

THE BEAT



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Family Day 2009—New Date Announced

Our 7th annual PCD Foundation Family Education Weekend originally scheduled last July has been rescheduled for the weekend of December 4 - 6, 2009 in Buffalo, New York. Details and registration information are available online at www.pcdfoundation.org or by email at info@pcdfoundation.org. In addition to our typical educational program, this event offers the opportunity for attendees to participate in focus groups that will help researchers develop a quality of life assessment tool for young people with PCD. This tool, in addition to existing tools for the adult community, will be used in clinical research trials to assess the impact of therapies on the patient experience. A preliminary program, subject to change, is available on page 2.

Hope to see you all there!

Looking Forward to 2010

In our continuing efforts to promote PCD research and awareness, the PCDF enjoyed a busy and productive year in 2009. Our plan to expand services into the growing PCD community in 2010 is very ambitious and relies on our ability as a community to raise the necessary resources—both financial and human. Our research partners at the Genetic Disorders of Mucociliary Clearance Consortium (GDMCC) program secured funding for the GDMCC for an additional five years to continue the specific PCD research and treatment network established back in 2002. However, the PCDF receives no direct funding from the GDMCC grant and PCDF identified priorities and goals rely solely on our ability to secure funding as a private patient group.

Here is our target list for 2010:

PCD International Scientific Meeting

Perhaps most exciting is the prospect for the first-ever international science conference devoted to PCD which will bring together medical and scientific experts from around the world who share a desire to advance the cause of PCD research. Efforts are underway right now to identify potential sources of funding for this meeting, which will be held in conjunction with a family education event, so that interested individuals in the PCD patient community will have the opportunity to participate in the science portion of the meeting if they wish.

Expanded PCD Family Education Event Program

Limited resources have forced us to focus our educational efforts on a single annual event. Starting in 2010, we plan to add additional family education events to improve access for as many families as possible.

Continued on page 3.

Mark Your Calendar!!!

**Family Weekend
2009
December 4-6
Buffalo, NY**

**Family Weekend
2010
Summer, 2010
St. Louis, MO
(tentative)**

New PCDF Contact Info:

**10137 Portland Ave S
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952-303-3155-Phone
866-371-7575—Fax**

PCD Foundation Family Education Day Tentative Program

PCD Foundation Family Education Weekend 2009 Buffalo, New York Program

FRIDAY, June 26, 2009

| | |
|-------------------|-------------------|
| 6:30 pm - 9:00 pm | Registration |
| 6:30 pm - 9:00 pm | Welcome Reception |

SATURDAY, June 27, 2009

| | | | |
|---|--|----------------------------|-------------------------------|
| 8:30 am - 9:15 am | Registration & Breakfast | | |
| 9:00 am - 9:15 am | Welcome--Michele Manion | | |
| 9:15 am - 9:30 am | Introduction of the Health-Related Quality Of Life (HRQL) Project Sharon Dell, MD & Alexandra Quittner, PhD | | |
| 9:30 am - 11:00 am Divide into HRQL Groups | Patients Age 5 to 12 Room: | Patients Age 13 + Room: | Parents & Caregivers Room: |
| 10:15 pm - 10:30 pm | Snacks Available in Breakout Rooms | | |
| 11:00 am - 11:30 am | Living with Chronic Illness--Alexandra Quittner, PhD | | |
| 11:30 am - 12:15 pm | What are Cilia and What Do They Do? John Carson, PhD | | |
| 12:15 pm - 1:15 pm | Lunch | | |
| 1:15 pm - 2:00 pm | When Good Cilia Go Bad: The Challenge of Recognizing & Diagnosing PCD Margaret Leigh | | |
| 2:00 - 2:45 pm | The Care and Feeding of PCD: Treatment Options to Help Improve Quality of Life Sharon Dell | | |
| 2:45 pm - 3:30 pm | Bronchiectasis and Advanced Lung Disease in PCD--Ken Olivier, MD | | |
| 3:30 pm - 3:45 pm | Afternoon Break | | |
| 3:45 pm - 4:30 pm | Airway Clearance Options for People with PCD--Jerry Reynolds, RT, PhD | | |
| 4:30 pm - 5:15 pm | Panel Discussion: PCD Research: Current Opportunities and Future Promise Margaret Leigh, MD, Sharon Dell, MD, Ken Olivier, MD, John Carson, PhD | | |

