The Inozyme Advocate

Your source for news, information, and events on Rare Calcification Disorders

Vol. 2 | December 2018

Welcome to The Inozyme Advocate, a semi-annual communication to bring you news, information, and events from the Patient Advocacy Team at Inozyme!

In the News – Classifying Genetic Conditions

In a recent Genetics in Medicine publication entitled "A proposed nosology of inborn errors of metabolism", Dr. Ferreira and his colleagues recommended a classification system for naming inborn errors of metabolism, called a nosology. A nosology is important because it provides a structure for diagnosing, studying, and treating a group of conditions. It also promotes awareness and advances communication and collaboration among physicians and researchers. The proposed classification system focuses on the specific disruptions in the underlying biological pathways that lead to a disease.

The proposed classification system was applied to Generalized Arterial Calcification of Infancy (GACI) and Autosomal Recessive Hypophosphatemic Rickets type 2 (ARHR2) since both conditions are due to disruptions in the ENPP1 pathway and a proposed nosology for ENPP1 Deficiency is included in the publication. GACI type 1 in infancy and ARHR2 post-infancy occur due to mutations or changes in the *ENPP1* gene, leading to a decrease in the amount of ENPP1 protein in an individual's body. The condition was named ENPP1 Deficiency since not all patients develop arterial calcifications (some develop only vessel narrowing, or join calcifications), and since rickets might not occur until later in life. Similarly, GACI type 2 in infancy and Pseudoxanthoma Elasticum (PXE) post-infancy are due to mutations in the *ABCC6* gene, leading to a decrease in the function of the ABCC6 protein in the body. Thus, it is named ABCC6 Deficiency, regardless of severity. The publication can be found at https://www.nature.com/articles/s41436-018-0022-8.

Announcement - Natural History Studies for Generalized Arterial Calcification of Infancy and Autosomal Recessive Hypophosphatemic Rickets Type 2 Near Completion!

The Natural History Studies for ENPP1 Deficiency (GACI type 1 and ARHR2) and ABCC6 Deficiency (GACI type 2) studies will complete enrollment by January 31, 2019. Anyone interesting in participating is encouraged to do so before then. To obtain more information or to participate in either study, please reach out directly to:

- **Dr. Frank Rutsch**, at the University of Muenster in Germany, by e-mail at frank.rutsch@ukmuenster.de or by phone at +49 251 8346439.

OR

- **Dr. Carlos Ferreira**, at the National Institutes of Health in the US, by e-mail at ferreiracr@mail.ig.gov or by phone at +1-240-393-5441.

Final results are anticipated by June 2019.

Meet the Team - Dr. Carlos Ferreira

Dr. Ferreira is a staff clinician at the National Institutes of Health (NIH)/ National Human Genome Research Institute (NHGRI) in Bethesda, Maryland, where he serves as a Principal Investigator (PI) of studies of various genetic conditions. He is also an Assistant Professor of Pediatrics at the George Washington University School of Medicine and Health Sciences, and an attending physician at Children's National Health System. Further, Dr. Ferreira is an advisor to Inozyme based on his specific research interest and experience in rare disorders of calcification.

Dr. Ferreira first became interested in rare disorders of calcification in 2013 when he encountered 2 families in the same week with *ENPP1* gene mutations: one with GACI, and one with ARHR2. Dr. Ferreira was so intrigued by the variable clinical history of these two families, with mutations in the same gene, that he was inspired to focus his research on rare disorders of calcification to learn more. He is pursuing this research as the Principal Investigator of the "Study of People with Generalized Arterial Calcification of Infancy (GACI) or Autosomal Recessive Hypophosphatemic Rickets Type 2 (ARHR2)". To learn more, visit: https://clinicaltrials.gov/ct2/show/NCT03478839.

Dr. Ferreira's accomplishments include directing the Children's National Health System research study of undiagnosed disease in partnership with Regeneron Genetic Center. Dr. Ferreira is also the author of numerous publications and book chapters. Read the highlights of his recent publication in the section entitled "In the News".

Inozyme is proud to have Dr. Ferreira as part of the team of dedicated clinicians and researchers involved with helping the ENPP1 Deficiency and ABCC6 Deficiency communities.

