

# ACDA NOTES

FROM THE ALVEOLAR CAPILLARY DYSPLASIA ASSOCIATION

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The ACDA is undertaking an audio project for Pregnancy and Infant Loss Awareness Month in October. Projects in prior years have included collages of our babies, a photo project of bereaved parents, a memorial wall, luminaries, calligraphy and a written word project about grief over time.

*This year we want to hear your baby's name.*

The purpose of this audio project is to record your child's name for inclusion in a larger compilation of names recorded by other ACDA families; we know saying and hearing their name spoken aloud is often a welcome expression of love. If you would like to participate, please visit the recording link below and submit your recording by **SUNDAY, SEPTEMBER 26:**

<https://www.speakpipe.com/AudioProject2021>

Please say your child's name and any special message within a ten second recording. We encourage you to use your native language.

All messages will then be compiled into one seamless file, to be shared by the ACDA on October 15. It is our hope that hearing your child's name along with the names of other children affected by ACDMPV will provide a sense of comfort and community within our ACDA families. A suggested idea is to listen to the final audio recording while lighting your candle of remembrance at 7:00 p.m. in your respective time zone on October 15 during the ACDA Wave of Light.

We hope you will participate and look forward to sharing the final version of this special audio project for Pregnancy and Infant Loss Awareness month.

Regards,  
Eliza Rista, President

## RESEARCH NEWS

### 2021 ACDA Grant (Cincinnati Children's):



In August 2021, the previously announced 2021 ACDA grant (see Issue #75 of ACDA Notes) for ACDMPV research was awarded in the amount of \$50,000 to **Dr. Allan Kenny** at **Cincinnati Children's Hospital Medical Center** in Cincinnati, Ohio, USA for the study entitled, *"Determining Safety and Efficacy of EF1a-FOXF1 Minicircle Plasmid-Containing Nanoparticles."*

As background, Cincinnati Children's is our NORD 2017 grant recipient and the ACDA has worked closely with Cincinnati Children's for a number of years (see Issues #57, #62-63, #68-69, #71-72 and #74-75 of ACDA Notes, from 2016-2021). The developmental biology research group at Cincinnati Children's also collaborates closely with other key ACDMPV research institutions, including the genetic research team at Baylor College of Medicine.

The ACDA circulated a [press release](#) in June 2021 from Cincinnati Children's that described their ground breaking research to develop a nanoparticle technology that will potentially be administered via IV within the first hours or days of life to an ACDMPV affected infant to rebuild lung tissue. The therapy works by delivering a high-tech engineered nanoparticle made of several polymers, fatty acids and a bit of cholesterol that carries the non-integrating *STAT3* gene, which in turn prompts blood vessel growth in the lung tissue. "We have developed a unique nanoparticle delivery system that can deliver genes capable of stimulating micro-vessel growth in the newborn lung," says Vlad Kalinichenko, MD, Ph.D., the senior author of the study. This is gene-driven therapy but not gene

editing. There is much work to be done before the therapy can be administered to a newborn but the awarding of this 2021 ACDA Grant will bring Cincinnati Children's one step closer to determining the safety and efficacy of such technology.

Dr. Kenny works closely with the **Kalinichenko Research Lab at Cincinnati**. The long-term goal of the Kalinichenko Research Lab is "to discover novel therapeutic approaches and generate novel FDA-approved drugs for treatment of these severe respiratory disorders." To learn more about the Kalinichenko Research Lab, please click [HERE](#) and read about their current projects.

### AT A GLANCE

In August 2021, the ACDA awarded one grant for ACDMPV research in the amount of \$50,000 (with funding raised in coordination with the ACDA and The David Ashwell Foundation). The 2021 ACDA grant to be distributed as follows:



Alan P. Kenny, M.D., Ph.D.  
**Cincinnati Children's Hospital Medical Center**  
 Cincinnati, Ohio, USA  
*Determining Safety and Efficacy of EF1a-FOXF1 Minicircle Plasmid-Containing Nanoparticles*

### 2022 Grant:

The 2021 grant recipient requested \$50,000 of the available \$100,000 grant option; therefore the remaining \$50,000 originally deferred due to the COVID-19 emergency will be reapplied to 2022 grant issuance. The ACDA is already looking ahead to the selection process for the 2022 grant, with partnerships and announcements to follow in early spring.



