UPCOMING MEETINGS

International Pachyonychia Congenita Consortium (IPCC) Annual Symposium
Atlanta, Georgia (prior to the SID Annual Meeting)
May 4th (Tuesday) 9am—4pm with dinner Tuesday evening
May 5th (Wednesday AM) 9am—11:30 with lunch after
(Note: The SID Translational Research Session will be held Wednesday PM)

CALL FOR PAPERS: We welcome submissions for presentations at the 2010 IPCC Annual Symposium. A small stipend will be available to those selected. The papers selected for the 2010 PC Update (see below) will also be invited to present at the IPCC Annual Symposium.

Please submit a 1/2 page summary/abstract to info@pachyonychia.org no later than 15 March 2010. Please register to attend the meeting at http://www.surveymonkey.com/s/QH5C735

GO Delivery! Delivery of Nucleic Acids to Skin
March 24-26, 2010, Stanford University (see invitation page 3)

PC 2010 JID Symposium Proceedings Update: AUTHORS INVITED

In 2005, the Symposium Proceedings for the first Pachyonychia Congenita Symposium held in 2004 were published. The goal of PC Project, sponsor of the IPCC, is ‘Find a Cure for Pachyonychia Congenita.’ Where are we in that search? What is the latest data from the International PC Research Registry? What have we learned about care and best practices for PC patients? Where is the science at this time?

A JID Symposium Proceedings 2010 PC Update has been proposed. We are excited to announce that Irwin McLean, Roger Kaspar and Sancy Leachman have agreed to serve as co-editors for this project so that we can produce a high quality and very valuable publication.

This is an excellent opportunity to publish the broad data gathered through the International PC Research Registry (IPCRR) and to provide more accurate information on Pachyonychia Congenita than any previous publication.

PC Project has pulled ‘bits and pieces’ of information together in a DRAFT list of ideas (see pg 2). This is a DRAFT and all ideas are welcome. We invite every author who has relevant data on PC care or PC research to participate in this publication.

If you have a suggestion for a paper (whether on the list on page 2 or not), please submit a 1/2 page summary/abstract to info@pachyonychia.org by March 15, 2010. You will be notified regarding acceptance by April 1, 2010 and the schedule dates will be established.

Also, if you are a physician treating PC patients and would like to be a co-author on one of the papers, please contact PC Project at info@pachyonychia.org. Please let us know your areas of interest and specialty.
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<th>Article Title or Description</th>
<th>Responsible author has been bolded; other authors and possible authors listed alphabetically (not listed in order for publication citation)</th>
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<td>Analysis of PC keratodermia from photographs of PC with mutation status known</td>
<td>Leachman, Majmudar, McLean, O'Toole, Smith, et al</td>
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<td>Botulinum toxin in the treatment of PC</td>
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<td>Case Reports: IPCRR data is available to study other groups of patients with specific mutations</td>
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<td>Case Reports: K6a N172del</td>
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<td>Case Reports: K16 R127C</td>
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<td>Correction of a mutant keratin 6a gene in HEK293 cells using small oligonucleotides</td>
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<td>Current Best Practices for PC</td>
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<td>Delivery: GO and MRC Grants</td>
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<td>EGFR Antibodies</td>
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<td>Phenotypic Effect of FLG on PC Mutations</td>
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<td>Gentian Violet and PC</td>
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<td>Humira study</td>
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<td>PC Blistering: Ultrasound Study</td>
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<td>PC Genetics: Discovery of PC Mutations</td>
<td>We'd like to invite authors of previous papers to work with us to have some fun and help end some of these misconceptions that were published prior to the availability of genetic testing.</td>
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<td>PC is NOT associated with... (A Top Ten List of features in the literature not supported by the IPCRR data)</td>
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<td>&quot;PC Tarda or Late Onset&quot; &quot;Alopecia&quot;</td>
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<tr>
<td>The PC Project Story: A Tale of Collaboration (include behind-the-scenes details on the organization and individuals involved in the Phase 1b clinical trial?)</td>
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Grand Opportunities in Transdermal Delivery of Nucleic Acids

Please join us for a symposium and workshop on the topic of delivering nucleic acids to skin cells

Stanford University
Clark Center
March 24-26

Keynote Speaker: Peter Marinkovich, MD (Stanford University)
“Epidermolysis Bullosa and Molecular Replacement Therapies”

Presentations by selected symposium participants
Remarks by Carl Baker, PhD (NIAMS)

To register go to: http://www.surveymonkey.com/s/GO_Delivery

The lectures and “hands on” workshop will focus on emerging formulations for delivery of nucleic acids to skin cells, and on imaging technologies for following effector molecules and assessing expression levels of target genes