Did You Know? – Patient Advocacy Groups

Patient advocacy groups (PAG) provide support services and educate patients and caregivers. Their mission is to improve the lives of patients and caregivers living with a condition. They work to increase public awareness of disease symptoms and treatment options, as well as promote research to cure or prevent that condition. Inozyme is supporting the formation of a formal GACI/ARHR2 PAG. To learn more, read the section entitled "Community Insights".

Community Insights – The GACI/ ARHR2 Community Meeting

On October 2, on the eve of the Global Genes 2018 Rare Patient Advocacy Summit in Irvine, CA, USA, Inozyme supported a meeting of members of the GACI/ARHR2 community.

13 GACI and ARHR2 community members around the globe participated, including 7 in-person participants (including 2 children) representing 4 familes, and 6 online participants representing 4 additional families.

In addition to community members, individuals from Children's Hospital of Philadelphia (CHOP), the PAG Soft Bones, and Dohmen Life Science Services (DLSS) participated in the meeting:

- Dr. Michael Levine, Medical Director of the Center for Bone Health at CHOP, shared the latest information on GACI and ARHR2 and potential treatments.
- Deborah Fowler and Denise Goodbar of Soft Bones discussed the elements needed to form a PAG and how best to proceed.
- Carey Stephenson and Pam Todd of DLSS highlighted advocacy-specific learnings from the 2017 landscape assessment and led the workshop to help the group identify tactics related to their preidentified goals.

Prior to the meeting, the community members identified four goals for the PAG:

1) **Educate** – provide searchable, shareable information
2) **Support** – offer hope and psycho/social connection, and let people know they're not alone
3) **Improve Access to Medical Care** – discuss diagnosis and healthcare provider awareness, and provide information about experts
4) **Improve Treatment** – share information on trials, and fund research

At the meeting, the group identified multiple tactics and classified them into 4 categories: high impact, difficult to accomplish; high impact, easy to accomplish; etc. Tactics discussed included promoting contacts with experts in the field, providing financial support to families in need, and advocating for calcification evaluation during mid-pregnancy ultrasounds. In the future, the group will need to prioritize the initiatives and make decisions about timing of execution. Additional ideas proposed, such as a disease education website and Healthcare Provider awareness, are initiatives Inozyme will put in place in 2019 in conjunction with the PAG.

The community engaged in subsequent discussions and decided to pursue formalizing a global GACI/ARHR PAG. This will allow the group to become a non-profit organization enabling them to accept donations and pursue fundraising activities, provide grants to researchers and clinicians to further treatments and ultimately a cure, and so much more.

Inozyme is excited for the GACI/ARHR2 community to take this next step! We are wishing them all the best in this new endeavor!

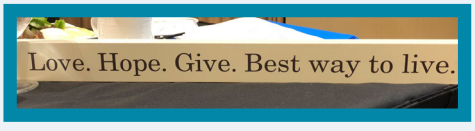
A summary of the meeting is available upon request. Please contact Lori Ann Correia at lori.correia@inozyme.com for a copy.

Engaging with Each Other

The meeting provided a forum for the community to form bonds and share their experiences.

"For tonight to actually happen is overwhelming. We always wondered how we were ever going to meet the people we have talked to for years over the phone and internet. This is a surreal moment," expressed one participant. And, a really touching moment occurred when the two children with GACI spoke of exchanging necklaces as a symbol of their bond.

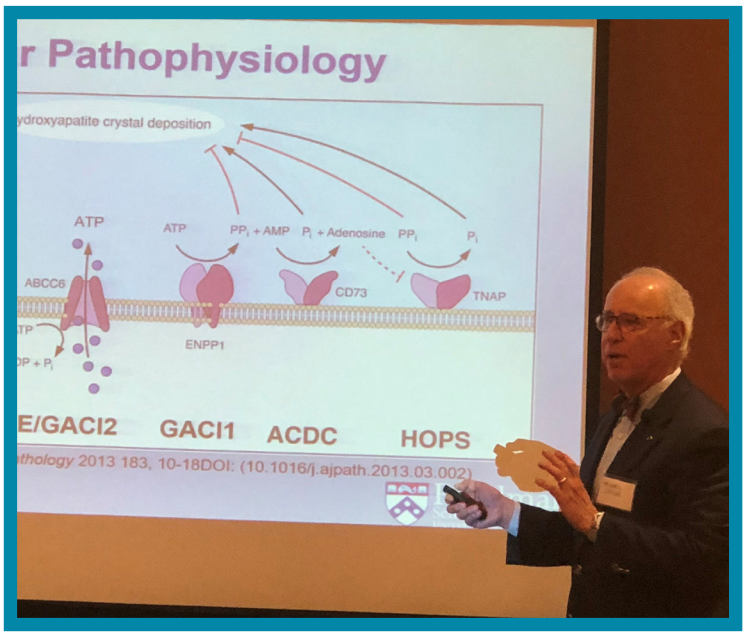
Another individual brought in a symbol of her feelings as seen in the below image.