### Journal Article (Circulation):

#### Circulation



The developmental biology research team at **Cincinnati Children's Hospital Medical Center** in Cincinnati, Ohio, USA (see Issues #57, #62-63, #68-69, #71-72 and #74-75 of ACDA Notes) recently published a manuscript entitled, *"Nanoparticle Delivery of STAT3 Alleviates Pulmonary Hypertension in a Mouse Model of Alveolar Capillary Dysplasia"* in the *Circulation* journal, which can be found [HERE](#). Please also view the press release from Cincinnati Children's linked on page 2 of this edition of ACDA Notes with respect to this ground breaking research.

Partial Abstract:

**Background:** Pulmonary hypertension (PH) is a common complication in patients with alveolar capillary dysplasia with misalignment of pulmonary veins (ACDMPV), a severe congenital disorder associated with mutations in the *FOXF1* gene. Although the loss of alveolar microvasculature causes PH in patients with ACDMPV, it is unknown whether increasing neonatal lung angiogenesis could prevent PH and right ventricular (RV) hypertrophy.

**Methods:** We used echocardiography, RV catheterization, immunostaining, and biochemical methods to examine lung and heart remodeling and RV output in *Foxf1*WT/S52F mice carrying the S52F *Foxf1* mutation (identified in patients with ACDMPV) [...]

**Results:** [...] Intravascular delivery of nanoparticles carrying Stat3 cDNA protected *Foxf1*WT/S52F mice from RV hypertrophy and PH, improved survival, and decreased fibrotic lung remodeling.

**Conclusions:** Nanoparticle

therapies increasing neonatal pulmonary angiogenesis may be considered to prevent PH in ACDMPV."

### Journal Article (Circulation):

#### Circulation



Dr. Jane Leopold, Division of Cardiovascular Medicine, **Brigham and Women's Hospital, Harvard Medical School** in Boston, Massachusetts, USA recently published an editorial article about Cincinnati Children's recent research developments discussed above, entitled *"Nanoparticle-Facilitated Gene Delivery in Congenital Pulmonary Vascular Disease: Roadmap for Other Forms of Pulmonary Hypertension,"* which can be found [HERE](#). Dr. Leopold surmises, **"These exciting findings are likely to advance gene therapy with STAT3 nanoparticles 1 step closer to the clinic for ACDMPV as a first-in-class therapeutic. One interesting aspect of this work is that it may have implications to other pulmonary vascular or lung diseases associated with reduced capillary density."**

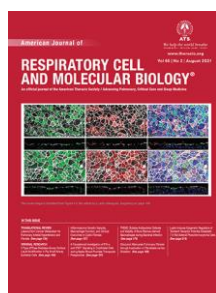
From the editorial, "Use of nanoparticle-facilitated gene therapy has the potential to modulate several of the molecular, structural, and functional complexities of pulmonary arterial and capillary abnormalities associated with ACDMPV that lead to pulmonary vascular dysfunction and pulmonary hypertension. The work of Sun et al demonstrates the efficacy of tailored gene therapy with nanoparticle delivery of STAT3 to the pulmonary vasculature in ACDMPV, a rare disease without pharmacotherapies. This first-in-class agent for ACDMPV further highlights the promise of nanoparticle-facilitated gene therapy for congenital diseases with pulmonary vascular involvement. It also emphasizes the potential of





nanoparticle-facilitated gene therapy to advance as a therapeutic in other heritable or acquired pulmonary vascular diseases and pulmonary hypertension associated with reduced capillary density. Once the genomic and molecular signals underlying pulmonary vascular remodeling have been discovered, precision nanoparticle-facilitated gene therapy may join the armamentarium of therapeutics available to treat other forms of pulmonary vascular disease.”