For meeting information contact:
Dr. Christopher Contag, Stanford, ccontag@stanford.edu
Dr. Roger Kaspar, TransDerm, roger.kaspar@transderminc.com
Dr. Leonard Milstone, Yale, leonard.milstone@yale.edu
International Pachyonychia Congenita Consortium (IPCC) Members 2009-2010

Medical & Scientific Advisory Board
*Sancy Leachman, MD, PhD (MSAB Chair)
Sherri Bale, PhD
*C. David Hansen, MD
*Peter R. Hull, MD
Roger L. Kaspar, PhD
E. Birgitte Lane, PhD
W. H. Irwin McLean, DSc, FRSE
*Leonard M. Milstone, MD
**Dennis R. Roop, PhD
Frances J.D. Smith, PhD

*Members of the PC Physician Panel
**Oversight of the IPCC Working Group Teams for 2009-2010 with Jouni Uitto
All MSAB members are ex-officio members of each of the IPCC Working Group Teams

The following IPCC Working Teams were organized in May 2009.

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<td>Leigh, Irene</td>
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IPCC General Members

Int'l PC Consortium
May 2010 Symposium

At the 2010 IPCC Symposium nearly 50 physicians and scientists actively discussed PC-related data and research to determine the best plan forward for 2010-2011.

If you would like more information on any of the presentations, please contact info@pachyonychia.org.

**Session 1**

**Pachyonychia Congenita Mutations**
Frances J.D. Smith, PhD
College of Life Science, University of Dundee, Dundee, UK

**IPCR Data 2010**
Mark Eliason, MD, David Hansen, MD
University of Utah, Salt Lake City, UT

**Specific Mutation Phenotypes**
Teresa Fu, MD, Jean Tang, MD, PhD
Stanford University, Stanford, CA

**Retinoid Treatment for PC**
Robert Gruber, MD
Innsbruck Medical University, Innsbruck, Austria

**PC Life History: Preliminary Data**
Amy S. Paller, MD
Northwestern University, Chicago, IL

**PC Nails: Preliminary Data**
Phillip Holler, MD, Adam I. Rubin, MD
Hospital of the University of Pennsylvania, Philadelphia, PA

**DISCUSSION: Organizing for Success**
Mary Schwartz, Director, Pachyonychia Congenita Project, Salt Lake City, UT

**Summary:** The identification and genotyping of PC patients and the resulting studies based on the data collection in the International PC Research Registry (IPCRR) were presented. There was extended discussion on how best to organize for educational outreach to share the data available more broadly and correct misinformation currently in the literature. An active Educational Outreach program and preparation of better diagnostic and ‘best practice’ guidelines are among the top priorities for PC Project/IPCC for the coming year, and these were confirmed as appropriate goals by IPCC participants.

Would you like to be involved with these objectives? Please contact Mary.Schwartz@pachyonychia.org.

**Session 2**

**Correction of a mutant keratin 6a gene in HEK293 cells using small oligonucleotides**
Hector Zambrano, MD, Leonard Milstone, MD
Yale University, New Haven, CT

**Development of Skin-Humanized Models of Type 1 PC**
Fernando Larcher, PhD
Epithelial Biomedicine Division, CIEMAT, Madrid, Spain

**Assessing delivery and quantifying efficacy of siRNA therapeutics in the skin using a dual-axis confocal microscope**
Hyejun Ra, PhD, Emilio Gonzalez, PhD, Chris Contag, PhD
Stanford University, Stanford, CA

**IPS Cells and Rare Skin Disorders**
Dennis Roop, PhD
University of Colorado, Gates Center for Stem Cell Biology, Aurora, CO

**Alternative approaches to therapy for keratin disorders**
Birgit Lane, PhD, FRSE, FMedSci
Institute of Medical Biology, Singapore

**Trans-splicing in autosomal dominant diseases**
Johann Bauer, MD
Paracelsus Medical University Salzburg, Salzburg, Austria

**Library Screening: Statins and Clinical Study**
W. H. Irwin McLean, DSc, FRSE, Peter Hull, MD
College of Life Sciences, University of Dundee, Dundee, UK

**DISCUSSION: The Future - Clinical Trials and Studies**
Sancy Leachman, MD, PhD, University of Utah, Salt Lake City, UT

**Summary:** The discussion identified many preclinical and clinical studies in progress in various locations and countries. These were prioritized as basic, early translational, later translational and clinical trials with botox, retinoids and siRNA currently underway.