SATURDAY DINNER PROGRAM

| | |
|-------------------|--|
| 6:00 pm - 8:00 pm | Group Dinner |
| 6:10 pm - 6:30 pm | The PCDF: Building a Foundation for a Healthier Future--Michele Manion |
| 6:30 pm - 8:00 pm | PCD Through the Ages: A Patient Panel Discussion |
| 8:00 pm - 8:20 pm | The State of the Foundation--John Carson, PhD |

| | |
|---------------------------------------|--|
| SUNDAY, June 28, 2009: 0am - 10:00 am | Continental Breakfast |
| 9:00 am - 12 noon | Open Discussion Time--All Attendees This session is designed as an opportunity for attendees to discuss things learned, ask any lingering questions and continue to get to know one another. Saturday is science time. Sunday is YOUR time and anyone is welcome to introduce new topics for discussion. The format for this session is casual so that attendees can leave for home as needed. |

Continued from page 1.

Expand Network of PCD Care Centers

We currently have 7 PCD 'centers of excellence' in North America. Our goal in 2010 is to identify physicians and centers with interest and expertise in PCD as referral centers for patients in our group. To qualify, centers will have to demonstrate the ability to accurately diagnose PCD and a desire to participate in efforts to develop standards of care for the treatment of PCD. If you know a physician (pediatrician, pulmonary specialists, etc.) who you think would be interested in participating in this process, please contact us at the PCDF: info@pcdfoundation.org.

Develop Strong Regional Chapters

As we continue to grow, we will need to rely on our designated regional chapters to help us accomplish our mission. In addition to taking the lead in regional fundraising efforts, chapter representatives will be responsible for promoting the educational and advocacy/support functions of the PCDF. We have had an informal regional chapter organization, but in 2010 plan to formalize these relationships and provide training and support for regional chapter representatives. If you are interested in a regional chair or volunteer position, please contact us: takeaction@pcdfoundation.org.

Fund One or More Research Grants

We have the opportunity to 'double our money' with a grant program offered by the American Thoracic Society (ATS). In 2010, we would like to take advantage of this program and provide PCDF funding that would be matched dollar for dollar by ATS. These grants can be used for research focused on improving the understanding and/or treatment of lung disease.

Add Staff and Volunteers

We are growing and need human resources in addition to financial resources! We hope to actually be able to add paid and volunteer staff for specific positions within the PCDF for more info: takeaction@pcdfoundation.org.

New Materials and Translations

In 2010, we will add to our inventory of published materials with new brochures, fact sheets and a new schedule for newsletter publication. We will also continue our progress in getting PCDF materials translated to Spanish. Our website remodel will include the ability to easily access standard publications and to sign up for the newsletters or other materials you want.

New Research on Potential Treatments for PCD

By Larry Ostrowski, PhD

Recent developments in two active research areas are beginning to show potential for novel treatment approaches to PCD. A new class of drugs is being developed to allow some production of a normal protein from genes that are mutated in a specific way. Normally, this type of mutation (nonsense mutation) causes the machinery that synthesizes proteins to "stop" at the site of the mutation. Drugs are being developed to allow the machinery to "read-through" the mutation and continue to make the rest of the protein. At least one of these drugs is being tested in Phase II trials in cystic fibrosis patients (*Lancet*. 2008 Aug 30; 372 (9640):719-27. Epub 2008 Aug 20.). Importantly, some of the mutations that cause PCD have been identified as this type of mutation.

