

# ACDA NOTES

From The Alveolar Capillary Dysplasia Association

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Dear Friends and Family,

It is not uncommon for us to fear that friends and family will forget or never mention our baby over time. *We never* forget and it is up to us to keep our babies' memory alive. By talking about your baby, others know that it will not upset you if they mention him/her. Just yesterday I mentioned in a conversation that Eric had a broken clavicle when he was born. Let your close friends and family know when you are missing your baby. Celebrate your babies' birthday and invite relatives and close friends. We are so moved that Steve's parents have faithfully been with us at the cemetery every June 7 for the last 12 years, and our other family members have also been very supportive. Talk to your children about their brother or sister. We can't even explain how much it means to us to hear our girls talk about Eric.

Include your baby in your activities, your celebrations and your conversations, and others will be more comfortable and do the same.

Fondly,

*Steve & Donna Hanson*  
ACDA Executive Directors

## Research News

As you know, the ACD research being conducted at Baylor College of Medicine resulted in recent findings that were published in the *American Journal of Human Genetics* on June 4, 2009. This publication is the first significant ACD genetics find and was led by Pawel Stankiewicz, M.D., Ph.D and Dr. Partha Sen, Ph.D at Baylor. This article was very technical so we asked Dr. Sen to provide a layman's summary of their findings. Thank you to Dr. Sen for providing the following synopsis:

"In the recently published study, we collaborated with Dr. Pawel Stankiewicz of BCM and Dr. Charles Smith-Shaw of the Wellcome Trust Sanger Institute of the UK who are involved in the genetic analysis of complex congenital disorders with a constellation of malformations involving different organ systems. These disorders are grouped under the acronym VACTERL and include congenital abnormalities of vertebra (V), the anus (A), the heart (Cardiac), Trachea-Esophageal fistula (abnormal connection between the trachea and the esophagus) with or without esophageal atresia, the kidney (Renal) and limb (L) abnormalities. In their studies, the genome is searched for abnormalities of chromosomal regions using methods that

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allow the recognition of smaller regions of deletion and/or duplication than can be seen with the usual chromosome analysis. The physicians of one of our ACD/MPV {Alveolar Capillary Dysplasia with Misalignment of Pulmonary Veins} patients had DNA sent for this analysis, and it showed a micro deletion on chromosome 16 in the region known as 16q24.1. A list of the genes present in this region of chromosome 16 included FoxF1, a gene known to be important in lung development. These findings prompted evaluation of this same region in our collected samples from ACD/MPV patients and their families. A total of fourteen DNA samples were tested for deletion in this region. Three of our confirmed ACD/MPV samples have a deletion that included the same chromosomal region, this genetic change was not present in any of their parents. Two of these ACD/MPV cases did not show deletion of the FoxF1 gene; instead there was a nearby deletion. This suggests that this nearby region of DNA missing in these patients might be responsible for expression of the FoxF1 gene, as these babies had ACD/MPV. Other cases analyzed in this study were not initially known to have ACD/MPV and were sent for genetic analysis because of their multiple congenital malformations. All those with lung tissue available to study had ACD/MPV; however for some there was no lung tissue available to review (Table 1). The figures in the paper document the precise deletion coordinates and suggest the likely process by which deletion occurred.

In addition to the deletion studies, we looked for mutations in the FoxF1 region in our collected group of ACD/MPV patients. DNA from 18 patients was sequenced and four separate mutations were identified in the coding sequence of the FoxF1 gene (Table 2). This added more support to the deletion studies, confirming involvement of FoxF1 in ACD/MPV since we had patients with either mutation of the FoxF1 gene or a deletion containing the FoxF1 gene. However, not all of our cases of ACD/MPV had deletion or mutation involving this region. This means that there are other genetic abnormalities that also can result in ACD/MPV and we think that these are likely to be in pathways that affect expression or activity of FoxF1.”