**Session 3**

**Ultrasound Studies of Pachyonychia Congenita**
Diana Gaitini, PhD, Eli Sprecher, MD, PhD
Rambam Medical Center, Haifa and Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
MRC Grant for siRNA Development
W.H. Irwin McLean, DSc, FRSE
College of Life Sciences, University of Dundee, Dundee, UK

Nucleic acid delivery to skin—update on GO Delivery! Project
Roger L. Kaspar, PhD
TransDerm, Inc., Santa Cruz, CA

SiRNA-mediated inhibition of mutant K6a in human skin equivalents
Robyn P. Hickerson, PhD
TransDerm, Inc., Santa Cruz, CA

Delivery of functional siRNAs using microneedles Emilio Gonzalez, PhD, Tycho Speaker, PhD
Stanford University, Stanford, CA, TransDerm, Inc., Santa Cruz, CA

DISCUSSION: Moving Forward on Nucleic Acid Delivery
Leonard Milstone, MD
Yale University, New Haven, CT

Summary: Presentations in the final session reported on progress on ‘delivery’ which was the major goal set at the 2009 IPCC Symposium. (Note: information on the GO Delivery! Grant is available at www.GO-Delivery.com. Request a password from Andrea.Burgos@TransDermInc.com.

2010 Publication UPDATE
Following the May 2010 IPCC meeting, discussions were held with several leading journals regarding an update to the 2004 Symposium Proceedings, which were published in a special issue of the Journal of Investigative Dermatology in 2005. The decision has been made to publish in a single issue of the JID, a review article and seven to eight research articles (in a “1st series”) in late 2010 or early 2011. These JID articles will be tagged with the IPCC logo to make them easy to identify. Additional articles will be published in the following months in a variety of journals. The articles proposed for the JID “1st series” include:

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<th>List of Proposed PC Update Articles—JID “1ST SERIES”</th>
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<td>IPCC Proceedings Review</td>
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Other articles being considered for 2010 and 2011 release in the JID (“2nd series”) and other quality publications include:
- PC Clinical Review (Hansen),
- siRNAs against specific keratin genes (Smith),
- Case Reports: K6aN172del (Smith, Hogendorf),
- PC Nails (Rubin),
- PC Life History (Paller),
- Phenotypic Effects of FLG and PC (Smith, Gruber, Schmuth),
- PC Mosaicism (Leachman), PC Transgrediens (Leachman, Harris).

Additional research is underway for future publications on
- Retinoids and PC (Gruber, Schmuth, et al [see below])
- PC Blistering-Ultrasound Study (Sprecher),
- PC Pain (possibly Chen and LiLi)

There is a wealth of data in the IPCRR that has not been evaluated or published. The IPCRR database is easy to query and provides a basis for quality publications. If interested, send proposal to info@pachyonychia.org.
Int'l PC Research Registry
IPCRR

IPCRR data published in 2005 reported on 50 PC patients. The IPCRR has extensive data, physician consultations and images on 254 of the 400 individuals and these data will be published as a key part of the 2010 PC Update.

The IPCRR data provide better information for diagnosis and understanding of PC. Some of the key findings include:
- Severe, intense PAIN is one of the most relevant features of PC across all genes and all mutations (although almost never referenced in the published literature)
- PC-1 and PC-2 subgroups do not correlate well with the genetics
- Not all PC patients have affected nails (despite the name of the disorder) and toenails are more often affected than fingernails
- No individual or family with 'nails only' has been found to date with a mutation in any PC-related gene

Based on the IPCRR data, the following features do not correlate with PC: bone deformities, cataracts, corneal lesions, deafness, hair loss (or hair abnormalities) and mental retardation. Although reported in the literature, these published studies usually involve single-case or single-family series and lack genetic confirmation of PC mutations.

Retinoids and PC

At the IPCC meeting in Atlanta, Robert Gruber presented data from the IPCRR on 35 PC patients who had used retinoids. Because the data were retrospectively gathered, some essential details were not available. The IPCC members concluded that a 'prospective' study should be conducted. Those interested will work together to plan and/or conduct the study including John DiGiovanna, Robert Gruber, Peter Hull, Sancy Leachman, Leonard Milstone, Amy Paller, Phoebe Rich, Laure Rittié, Matthias Schmuth, Jean Tang and Xue-Jun Zhang. If you would like to assist in this project, contact Mary.Schwartz@pachyonychia.org.

Before holding the initial web meeting to plan a new study, discussions were held with Peter Hull who has an on-going PC study involving statins and retinoids. Robert Gruber and Matthias Schmuth agreed it is best to wait for the results of Hull's study before moving forward with the prospective study.

IPCC GOALS: Educational Outreach, PC Diagnostics and PC Best Practices

The PC Physician Network will include all interested in helping with these goals and includes MSAB members David Hansen, Peter Hull, Sancy Leachman, Leonard Milstone, Jean Tang as well as Gerald Asin, Giselly de Cringnis, Takashi Hashimoto, Mark Eliason, Edel O'Toole, Amy Paller, Lori Paragas, Phoebe Rich, Adam Rubin, Virginia Sybert, Antonella Tosti and Maurice van Steensel. The first planning session will be held in July.