In another approach, researchers at the University of North Carolina-Chapel Hill have submitted an abstract to the upcoming American Society of Gene Therapy's annual meeting in which they report that they were able to restore ciliary activity to mouse PCD cells using a gene transfer vector expressing the normal ciliary protein. Drs. John C. Olsen and L. E. Ostrowski caution that this is a proof of concept study, and much more work remains to be done. It should be emphasized that these two studies would not have been possible without the tremendous amount of basic research that has been performed to identify the genes and the specific mutations involved in PCD. Additional funding for both basic and translational research is needed to further improve the diagnosis and treatment of PCD.

New Gene Linked to PCD–PCDF Research Committee Review

Article: Ktu/PF13 is Required for Cytoplasmic Pre-Assembly of Axonemal Dyneins.
Publication: Nature 456: 611-616 (2008)
Author(s): Omran H, Kobayashi D, Olbrich H, Tsukahara T, Loges NT, Hagiwara H, Zhang Q, Leblond G, O'Toole E, Hara C, Mizuno H, Kawano H, Fliegau M, Yagi T, Koshida S, Miyawaki A, Zentgraf H, Seithe H, Reinhardt R, Watanabe Y, Kamiya R, Mitchell DR, and Takeda H

This paper describes the findings by Omran et al (2008) that mutations in *KTU* (also known as *ktu*, *ktn* or *Kintoun* or *PF13*) gene causes Primary ciliary dyskinesia (PCD) / Kartagener syndrome (KS) in a subset of PCD patients.

A group in Japan studying a small aquarium fish found in the rice fields (known as Medaka fish) identified mutant fish that presented with situs inversus, polycystic kidney disease, and impaired motility of cilia and sperm flagella. Further, electron microscopic (ultrastructural) examination of cilia and sperm flagella revealed defective outer and inner dynein arms, similar to what is observed in PCD patients. Additional studies revealed that the mutant fish had mutations in the gene *KTU*.

Further studies were done in the unicellular algae known as *Chlamydomonas*. This organism is used as a model organism for PCD since it has two flagella and the structure of the *Chlamydomonas* flagella is similar to the structure of the human cilia and flagella. The *Ktu* gene (known in *Chlamydomonas* as PF13) was again found to be required for the assembly of inner and outer dynein arms. Mutant *Chlamydomonas* lacking the PF13 gene product had paralyzed flagella and hence could not swim. Electron microscopic examination of the flagella revealed defective outer and inner dynein arms.

Since *situs inversus* (observed in fish) and missing dynein arms (observed in fish as well *Chlamydomonas*) are cardinal features of PCD, the human *KTU* gene was tested as a candidate gene in 112 PCD/KS patients. Two unrelated families with PCD out of 112 studied showed mutations in the *KTU* gene. It is pertinent to mention that of all 112 patients with PCD/KS tested, only 17 had defective outer and inner dynein arms, which leads to the frequency of *KTU* gene mutation as a 12% (2/17) in patients with outer and inner dynein arms defects. Protein analysis showed that *KTU* protein was indeed absent from the PCD patients who harbored the mutation, showing that the mutations lead to the absence of normal *KTU* protein. Unlike fish, the kidneys of the affected individuals who harbored *KTU* mutations were normal. This difference is attributed to the fact that kidneys in fish and human are originated from different cell types.

It was noted in these studies that the *KTU* protein was not actually part of the cilia or flagella. Instead, the function of *KTU* protein is to preassemble the dynein arm complex before it is transported into the cilia or flagella. This is the first report which shows that mutations in a non-ciliary protein can cause PCD. Importantly, this study adds *KTU* to the list of known PCD genes, which will aid diagnosis and ultimately, treatment.

HAVE A STORY TO SHARE?

We'd love to hear from you! Patient stories are an important feature of our printed and online materials. Worried about writing it? We can help! Please contact Lynn Ehrne or Michele Manion at the PCDF if you would like to participate:

info@pcdfoundation.org

LOOKING FOR WAYS TO GET INVOLVED?