### Journal Article (*Am J Respir Cell Mol Biol*):



The developmental biology research team at **Cincinnati Children’s** Hospital Medical Center in Cincinnati, Ohio, USA (see above and Issues #57, #62-63, #68-69, #71-72 and #74-75 of ACDA Notes) also recently published a manuscript entitled, “*Therapeutic Potential of Endothelial Progenitor Cells in Pulmonary Diseases*” in the American Journal of Respiratory Cell and Molecular Biology, which can be found [HERE](#).

As introduced previously, Dr. Kalinichenko and his team in Cincinnati are pursuing two possible therapeutic approaches for ACDMPV, pending the development of clinical trials. The first approach is the evolving **nanoparticle technology** discussed above and in prior Issues of ACDA Notes. The manuscript discussed below describes a second possible therapeutic approach in development in the years to come, a potential **cell therapy** for ACDMPV, as also previously discussed in prior Issues of ACDA Notes. Abstract:

“Compromised alveolar development and pulmonary vascular remodeling are hallmarks of pediatric lung

diseases such as bronchopulmonary dysplasia (BPD) and alveolar capillary dysplasia with misalignment of pulmonary veins (ACDMPV). Although advances in surfactant therapy, corticosteroids, and anti-inflammatory drugs have improved clinical management of preterm infants, still those who suffer with severe vascular complications lack viable treatment options. Paucity of the alveolar capillary network in ACDMPV causes respiratory distress and leads to mortality in a vast majority of ACDMPV infants. The discovery of endothelial progenitor cells (EPCs) in 1997 brought forth the paradigm of postnatal vasculogenesis and hope for promoting vascularization in fragile patient populations, such as those with BPD and ACDMPV. The identification of diverse EPC populations, both hematopoietic and nonhematopoietic in origin, provided a need to identify progenitor cell selective markers which are linked to progenitor properties needed to develop cell-based therapies. Focusing to the future potential of EPCs for regenerative medicine, this review will discuss various aspects of EPC biology, beginning with the identification of hematopoietic, nonhematopoietic, and tissue-resident EPC populations. We will review knowledge related to cell surface markers, signature gene expression, key transcriptional regulators, and will explore the translational potential of EPCs for cell-based therapy for BPD and ACDMPV. The ability to produce pulmonary EPCs from patient-derived induced pluripotent stem cells (iPSCs) in vitro, holds promise for restoring vascular growth and function in the lungs of patients with pediatric pulmonary disorders.”

### Journal Article (*Clinical Epigenetics*):

The genetic research team at Erasmus University Medical Center in Rotterdam, The Netherlands recently published a manuscript



entitled, “*Genome wide DNA methylation analysis of alveolar capillary dysplasia lung tissue reveals aberrant methylation of genes involved in development including the FOXF1 locus*” in the Journal of Clinical Epigenetics, which can be found [HERE](#). Partial Abstract:



**“Background:** Alveolar capillary dysplasia with or without misalignment of the pulmonary veins (ACD/MPV) is a lethal congenital lung disorder associated with a variety of heterozygous genomic alterations in the FOXF1 gene or its 60 kb enhancer. Cases without a genomic alteration in the FOXF1 locus have been described as well. The mechanisms responsible for FOXF1 haploinsufficiency and the cause of ACD/MPV in patients without a genomic FOXF1 variant are poorly understood, complicating the search for potential therapeutic targets for ACD/MPV. To investigate the contribution of aberrant DNA methylation, genome wide methylation patterns of ACD/MPV lung tissues were compared with methylation patterns of control lung tissues using the recently developed technique Methylated DNA sequencing (MeD-seq).

**Results:** Eight ACD/MPV lung tissue samples and three control samples were sequenced and their mutual comparison resulted in identification of 319 differentially methylated regions (DMRs) genome wide, involving 115 protein coding genes. The potentially upregulated genes were significantly enriched in developmental signaling pathways, whereas potentially downregulated genes were mainly enriched in O-linked glycosylation. In patients with a large maternal deletion encompassing the 60 kb FOXF1 enhancer, DNA methylation patterns in this FOXF1 enhancer were not significantly different compared to controls. However,

two hypermethylated regions were detected in the 60 kb FOXF1 enhancer of patients harbouring a FOXF1 point mutation. Lastly, a large hypermethylated region overlapping the first FOXF1 exon was found in one of the ACD/MPV patients without a known pathogenic FOXF1 variation.