Ideas from the IPCC discussion and follow-up survey forms have been collected, entered in the PC database and are being implemented:
- Promote the concept of primary features of PC or likely not PC (ed note: these primary features seem to be pain, plantar keratoderma (not necessarily focal) and usually one other feature such as thickened toenails and/or cysts)
- Broaden PC publication outreach to include pediatrics, pain, podiatry, genetics and other fields – a list of some of the leading journals in these areas was created
- Sponsor IPCC members as lecturers at medical schools
- Search engine optimization and improve tags, use Wikipedia, PC Website for outreach
- Contact GPs via mailings, offer Grand Rounds opportunities and provide PC informational publications
- Arrange patients for educational outreach programs at universities

Stanford Medical Practice Course Hosts 4 PC Patients

Jean Tang (newest PC MSAB member) facilitated this opportunity with 4 PC patients participating in the Stanford Medical Practice Course on May 28, 2010. This multi-patient approach is much more informative than single-case or single-family events.

Nashville Derm Society Grand Rounds will include PC Patients

Another group of four patients will participate in the Nashville Derm Society Grand Rounds (June 18, 2010) under the leadership of Amy Valet of Vanderbilt University School of Medicine.

NOTE: PC Project sponsors patients for these events, ensures that the patients are genetically confirmed for PC and offers a comparison of genes/mutations for the most comprehensive educational experience. Slides and handouts are provided. If you would like to schedule an event for your institution or organization, view or use the slides, or see a sample of the handouts, email info@pachyonychia.org.
International Pachyonychia Congenita Consortium (IPCC) Members 2010-2011

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W. H. Irwin McLean, DSc, FRSE
Leonard M. Milstone, MD
Dennis R. Roop, PhD
Frances J.D. Smith, PhD
Jean Tang, MD, PhD*
*appointed May 2010

PC Physician Network
PC Consultation Team for the IPCRR
David Hansen, Peter Hull, Sancy Leachman,
Leonard Milstone, Fanny Morice, MD (France)

Clinical Studies, Educational Outreach,
PC Diagnostics and PC Best Practices Teams
Gerald Asin, Eulalia Baselga, Susan Bayliss, Bernard Cohen, Giselly De Cignis, John DiGiovanna,
Mark Eliason, Ramon Grimaud, Robert Gruber,
Peter Hull, Takashi Hashimoto, Alain Hovnanian,
Alan Irvine, Aleksey Kansky, Sancy Leachman,
Irene Leigh, Jemima Mellerio, Leonard Milstone,
Fanny Morice, Colin Munro, Edel O’Toole, Amy
Paller, Lori Paragas, Phoebe Rich, Adam Rubin,
Matthias Schmutz, Eli Sprecher, Virginia Sybert,
Jean Tang, Antonella Tosti, Jouni Utto, Maurice
van Steensel, Hector Zambrano, Xue Zhang, Zue-Jun Zhang, Pingu Zhou

Genetics Team
Frances Smith, PhD
David Hansen, Peter Hull, Sancy Leachman,
Leonard Milstone

Research Team
Roger Kaspar, PhD
Sherri Bale, Jiang Chen, Chris Contag, Marcela Del Rio, Marianne Foldvari, Daniel Gibson, Emilio Gonzalez, Richard Heller, Robyn Hickerson, Yeu-Chun Kim, Birgit Lane, Maria Fernanda Lara, Fernando Larcher, Sancy Leachman, Samir Mitragotri, Leonard Milstone, Irwin McLean, Dennis Roop, Frances Smith, Tycho Speaker, Jean Tang

IPCC General Members—All Interested Physicians and Scientists are invited to join the IPCC
First Series of Articles Submitted to JID
As planned and announced in several recent IPCC Newsletters, the first group of nine PC-related articles were completed, reviewed by the editors for PC Project (Roger Kasparr, Irwin McLean and Sancy Leachman) and submitted to the JID. We hope all will be accepted for publication.

We are striving to move the next group of articles forward to publication and encourage any who desire to publish in collaboration with PC Project to contact us right away. Some of the articles being proposed and considered include the following. Other authors and other articles are welcome. There is a wealth of data in the IPCRR that has not been evaluated or published. The IPCRR database is easy to query and provides a basis for quality publications. If interested, send your proposal to info@pachyonychia.org.

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<td>Rubin, et al</td>
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<td>Phenotypic Effects of FLG and PC</td>
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<td>PC Mosaicism [has been submitted]</td>
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<td>Retinoids and PC [has been submitted]</td>
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<td>Genotype-Phenotype Correlation Using Photo Images</td>
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<td>O’Toole, et al</td>
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IPCC Meeting
May 3– May 4, 2011
Prior to the SID
Phoenix, Arizona

The presentation spots for this meeting are limited. Please submit your abstract to PC Project before February 1, 2011 for consideration for oral presentation at the IPCC Meeting in May 2011.

