoints).

**NIH/NIAMS Coalition**

The National Institutes of Health (NIH) is the major government funding organization for health research in the USA. There are 27 institutes and PC is served by the National Institute of Arthritis, Muscular Skeletal and Skin (NIAMS).

The NIAMS Coalition 2013 Outreach & Education Meeting was held November 6, 2013 in Washington DC. PC Project (Mary Schwartz) was grateful to be invited to this meeting with all expenses covered. There were about 40 other patient organizations and we able to hear excellent presentations about NIAMS. As most understand, funding for the NIH grants is at an all time low point making grant funding very difficult to obtain.

In this meeting, PC Project was singled out for our scientific research achievements. This was surprising with the many large patient advocate organizations present that have large budgets and many staff members.
We gratefully acknowledge the estate planning gift received last week from the Estate of David Wittmer in the amount of $165,000.

David first contacted PC Project by telephone in April 2005 and immediately joined the IPCRR. He attended the 2005 Patient Support Meeting held near Niagara Falls, Ontario and became a dear friend. Over the years, he quietly made donations and provided scholarship funds for others to attend PC Patient Support Meetings. At some point before his stroke, he included PC Project in his Will.

This generous gift will be matched $2-for-$1 by our sponsor. The funds come at a very special time and provide the needed funding to move the topical rapamycin clinical trial forward. We had faith that funds would be found for this inasmuch as the government funding has been delayed (or possibly denied). The contract with Stanford for the administration of the trial costs is almost exactly the amount of this gift. We are grateful to our friend, David Wittmer.
TOP 10 CURRENT PROJECTS
There are many, many different projects at many different stages at PC Project. Here are just a few of those at the top of the current list:

1. **Topical Rapamycin Clinical Trial.** Headed by Roger Kasp- par, TransDerm, Inc. this is the leading project at this time. If successful, the goal is to have a product that will be manufactured and available. We are not taking short cuts (however tempting that might be) because that would mean only a few patients might ever benefit. The road through the FDA to an approved treatment is challenging. We are moving on that pathway day-by-day. We expect to contact patients before December 15, give a final list to Stanford at that time. The six-month trial, will enroll 15 PC patients with specific PC-types. It will involve seven trips to Stanford University in California. The pre-trial work in animals and humans has been very encouraging.

2. **siRNA.** The initial steps for the second siRNA clinical study have been completed. While only 17 patients have the targeted mutation, this is the ‘longshot’ therapy that has great promise. It directly targets the condition.

3. **Botulinum toxin (Botox or Dysport).** We will soon hold the first teleconference with physicians to discuss this procedure. No standards have been established so each patient is a type of ‘science experiment.’ We want to establish a better protocol and have some meaningful studies to determine why it is sometimes effective and other times not effective.

4. **PC PhotoBox.** You can see a video of the PhotoBox at http://youtu.be/ZW1ytC2a6aU. This tool was designed and produced at PC Project to meet the need for consistent photos during the clinical study.

5. **Objective Data Gathering Using Digital Monitors.** We are working with Gecko Enterprises (a group of creative technical experts) to identify devices which may allow us to gather objective data to measure improvement. Most of the data available is subjective (patient reported) and has great value, but FDA and others want objective data as well. In a study with Parkinson’s disease this group was able to gather essential information. We believe this will have application for PC as well. Some of you may have used a FitBit or other tracking device. If so, please let us know about your experience. There are other devices being developed such as a mat designed for diabetics that gives a heat image of feet simply by pressing the feet lightly on the mat. It is a very interesting predictors for blister formation, etc. And more ideas are in discussion…

6. **Educational Outreach.** The next opportunity is in January 2014 in Innsbruck, Austria. Seven PC patients will attend from Austria, France, Hungary, Sweden and Switzerland.