**Conclusion:** This is the first study providing genome wide methylation data on lung tissue of ACD/MPV patients. DNA methylation analyses in the FOXF1 locus excludes maternal imprinting of the 60 kb FOXF1 enhancer. Hypermethylation at the 60 kb FOXF1 enhancer might contribute to FOXF1 haploinsufficiency caused by heterozygous mutations in the FOXF1 coding region. Interestingly, DNA methylation analyses of patients without a genomic FOXF1 variant suggest that abnormal hypermethylation of exon 1 might play a role in some ACD/MPV in patients.”

### Journal Article (Respir Res):



The genetic research team at Baylor College of Medicine in Houston, Texas, USA recently collaborated with an international team in Poland to publish a manuscript entitled, “*Perturbation of semaphorin and VEGF signaling in ACDMPV lungs due to FOXF1 deficiency*” in the Respiratory Research journal, which can be found [HERE](#). Partial Abstract:

**“Background:** Alveolar capillary dysplasia with misalignment of pulmonary veins (ACDMPV) is a rare lethal congenital lung disorder in neonates characterized by severe progressive respiratory failure and refractory pulmonary hypertension, resulting from underdevelopment of the peripheral pulmonary tree. Causative heterozygous single nucleotide variants (SNVs) or copy-number variant (CNV) deletions

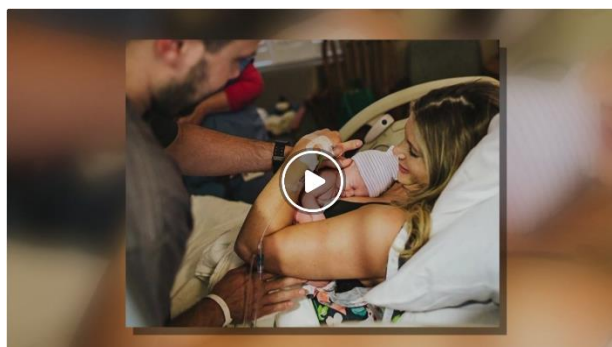


involving FOXF1 or its distant lung-specific enhancer on chromosome 16q24.1 have been identified in 80–90% of ACDMPV patients. FOXF1 maps closely to and regulates the oppositely oriented FENDRR, with which it also shares regulatory elements.

**Conclusions:** Our transcriptomic data imply potential crosstalk between several lung developmental pathways, including interactions between FOXF1-SHH and SEMA-NRP or VEGF/VEGFR2 signaling, and provide further insight into complexity of lung organogenesis in humans.”

## AWARENESS NEWS

### *Families in the News (Barrett Bone):*



**“As loved ones continue spreading blessings, Barrett's parents said it's acts like that from complete strangers that are some of the most powerful. "You're thinking of my child. It's incredible," said Katy Bone.”**

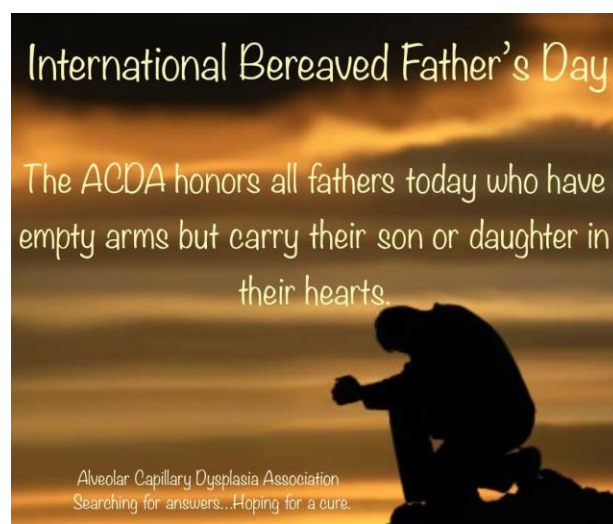
Katy and Tyler Bone, ACDA parents to Barrett (June 14, 2019 – July 12, 2019), recently shared how they celebrated Barrett's second birthday by performing random act of kindness towards others. Please read the touching story below:

[‘Blessings for Barrett’ movement inspires random acts of kindness](#)



### *International Bereaved Father's Day (August 29, 2021):*

Love and light to our bereaved ACDA fathers this past International Bereaved Father's Day, which is observed annually on the last Sunday in August.