GO Delivery! Project
Begins Year 2
Efforts to develop skin model systems and common reagents useful to comparatively study nucleic acid delivery technologies continue to progress. A second meeting for participants and interested parties is in the planning stages for the beginning of 2011. We hope many of you will be able to participate in this important program as topical skin DELIVERY continues to hamper progress of promising drug candidates for treatment of PC. This effort is led by TransDerm (Roger Kasparr), Stanford (Christopher Contag) and Yale (Leonard Milestone).
PC Project Sponsored Educational Outreach
Following discussion and guidance at the IPCC meeting in May 2010, PC Project is sponsoring Grand Rounds or similar educational outreach events. It is clearly more advantageous for those attending a Grand Rounds to meet a variety of patients with different genetically-confirmed PC mutations, rather than just a single case or single family. Also, the experience is more beneficial and positive for patients who attend such an event together.

PC Project will provide travel and housing for patients as well as detailed handouts documenting the various mutations, patient images and information on Pachyonychia Congenita. If needed, slide presentations can be made available.

Since May, two such events have taken place and we have had positive feedback from the organization and the patients after each event.

- May 28, 2010. Four PC patients were at the Stanford University two-hour “practice of medicine” course. About 50 residents attended the class. Many thanks to Jean Tang for her efforts in including PC in this worthwhile event.
- June 18, 2010. Four PC patients participated in Grand Rounds at the Nashville Dermatology Society meeting.

If you would like to schedule patients for an event at your institution or organization, please contact info@pachyonychia.org.

IPCC Physician Network: Best Practices Team Holds First Web Meeting
Members of the IPCC Physician Network and other active IPCC members, held the first web meeting on ‘Best Practices and Educational Outreach for PC’ to discuss and develop a strategy for developing a ‘best practices’ guideline for PC.

It is clear that we are at the very beginning of this process and we have only ‘soft’ data from patient experiences and no data based on clinical trials. Still, we have information from over 300 genetically-confirmed PC patients and we need to find effective ways to share this information to benefit both physicians and patients.

Real Timeline for Best Practices

- 1995 McLean/Smith identify the genes that cause PC
- 2004 IPCRR (International PC Research Registry) begins with three PC patients
- 2004 First PC Symposium held in Park City, UT with 23 physicians and scientists
- 2005 Symposium Proceedings published JID Special issue
- 2008 siRNA TD101 Clinical Trial
- 2008 PC Project advertises in the IPCC newsletter for authors to publish IPCRR data
- 2009 the IPCC Physicians Network holds quarterly web meetings
- 2010 IPCRR has identified and confirmed over 300 patients with PC
- August 23, 2010 “Best Practices” web meeting to develop PC Clinical paper based on IPCRR data
- FUTURE DATE PC Best Practices Guidelines will be possible based on clinical studies.
IPCC Physician Network continued
Right now it is “Best Observations” or “Best Guesses”. However, we believe that by focusing on this goal, new clinical studies may evolve which will help to clarify and validate the data now available in the IPCRR.

Dave Hansen has been working with the IPCRR data for the past several years and will lead the effort to publish a clinically-oriented publication as a companion to the science-oriented manuscript recently submitted to the JID.

If you are interested, but were not able to attend the web meeting, you can listen to the recorded meeting and you are welcome to participate with us. To get the link, email info@pachyonychia.org.

News and Notes Publications
Gonzalez-Gonzalez E, Speaker TJ, Hickerson RP, Spitzer R, Flores MA, Leake D, Contag CH, Kaspar RL. Silencing of reporter gene expression in skin using siRNAs and expression of plasmid DNA delivered by a soluble protrusion array device (PAD). Mol Ther. 2010 Sep;18(9):1667-74. This article merited a front cover image. The work is part of the GO! Delivery! Grant research.

Rowe, Aaron. Shoestring Gene Therapy, The Scientist (Vol 24, Issue 8, Pg 20). This article briefly tells the story of how the PC clinical trial came to be. There are few errors and overall a nice article.

Presentations
Hector Zambrano, in the lab of Leonard Milstone at Yale, recently attended the 1st International Congress of Therapeutic Dermatology organized by the Ecuadorian Society of Dermatology and Related Sciences in Bahia de Caraquez, Ecuador. His presentation Treatment of congenital Pachyonychia: results of a clinical trial was well received by the audience.