2018 Frederic C. Batter Award - Dr. Michael Levine

Dr. Levine is the recipient of the 2018 Frederic C. Batter Award from the American Society of Bone and Mineral Research (ASBMR)! This award is presented to an ASBMR member in recognition of outstanding clinical investigation in disorders of bone and mineral metabolism. Dr. Levine specializes in endocrine diseases that affect bone and mineral metabolism, including rickets and genetic bone disease, at CHOP. He is also a Professor of Pediatrics and Medicine at the Perelman School of Medicine at the University of Pennsylvania. His long list of accomplishments includes studying the molecular basis of unusual metabolic bone conditions to provide insights into the etiology of more common bone disorders. His critical research has revealed the causes of various forms of rickets.

Inozyme is proud to have Dr. Levine as the Chair of Inozyme's Clinical Advisory Board and a member of the dedicated team of physicians caring for individuals with ENPP1 and ABCC6 Deficiencies. Congratulations to Dr. Levine on receiving this distinguishing award!



Meeting Highlights – Global Genes 2018 Rare Patient Advocacy Summit

Global Genes 2018 Rare Patient Advocacy Summit took place in Irvine, CA, USA from October 2-4. A total of 724 people attended the summit including patients, caregivers, and representatives from the medical community and industry. Meeting highlights include:

- The Freshman Orientation provided first-time attendees with an overview of the conference.
- The 4 Summit tracks: Living with a Life-Altering Condition, Architecting Your Disease Community, Patients as Partners and Drivers, and Science and Technology. View the recorded sessions at the Global Genes Vimeo channel.

- The two-day event concluded with the RARE Champions of Hope Celebration, which honors individuals for their notable efforts in rare disease advocacy. Learn more about the 2018 Rare Champions of Hope at https://globalgenes.org/2018-rare-champions-of- hope-honorees/.

Mark your calendar for the 2019 RARE Patient Advocacy Summit **on September 18-20th in San Diego, California at the Sheraton San Diego Marina Hotel. Hope to see you there!**

Ways to Get Involved - Rare Disease Day 2019

Rare Disease Day (RDD) 2019 will be celebrated on Thursday, February 28. RDD is observed worldwide annually on last day of February to raise awareness for rare diseases and the daily impact living with a rare disease has on patients and families. Each year, the RDD organization has a unique campaign. **The 2019 RDD theme is Bridging Health and Social Care.** Mark your calendars, get involved and learn more at https://www.rarediseaseday.org/.

RARE DISEASE DAY®

Upcoming Events - Winter and Spring 2019

The following meetings maybe of interest to patient, caregivers and healthcare providers. Visit the below websites to find the ones of interest to you.

- **April 2–6, 2019: American College of Medical Genetics (ACMG),** Seattle, WA
  https://www.acmgmeeting.net/acmg2019
- **April 10–12, 2018: World Orphan Drug Conference,** Washington, DC
  https://www.terrapinn.com/conference/world-orphan-drug-congress-usa/index.stm
- **April 27–April 30, 2019: Pediatric Endocrine Society,** Baltimore, MD https://2019.pas-meeting.org/about/
- **May 10, 2019: Rare Bone Disease Workshop and May 11-14, 2019: European Calcification Tissue Society,** Budapest, Hungary
  https://www.ects2019.org/wp-content/uploads/2018/09/ECTS_2nd_announcement_web.pdf
- **June 7, 2019: Global Genes Rare Patient Advocacy Symposium,** Philadelphia, PA
  https://globalgenes.org/2019-rare-drug-development-symposium/
- **June 21-23, 2019: NORD Patient & Family Forum,** Houston, TX
  https://rarediseases.org/living-rare-living-stronger-nord-patient-family-forum/

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