Reports from **Stichting ACD** (The Netherlands) and **The David Ashwell Foundation** (UK) will return in the next edition of ACDA Notes.





## FUNDRAISING NEWS

**Donations:**

**To make a secure tax deductible donation to the ACDA, please visit our website.**



[acdassociation.org/donate](http://acdassociation.org/donate)

The ACDA is a 501(c)(3) non-profit, tax-exempt organization as designated by the Internal Revenue Code of the United States.

**Balance of ACDA account:**

The balance of the ACDA bank accounts as of August 23, 2021 is [REDACTED] [REDACTED]

[illegible]

**Update from AmazonSmile:**

The ACDA was issued a [REDACTED] donation from the AmazonSmile Foundation as a result of AmazonSmile program activity between January 1 and March 31, 2021. To designate the ACDA as your charity, please follow the link below so that all of your eligible shopping will benefit the ACDA:

<http://smile.amazon.com/ch/46-2915711>



### Update from Spreadshirt:

Items with the ACDA logo are available for purchase in our Spreadshirt store [HERE](#). The accrued commission payment from Spreadshirt between March 16 and August 29, 2021 is [REDACTED]. Please continue to shop at our store as new items and new features are added regularly. You have the option to customize your products by choosing “Create,” including adding your child’s name or picture to most items featuring the ACDA logo. Don’t forget the ACDA earns a commission equal to **20% of every product sold!** **Look for free standard shipping from September 7-9, 2021!**

### **Donations Received:**

Thank you to the following families and friends that have made donations to the ACDA since the last ACDA Notes:

[illegible]

*\*We are sorry we do not know the child for whom the memorial contribution was made. Please contact us to let us know.*

### T-shirt fundraiser (Barrett Bone):



**Katy and Tyler Bone raised \$600 from t-shirt sales in honor of Barrett Bone! Thank you Katy and Tyler!**

Katy and Tyler Bone, ACDA parents to Barrett (June 14, 2019 – July 12, 2019), continue to **raise funds for ACDMPV research in Barrett's honor!** As a follow-up to Issues #69, 70 and 72 of ACDA Notes, the Bone family worked with a designer to create special t-shirts for Barrett. In March 2021, they organized a third round of their t-shirt fundraiser and **donated \$600 from the sales to the ACDA in June 2021!** This is in addition to the \$400 in July 2020 and \$500 on #GivingTuesday2019 donated from the sales. In Katy's own words from the March 2021 fundraiser, "T-shirt sale update!!! In March we did a T-shirt sale to raise money for the ACD association. We raised \$600!!!! Thank you thank you thank you!!!!!"

**Because of Barrett | We Love Harder!** Donations will be made to the Alveolar Capillary Dysplasia Association in honor of Barrett. These donations help with research in hopes to find a cure for other babies who will be born with this disease."

### Pampered Chef fundraiser (Barrett Bone):



In July 2021, a friend of Katy and Tyler Bone, ACDA parents to Barrett (June 14, 2019 - July 12, 2019), organized a Pampered Chef fundraiser for **ACDMPV research in honor of Barrett Bone.** In Katy's own words, "My sweet friend is hosting a pampered chef fundraiser to donate money to the ACDA in Barrett's honor... Lisa recently started selling and I thought it was the sweetest that she wants to give back in honor of Barrett." 💙🐝💙