NIAMS K01 Grant
Laure Rittie, PhD, University of Michigan at Ann Arbor has been awarded a K01 grant entitled Mechanisms of Altered Skin Re-Epithelialization in Aging. The grant began September 2010 and will end May 2014. Impaired wound healing is a common clinical problem in elderly individuals, for whom the wound healing reaction is commonly described as "slow" and "of poor quality". Our recent results demonstrate that rather than slow, the wound repair reaction appears prematurely terminated, due to an early cessation of epidermal cell (keratinocyte) proliferation in aged skin compared to young adults. The specific focus of this project is to investigate the mechanisms that cause this age-dependent cessation of keratinocyte regenerative capacity in aged skin wounds.

Based on preliminary data, we hypothesize that PC keratins, which are major cytoskeletal components induced in wounded skin, play important functions in regulating epidermal cell growth during normal wound repair, and are defective in aged skin. Our specific aims are designed to establish a working model, and directly test this hypothesis. In addition to shedding light on the mechanisms of impaired wound healing in aged human skin, our proposed studies will likely provide useful information on the functions and regulation of PC keratins in skin.

We apologize that this IPCC News section is incomplete. Please let us know of grants, presentations and publications of IPCC members. We would like to recognize and include all of these in the IPCC Newsletter.

PC Patient Support Meetings Edinburgh, Scotland October 22-24, 2010
The meeting will be held at the Best Western Capital Hotel in Edinburgh. If you would like to attend and participate, please contact us. We expect about 40 PCers will be at the meeting, as well as several physicians and scientists interested in PC and other keratin disorders.

Roissey, France
June 18-19, 2010
This meeting was co-sponsored by the Association Le Cœur au Pied and PC Project. Presentations were translated or given in French by Sylvia Cierpucha (PC Patient and Le Cœur au Pied President), Irene Leigh, MD, W.H. Irwin McLean, DSc, FRSE, Mary Schwartz (PC Project Director), Frances Smith, PhD, and Eli Sprecher, MD. There was an excellent question and answer session followed by PC care demonstrations.
International Pachyonychia Congenita Consortium (IPCC) Members 2010-2011
Sponsored by PC Project

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*Members of the IPCC 2010 Best Practices, Educational Outreach, Clinical

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GENETICS TEAM
Frances J.D. Smith, PhD
C. David Hansen, Peter R. Hull, Sancy A. Leachman,

PC CONSULTATION TEAM FOR THE IPCRR
C. David Hansen, Peter R. Hull, Sancy A. Leachman, Leonard M. Milstone, Jean Y. Tang

PC PHYSICIAN NETWORK


IPCC GENERAL MEMBERS

Interested Physicians and Scientists are invited to join the IPCC

PLEASE HELP US
With all of the progress made by the IPCC members since 2004, the most heart-breaking thing I experience is seeing current (2009-2010) publications which contain false, incorrect, incomplete, outdated and erroneous information about Pachyonychia Congenita.

In two recent 2010 publications, I noted the following:
1. There is NO genetic testing done to establish the basis for diagnosis. PC Project offers free genetic testing; the patients in these articles may have other conditions and not Pachyonychia congenita.
2. Many characteristics known now to NOT be connected with PC are listed as PC-related (see IPCRR registry data on over 400 patients).

I know many of you review articles. Will you please help us? Insist on genetic testing! Why?
- Baldness is reported in one article. There is no baldness connected with PC. That is an important clue the patient may have a connexin mutation (not a PC mutation).
- Although no one with ‘nails only’ has yet been found to have a mutation in one of the PC genes, the case study says it is Pachyonychia congenita.

There are dozens of additional points like this. The authors do not contact PC Project and do not use any of the statistics or data available on the PC website. Will you please help us? We welcome your suggestions. We must find a way to stop the flow of misinformation.

2011 MEETINGS
IPCC Physician Quarterly Web Meeting
February 1st (Tuesday) 7am MST
Current clinical study results will be reported and we will continue discussion to develop information on treatments to lead to further PC clinical studies.
For a link to the meeting, send an email request to info@pachyonychia.org

Go Delivery! Second Annual Conference. ALL ARE WELCOME!
February 10-12 (Thursday through Saturday)
The Canyons Resort Hotel, Park City, Utah (see attached flyer)
Register at www.TransDermInc.com/GOregistration
Results generated using the model systems provided by the GO Delivery consortium will be presented by program participants.