Consider membership on a PCDF committee. We have three standing committees: Research, Education and Development and several less formal ad hoc opportunities. For more info contact us at:

info@pcdfoundation.org

Conor's Story

by Carey Kauffman

I first learned about PCD 12 hours after my son was born. Conor was born a full-term, 9lb 4oz "healthy" baby boy by all measures. After staying with us the first night, Conor couldn't seem to get rid of a tiny bit of congestion which led to a chest x-ray and a '*situs inversus totalis*' diagnosis. After telling us they had never seen *situs inversus* before, they informed us that there was a 25% chance of Kartagener Syndrome. From that point, we heard a number of comments from the doctors that are concerning – if not alarming - in light of what would happen a few hours later:

- "Even if he has it, you won't need to worry about it until later in his life. It doesn't manifest itself until later."
- "How bad can it be if it's not diagnosed until later in life?"
- "Donny Osmond has *situs inversus totalis* – and he's just fine!"
- "Don't worry – he'll just have a snottier nose than the other kids. All kids have runny noses."



Carey, Keagan and Todd

Conor passed away the next day shocking every doctor and nurse involved in his care. His lungs collapsed causing his heart to shut down and they couldn't save him.

The doctors said that they had never seen or heard of anything like it and couldn't tell us what happened. After doing our own research on our Blackberries in the hospital and learning more about how PCD patients are misdiagnosed as having cystic fibrosis among other disorders (therefore the 'delayed' diagnosis) and about neonatal respiratory distress, pneumonia, etc. related to PCD during his few hours, we were adamant that he be tested for it during the autopsy. The doctors said though it would not be seen as a cause of death, they would do it because we were so serious about it.

The autopsy came back 'acute pneumonia' which again shocked the doctors who had taken multiple 'clear' x-rays of his chest and were unable to grow bacteria on tracheal samples when he was alive. They had also given him 2 antibiotics that would have addressed "90% of any infections out there." Our only thought was - if your cilia don't work, they don't work from day one. We aren't doctors and have no medical training, but that made sense to us.

He tested positive for PCD.

I don't want any parents to have to lose a child like this. I think Conor's situation is rare, and I'm not sure he could have been saved – maybe he had a more severe form if it? Or maybe the pneumonia he got would have been too much for any child? Or, maybe if he had gotten through the first couple of days, he'd be here right now. But we don't really know, and never will.

What I do know is that through the PCDF and the voices and talents of everyone touched by this disorder, doctors can be more informed, patients can live healthier lives and perhaps one day PCD will no longer need to be on any radar anywhere in the world.

News About Primary Ciliary Dyskinesia

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We're on the Web!!!

www.pcdfoundation.org

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Education & Advocacy for
People with Primary Ciliary
Dyskinesia*

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DISCLAIMER

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Journal Watch NEW ARTICLES OF INTEREST TO THE PCD COMMUNITY

The National Library of Medicine (NLM) maintains a database of peer-reviewed articles from international medical journals. The peer-review process means that the article is subject to vigorous critical review by a panel of experts prior to being accepted for publication. This information can be accessed by the public at: <http://www.ncbi.nlm.nih.gov/pubmed/> or by typing "Pubmed" into your internet provider search function.

Health-related quality of life and unmet needs in patients with primary ciliary dyskinesia. Pifferi M, Bush A, Di Cicco M, Pradal U, Ragazzo V, Macchia P, Boner ALEur Respir J. 2009 Sep 24.

From abstract: "PCD is associated with a progressive and continuous impact on physical and mental health of the patients. Earlier identification of the patients and better strategies aimed at improving compliance with care are urgently needed."

Management of otitis media with effusion in children with primary ciliary dyskinesia: A literature review. Campbell RG, Birman CS, Morgan L. Int J Pediatr Otorhinolaryngol. 2009 Sep 29.

From abstract: "...otitis media with effusion in primary ciliary dyskinesia does not resolve by the age of 9 years, regardless of treatment, as previously assumed. Ventilation tube insertion improves hearing in primary ciliary dyskinesia, but may lead to a higher rate of otorrhoea when compared to the general population. Tympanic membrane changes were clinically insignificant. Our patient eventually underwent successful insertion of bilateral ventilation tubes with a marked improvement in hearing and language with minimal otorrhoea."