### Matching Gifts:

**MATCHING GIFTS**

1. YOU DONATE.
2. THEY MATCH.
3. DOUBLE THE IMPACT.

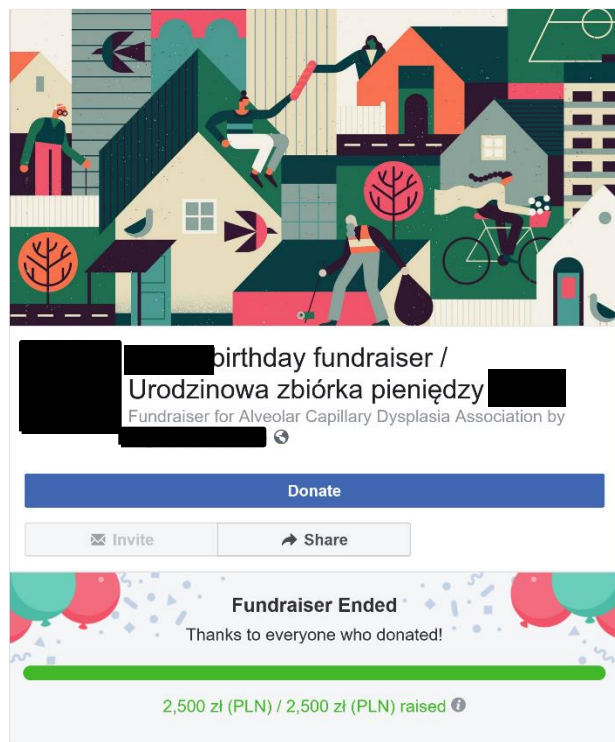
**Don't forget about Matching Gifts** – If your employer has a Matching Gifts Program for charitable organizations, your contributions to ACDMPV research can grow! Please check with your Human Resources department. The ACDA Tax Identification Number is **46-2915711.**

The ACDA extends our sincere thanks to **AMC Theaters, Bank of America, Chevron, Goldman Sachs, Schneider Electric, Tokyo Electron and Verisk Analytics** for their matching gifts for ACDMPV research!





### Birthday Fundraiser (████):



████ raised 2,500 zł (PLN) through a Facebook birthday fundraiser in honor of her son, █████. Thank you, █████!

In August 2021, █████, ACDA mother to █████, organized a birthday fundraiser for **ACDMPV research in honor of █████**. In █████'s own words, "Thank you very much to all the donors for supporting my birthday fundraiser so far ❤️ I have already increased my goal three times, your response is amazing. The goal is lofty, we are adding a small brick to groundbreaking research 🙌 Thank you."

This year, instead of birthday wishes and gifts, I am asking for support of ACDA - Alveolar Capillary Dysplasia Association. This organization's mission is very important and any donation will help to achieve the goal. ACDA information is provided below."

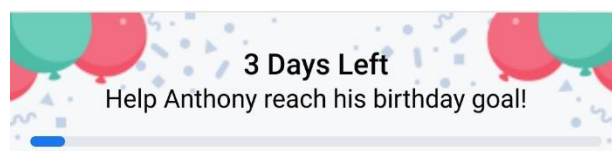


### Birthday Fundraiser (Merrideth Kateridge):



#### Anthony's birthday fundraiser for Alveolar Capillary Dysplasia Association

Fundraiser for Alveolar Capillary Dysplasia Association by █████



Anthony is on his way to his goal ([donate here!](#)) through a Facebook birthday fundraiser in honor of his daughter, Merrideth Kateridge. Thank you, Anthony!

In August 2021, **Anthony Kateridge**, ACDA father to Merrideth (March 9, 2017 – April 5, 2017), organized a birthday fundraiser for **ACDMPV research in honor of Merrideth Kateridge**. In Anthony's own words, "For my birthday this year, I'm asking for donations to Alveolar Capillary Dysplasia Association. I've chosen this nonprofit because their mission means a lot to me, and I hope you'll consider contributing as a way to celebrate with me. Every little bit will help me reach my goal. I've included information about Alveolar Capillary Dysplasia Association below. Anyone who knows me, knows how this has affected me and my family. for those of you that dont know **My sweet little Shield maiden, Merrideth Lilly Kateridge was only 27 days old when she lost her battle. Daddy will always love you. I miss you every second of every day. Please give what you can so no other family has to go through what we have gone through.** To find the cause of and cure for Alveolar Capillary Dysplasia with misalignment of the pulmonary veins (ACDMPV), a rare infant lung disorder."