International PC Consortium (IPCC) Annual Symposium
May 3-4 (Tuesday all day and Wednesday AM only) prior to SID
The SID Translational Research Session will be Wednesday PM
JW Desert Ridge and Resort Phoenix, Arizona
CALL FOR SPEAKERS: We welcome submissions for presentations at the 2011 IPCC Symposium. A small stipend will be available to those selected. Please send your application/abstract to info@pachyonychia.org no later than 15 Feb 2011.
Please register to attend the meeting at http://www.pachyonychia.org (link is at lower left of website Home Page)

Pachyonychia Congenita Patient Support Meeting
August 5-7 (Friday evening, Saturday all day, Sunday AM only)
Philadelphia, Pennsylvania
CALL FOR SPEAKERS: We invite physicians and scientists interested in PC or related keratin or skin disorders to participate in the meeting. We anticipate approximately 50 genetically-confirmed Pachyonychia Congenita patients will participate.
Please register to attend the meeting at http://www.pachyonychia.org (link is at lower left of website Home Page)
THANKS! Thanks, thanks, thanks, thanks... is the main message of this IPCC Newsletter.

The IPCC was organized in Feb 2004 and IPCC members have been actively involved in collaborations since then to identify effective treatments for Pachyonychia Congenita and other painful skin disorders.

THANKS! to IPCC members who serve on the Medical and Scientific Advisory Board for Pachyonychia Congenita Project, the support organization for PC.

THANKS! to IPCC members who are leading the research efforts of the GO! Delivery Grant funded through NIH/NIAMS under the American Recovery and Reinvestment Act of 2009 (ARRA). The goal is to find effective methods to deliver nucleic acids to skin. All interested researchers can participate, use resources and share data.

THANKS! to all the physicians who conduct telephone consultations with those reported to have PC and to the genetic scientists who conduct the PC genetic testing.

THANKS! to the IPCC researchers who share mice, formulations, tips, techniques, time and other resources and know-how to move the efforts forward more quickly.

THANKS! to the IPCC members who have participated in the monthly Genetics team web meetings to discuss ongoing genetic testing. The findings include more than 60 PC mutations, a significant group diagnosed with PC who do not have PC but other genetic conditions and a group for whom no mutation can yet be identified.

THANKS! to the IPCC members who participate in the Quarterly Physician Network web meetings to discuss differential diagnosis for PC as well as to identify proper and meaningful treatments for those with genetically confirmed PC.

THANKS! to the authors who have submitted quality publications on Pachyonychia Congenita and on PC-related research.

THANKS! to the authors who have submitted quality publications on Pachyonychia Congenita and on PC-related research.

THANKS! to researchers and physicians who attend and present at PC Patient Support Meetings. Your participation is helping to educate PC patients and we learn a lot from you.

THANKS! to IPCC members who travel around the world to present accurate and current information on PC and related research.

Patient Support Meeting
A successful PC Patient Support Meeting sponsored by PC Project UK under the direction of Irwin McLean and Frances Smith (University of Dundee) was recently held in Edinburgh, Scotland.

37 patients attended, most with genetically confirmed PC. Presentations were given by Robyn Hickerson, Roger Kaspar, Brigit Lane, Irene Leigh, Irwin McLean, Colin Munro, Edel O'Toole, Frances Smith, Eli Sprecher and Mohzeh Zamiri.

Presentations were given on the family of keratin disorders, current research around the world, patient care techniques, and other topics essential for PC patients.

Physicians Web Meeting
Many dermatologists have participated in the recent PC Physician Web Meetings. (See the asterisks* on page 4 for names of those participating on the IPCC Best Practices team).

The current web discussions seek to capture the most critical treatment needs for PC patients and to discuss those techniques, tips and treatments which may be considered 'best practices for PC.' See the IPCC Newsletter Vol 7 No 3.

Dr. Albert Bravo, DPM and a PC patient, provided a detailed outline to lead the discussion. Following are notes from the meeting which will be continued in the Feb 1st web meeting.

Infection - Infection is frequently what will bring a PC patient to a physician's office. In addition to the active treatment of the current infection with antibiotics, local wound care, etc., preventative measures are stressed to help avoid recurrent infections. Measures to avoid cracking and splitting of the skin, etc., are important.

DISCUSSION:
- Has anyone ever cultured bacteria from nails? (none available)
- What type of infections are involved? Are they actually bacterial infections? For paronychial infections, topical steroids have been effective, saline or saline compress.
- Use a bleach bath soak to prevent infection (recipe available from Len Milestone). How often? 1xweek or 3xweek; generally ½ hour. Can be overall (bath) or just feet or just nails, etc. Used for years; now pediatricians are finding helpful. PC Project has had good feedback from patients using this especially for children, or those who get extended moist/infected areas at times.
REQUEST: PC Project to try to obtain good photos of nail infections (and plantar infections as well).

**Appearance** - Though certainly a consideration, particularly when there is involvement of the hands and fingernails, and particularly in younger patients, appearance is often a secondary consideration with PC patients due to the extent of pain which is frequently involved. Reduction of the rapidly accumulating keratotic lesions, and persistent and aggressive nail care, done with the purpose of reducing the pain will help with the appearance of the hands and feet. Fungus nail remedies can help if there is superimposed or coexistent fungal infection of the nails, however rarely will provide a cure as the nail deformity is part of the PC, and usually does not involve fungal infection.