7. **Publications.** The most important method for improving awareness of PC and attracting researchers to work on basic science and translational research projects that will benefit PC. We have just submitted an article to The Dermatologist. (This opportunity came to us because a PCer, Janie Youhas, contacted the publishers and suggested it!) We have approximately 20 other articles underway with various authors around the world including an update to the IPCRR data published in 2012. We now have more than 500 genetically confirmed PCers!

8. **BioBank.** One of the important efforts is creating PC cell lines using skin samples donated by patients. In addition, we have projects using PC samples for microarrays, nerve staining regarding pain, stem cell research projects and more. From time to time, we will contact patients about donating a sample. Some of these are from affected areas and other times the sample can be from any location. We are careful to ensure that the most possible research success is obtained from each sample.

9. **IPCC Annual Symposium.** This is the meeting where the research goals are set. We are delighted that so far every specialist selected has accepted our invitation to speak. We are so pleased that we are able to continue to engage the top specialists in each area we need.

10. **Updating Brochures.** It is time to update the PC Brochures. If you have suggestions, please let us know. We’ll try to include a few projects each month as time/space allows.
A TRIBUTE TO HOLLY EVANS-

Holly joined PC Project on Monday, August 20, 2007. She had just returned home from serving as a missionary for The Church of Jesus Christ of Latter-day Saints in the South Carolina, Columbia Mission, about a week earlier. Holly is the youngest of 14 children. Mary and Holly decided to ‘try it out for a few weeks’ — and, as they say, the rest is history.

Most of you have spoken with Holly on the phone and know that she is always pleasant, upbeat, happy and ready to help.

What you don’t see or know is that she is a mind reader! Truly. If Holly hears Mary talking on the phone about something, before the conversation is over, Holly will have the information researched and ready either to send out — or ready for Mary to use.

Holly attends the University of Utah majoring in Information Systems. She will graduated in May. She is a natural with computers (and screens of all types)! For example, she was the videographer and editor of the PhotoBox video (see pg 2 for link) but, of course, did not list her name in the credits!

She is truly a behind the scenes magician. Mary adds a bit of ‘spit and polish’ but a lot of the heavy lifting is accomplished by Holly. December 21 is Holly’s birthday and a good time for all of us to acknowledge that she is a great part of all of our success. After more than six years at PC Project Holly still says she “is really excited to be working for PC Project.”

FACEBOOK UPDTE

By Julie Peconi
PC Project Social Media Co-ordinator

We are working hard to increase PC Project’s presence on social media, starting with Facebook. For those of you unaware of how Facebook works, people on Facebook can ‘like’ our page: Pachyonychia Congenita Project. This means that when we put information on the Page (called posting) our posts will show up on our likers’ personal news feed. This then provides them with what are essentially mini newsflashes about PC! Below are just a few of the ways in which we believe we can use Facebook to promote the great work for PC:

1. Drawing attention to changes or updates in the website
2. Explaining the Research Registry; its benefits and encouraging people to join
3. Highlighting new research and providing updates to ongoing studies
4. Promoting the patient support meetings and teleconferences
5. Fundraising ideas/activities

We also plan to post general information concerning PC, for example, the numbers of those genetically confirmed and the worldwide locations of PC. Most people don’t know these facts and may find them interesting.

As we have just begun, not many people are aware we are on Facebook and we need your help! If you are on Facebook please like our page so that you will be able to see our posts. And if you like what you read, please let us know! Every ‘like’, ‘comment’ or share’ on our posts greatly improves the reach of our page, thus getting more knowledge and information out to the PC Community and our friends and family.

You can find us at https://www.facebook.com/pages/Pachyonychia-Congenita-Project/139161046150358

SOUPS ON! YOU ARE MAKING IT HAPPEN!!

As invited in our Year End Letter, 31 new donors have contributed to the PC pot! Every donation matters — small or large — and every donation is matched in 2013 $2-for-$1 so the funds triple. We appreciate each person doing whatever they can — so we can provide ‘soup’ (or services) to truly benefit all those with PC everywhere. Thank You!