### Birthday Fundraiser (Ethan Kimberlin):



#### Kat's birthday fundraiser for Alveolar Capillary Dysplasia Association

Fundraiser for Alveolar Capillary Dysplasia Association by [REDACTED]



1 Week Left

Kat reached her birthday goal! You can still donate to show your support.

\$495 raised of \$180

Kat raised \$495 of her \$180 goal (still time to [donate here!](#)) through a Facebook birthday fundraiser in honor of her son, Ethan. Thank you, Kat!

In August 2021, **Kat Kimberlin**, ACDA mother to Ethan (October 23, 2017 – October 24, 2017), organized a birthday fundraiser for **ACDMPV research in honor of Ethan Kimberlin**. In Kat's own words, "For my birthday this year, I'm asking for donations to Alveolar Capillary Dysplasia Association. I've chosen this charity because their mission means a lot to me, and I hope that you'll consider contributing as a way of celebrating with me. Every little bit will help me reach my goal. I've included information about Alveolar Capillary Dysplasia Association below.

To find the cause of and cure for Alveolar Capillary Dysplasia with misalignment of the pulmonary veins (ACDMPV), a rare infant lung disorder."

### Birthday Fundraiser (Felina Aßmann):



#### Jans Geburtstags-Spendenaktion für Alveolar Capillary Dysplasia Association

Fundraiser for Alveolar Capillary Dysplasia Association by [REDACTED]



1 Week Left

Help Jan reach his birthday goal!

Jan is on his way to his €150 EUR goal (with a week left to [donate!](#)) through a Facebook birthday fundraiser in honor of his daughter, **Felina Aßmann**. Thank you, Jan!

In August 2021, **Jan Aßmann**, ACDA father to Felina (October 2, 2017 - October 20, 2017), organized a birthday fundraiser for **ACDMPV research in honor of Felina Aßmann**. In Jan's own words, "This year on my birthday I am asking you to donate to Alveolar Capillary Dysplasia Association. I have selected this nonprofit because I care deeply about their concern. I hope you celebrate my birthday with a donation to this organization. Any amount that small helps to reach my goal. Here you can find more information about the Alveolar Capillary Dysplasia Association. To find the cause of and cure for Alveolar Capillary Dysplasia with misalignment of the pulmonary veins (ACDMPV), a rare infant lung disorder."



## REMEMBERING OUR BABIES

[REDACTED]

[REDACTED]

## WELCOME TO NEW FAMILIES

A sad but warm welcome to the following newly registered families:

- [REDACTED]
- [REDACTED]





## SAFE ARRIVALS!

Congratulations on the birth of the following little siblings in our ACDA registered families:

- [REDACTED]
- [REDACTED]

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## ACDA COMMITTEE POSITIONS

Please check our website for a full listing of Board and Committee members and let us know if you would like to get involved.

<http://acdassociation.org/board-members>

At the quarterly ACDA Board of Directors meeting in August 2021, Eliza Rista, Renee Murray and John Rista were unanimously reelected to serve as President, Secretary and Treasurer, respectively, of the ACDA Board of Directors until August 2022.

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## CONNECT WITH US

### Facebook:

- [Official ACDA Public Page](#)
- [Parent Group](#) (private)
- [Family Group](#) (private)

Read about the private groups with information on how to join:

<http://acdassociation.org/support-groups/>

### Twitter:

- Follow us [@acdassociation](#)

### Website:

- [acdassociation.org](http://acdassociation.org)

### Email:

[President@acdassociation.org](mailto:President@acdassociation.org) (Eliza Rista)  
[Secretary@acdassociation.org](mailto:Secretary@acdassociation.org) (Renee Murray)  
[Treasurer@acdassociation.org](mailto:Treasurer@acdassociation.org) (John Rista)

**A note from the President:** We absolutely want to hear from you as to how we can best meet your needs with respect to information about ACDMPV and also grief support. We are here to help in any way we can. Please know we always want to hear your ideas and we love community involvement on any level. Please never hesitate to contact me at [President@acdassociation.org](mailto:President@acdassociation.org).

Regards, Eliza Rista, mom to Johnny  
(February 20, 2013 – March 4, 2013)