**DISCUSSION:**
- **Functionality** is another consideration. The first thing for a child is often manipulating objects with the thickened nails; this leads to trying to file, clip, etc. and those actions may contribute to pain.

**Pain** - The pain from PC can vary greatly, with some days being extremely painful, and other days being much less uncomfortable. Likewise, treatments for the lesions caused by PC vary, and on certain days one treatment will feel much better than other treatments. The challenge is to try to tailor the treatment for the circumstances of each day.

**DISCUSSION:**
- Does trauma exacerbate the keratoderma and pain? Bed rest, casts, etc. do reduce the amount of keratoderma, but do not seem to eliminate the pain or keratoderma. Unclear how to test/capture this or what to do with the information. The question is the effect of trauma on the condition and how to get at that.
- Topical pain treatment - IRB approved PC Project study for topical ibuprofen; however, drug was pulled by FDA right as the study was to begin. Patients are finding this online and using it, reporting that it is as effective as systemic ibuprofen.
- New product from Tylenol - topical cream (too new to have any information)
- Other topicals?

**CARE FOR CALLUS LESIONS**

**Manual Debridement:**
Shaving the calluses or draining the blisters needs to be done judiciously. Most people with PC will quickly find that if they shave the lesions too far, it can cause pain, however if they do not shave enough, it is also painful. I find it most helpful to "prick" the blisters in order to let the fluid out, however leave the roof of the blister in place. It will take some trial and error to determine how far to shave the calluses. However, particularly for very thick lesions, daily use of a Ped-Egg callus shaper, done when the lesions are dry and have not been soaked, can be extremely helpful. This certainly will not by itself suffice for severe lesions, however can be an excellent adjunct. This should be done every night before bedtime, without soaking the feet, and using the Ped-Egg only for about 30 seconds on each lesion. This can be extremely helpful, as long as it is done every night.

**PC patients** quickly become quite skilled in shaving the calluses with a razor blade, knife, fingernail clippers, etc. Despite the inherent danger in using razor blades, they tend to be the quickest and therefore preferred method. Even in skilled hands, a double-edged razor can be quite dangerous, and a single-edged razor is safer, though it is not as flexible. Podiatrists often use a scalpel blade called a 312 blade, which is about half an inch wide, attaches to a scalpel handle, and is much safer.

Use of power instruments such as a Dremel tool, with the proper burr installed, can also be of some value. See IPRCC data information on various manual methods.

**DISCUSSION:**
- Patients settle into their own self-care methods; difficult to alter. Likely would participate in studies if we have basis for what we are trying.

**Soaking/Moisturizing Creams**

Many times, a brief, cold soak will provide significant relief. Sometimes warm soaks and Johnson's foot soap, Epsom salts, or even plain water will feel better, but most of the time a cool soak is more comfortable. At times moisturizing creams can be helpful, as this can reduce the cracking and splitting of the skin, reduce friction, and aid in reducing blister formation.

**Chemical**

Several types of topical medications to help debride the callus formation are sometimes used, primarily salicylic acid and urea. The salicylic acid can at times be helpful, however frequently will cause chemical irritation to skin and at times can be aggravating to the situation. Patients frequently will try the salicylic acid, however many abandon its use. Urea pastes can be used under occlusion to soften the thickened nails to the point where they can be more easily trimmed away or removed.

**CHAT:**
One has to bear in mind that different things work for different people. For example, some patients like Flexitol heel balm (40% urea) and others do not.

**DISCUSSION:**
- In Europe, Onyster (Fabre) is a urea for nails that comes with a plastic covering. We could possibly obtain some for a small study.
- For some young children, urea creams have been helpful. Once they are larger (by age 10), the urea seems less helpful.

**ANTIPERSPIRANT METHODS.**

Web Meeting – only a few minutes discussion on the following (to be cont’d)

Controlling perspiration of the feet can make a big difference.

Botox (actually Dysport is used in the PC study). Published studies claim effective pain reduction.

**Iontophoresis.** A simple device using water to conduct a mild electric current through the skin's surface. It is used in clinics or at home for people who have excessive sweating.

Very old method. PC Project will try to find more information on newer devices and gather information for future discussion.

**Glucopropyolrolate** (brand name Robinul). Would be an off-label use; could try a small study.

The Web Meeting Discussion will continue in the next meeting February 1st. If you would like to participate, please email info@pachyonychia.org.
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PC PHYSICIAN NETWORK


* Members of the IPCC 2010 Best Practices, Educational Outreach, Clinical Studies Team

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Interested Physicians and Scientists are invited to join the IPCC


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