ACDA members had several questions following the publication of the Baylor article. We wanted to share those questions and the answers that were provided by Dr. Sen:

- 1) I am trying to interpret the point that the children but not the parents had abnormalities. Does that mean that the mutation might have had an environmental rather than hereditary cause?

It is correct that the parents do not have the mutations that cause ACD/MPV. Mutations may occur for various reasons. All of us have unique mutations that are known as *de novo* mutations. However, these random mutations sometime may cause serious problems as in ACD/MPV. The mutation occurred in one of the sex cells of the parents (either sperm or egg). It is very unlikely that the environment had a role to play. We do not have enough information to conclude that.

- 2) I was wondering if you know anything about their animal testing policy. I am assuming they don't test on animals? I know they used families to test but wondering about animals?

We are not doing any animal testing studies. [In other researcher's studies], the gene (*Foxf1*) has been mutated in mice and the animals show some characteristics similar to ACD/MPV. However, the authors of that research publication state that only half of the littermates died and the other half was healthy.

- 3) Does this mean they believe it is genetic?

It is definitely genetic at least in the cases where we have identified deletion/mutation in FoxF1. But it was not present in the parents. As I stated earlier, the mutation and deletion might have occurred *de novo* in the sex cells of the parents. I believe other cases also have a genetic condition. It is just that we don't know enough yet to identify them.



# 3 Angels Update

By Craig Snyder, Founder of 3 Angels

In the wake of the publication of significant findings on the genetics of ACD, the research team at Baylor College of Medicine continues to dig deeper in an effort to find the genetic underpinnings of cases of ACD not explainable by the first discovery. Although additional time, resources and samples will be necessary before the complete picture becomes clear, the discovery of a genetic defect which causes perhaps 40% of ACD cases, has strongly pointed researchers in what are most likely to be the most fruitful directions.

The first year of the collaborative agreement on physician awareness of ACD, between the 3 Angels Memorial Fund and the Centers for Disease Control, will come to an end in September. The CDC is currently reviewing and is expected to approve an extension of the project for a second year, commencing on October 1, 2009. Design work on a website for physicians about ACD is now in the final stages of design and programming, based on input from researchers gathered at the ChILD (Children's Interstitial Lung Disease) research consortium conference in Denver last spring.

Once the additional funding for the second year of the project is approved by the CDC, the site will "go live" on the internet and a marketing campaign will begin to drive relevant medical professionals to the site where they will learn how best to diagnose ACD and how to document cases for further research.

Finally, in July, the United States Senate voted funds to extend the CDC work on ACD for a third year, which would commence in October 2010.

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- If you have recently moved or changed your email address, be sure to let us know. If you have approved release of your information, we share your contact information with new families so they have others to reach out to for support and understanding.
- You can make a tax-deductible donation for ACD research. Make a general or "In Memory Of" donation on the 3 Angels website at:  
<http://www.3angelsfund.org/contribute.php>  
or by mail with a check or money order to:

*3 Angels Memorial Fund for ACD Research  
PO Box 12251  
Arlington, VA 22219*

# Fundraising Activities

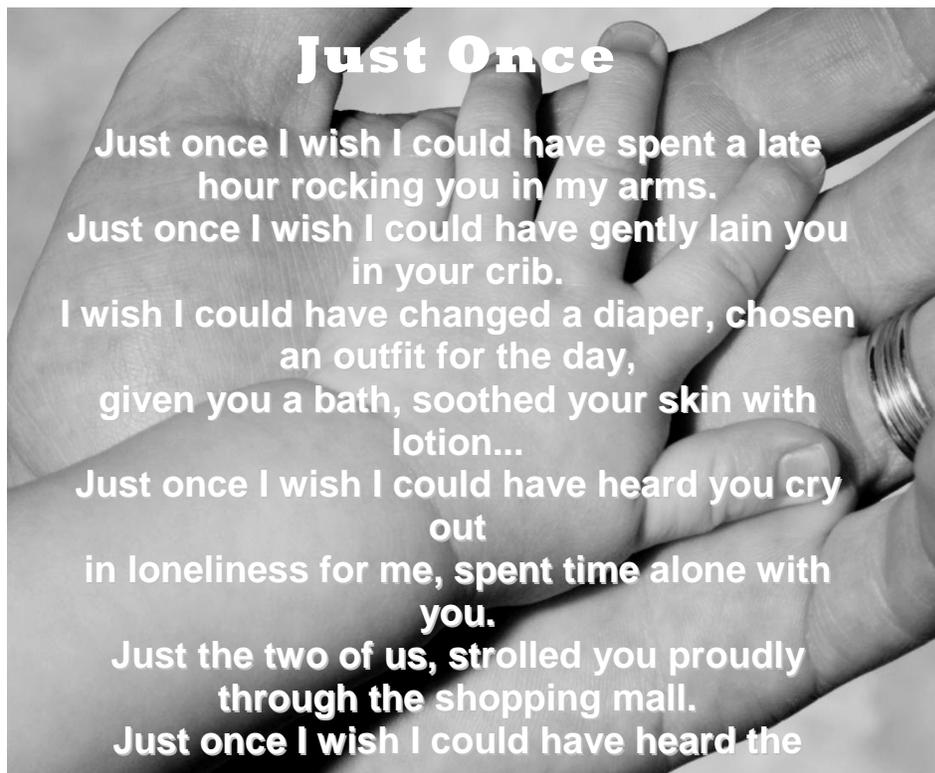
**NEW YORK** - [REDACTED] of New York and mom to [REDACTED], struggled with trying to find a way to raise money for ACD. She thought a walk for ACD would be great but with such a diverse group living all over the world, it would be difficult to gather all of us and our families for one day of fundraising. Then, [REDACTED] recently attended a Home & Garden Party (aka Celebrating Home) given by a friend at her home. After contacting the representative that hosted her friend's party, [REDACTED] decided to have her own party on October 24. She has contacted friends and gotten a room donated for the party. All of us can participate in this fundraiser by going to the following website that was established exclusively for this fundraiser:

[www.celebratinghome.com/parties/three angelsfund40426](http://www.celebratinghome.com/parties/three%20angelsfund40426).

Shop on line and your order will be shipped to you. If you are interested in hosting your own fundraiser, you can also find a representative in your area at <http://www.celebratinghome.com>. [REDACTED] also offered her assistance for anyone that wants more information. She can be reached at [REDACTED]

**HAWAII** - [REDACTED] are pursuing a similar effort in raising money for ACD. [REDACTED] and her husband, parents of [REDACTED], work at a Sam's Club in Pearl City, Hawaii. Their store prides itself on doing lots of community service and providing grants and donations to different organizations in need. [REDACTED] approached her General Manager, Mr. [REDACTED], regarding the fundraising that she was interested in doing. She has asked the ACDA and 3 Angels to send a letter to Mr. [REDACTED] in support of their efforts which is the first step in requesting grant money from the Sam's Club/Walmart Foundation. In addition to the grant money, the [REDACTED]'s are organizing an in-store fundraiser for the employees in which the company makes lunches and the proceeds get donated. In addition to the fundraising at Sam's Club, [REDACTED] is investigating other ways to raise money for ACD research. More details to come on this but contact [REDACTED] for more information at [REDACTED]

Hopefully, [REDACTED] and [REDACTED] have inspired you to get involved.



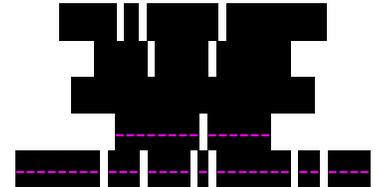
# Remembering Our Babies

May you find a meaningful way to celebrate the precious life of your baby.



# New ACDA Member

Please introduce yourself and share the story of your family with our new ACDA member.



Other Children



*Contact Information*

## ACD Association

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## 3 Angels Memorial Fund for ACD

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