Hope Springs Eternal
By Kerry Molina & Sean Nohelty

With the arrival of Spring, we are excited to bring you this second issue of “Fighting For Fiona & Friends / NKH-ND News Today”. Since the inaugural launch last Fall, we have seen tremendous progress in both accelerating research and spreading awareness of our shared fight against Non-Ketotic Hyperglycinemia.

In early March at Notre Dame’s 2019 Rare Disease Day Conference, Dr. Kasturi Hal-dar and her team updated the NKH community on some very exciting developments in their four-pronged research initiative. Read more about their news and meet one of the team’s lead researchers, Dr. Rebecca Wingert.

Also, meet the O’Sullivan’s and the Archibald’s - two incredible NKH families and their foundations (the Drake Rayden Foundation and NKH Crusaders) whose tireless efforts as parents and patient advocates are making a profound and lasting difference. Hear their inspiring stories and how their families are helping fund research at Notre Dame and beyond.

And just around the corner is ND Day on April 28-29, the annual fundraising ‘telethon’ where we need you (and as many people as possible) to donate $10 and cast your 5 votes for BP-CRND. The more votes, the larger share of a $1.2M Matching Challenge Fund that NKH research will be awarded. Last year, BP-CRND came in 5th place out of more than 800 clubs and was awarded over $22,000 for NKH research in addition to over $10,000 in direct contributions. Read about how you can participate and get others involved too.

As with Spring, our hope springs eternal in the fight against NKH. Thank you for joining us, get ready for ND Day and spread the word!

Notre Dame Day 2019: April 28–29
By Corianne Kellems

With a gift of $10 (or more) you earn 5 votes to cast for the Boler-Parseghian Center for Rare & Neglected Diseases (BP-CRND) supporting NKH research. We need as many individual people to donate $10 and cast their 5 votes for BP-CRND.

https://notredameday.nd.edu/organizations/boler-parseghian-center-for-rare-and-neglected-diseases

Voting is open NOW thru midnight on April 29. Donate. Vote. Spread the Word!

(see Notre Dame Day, continued on page 9)
We have overcome a major hurdle to developing patient-centered treatments by building successful mouse models that mimic NKH disease as seen in patients with genetic mutations.

Last year we reported creation of a mouse model with mutations in GLDC/P protein (defect in which is a major cause of NKH. These mice showed severe disease and died within 1-2 days of birth and also in utero. We now report rescue of mutant mice through formate treatment of pregnant mothers. These mice have elevated glycine and are being evaluated for neurological symptoms of NKH before we initiate testing of genetic and epigenetic treatments. To the best of our knowledge previously developed NKH mouse models have not been reported (either published or unpublished) to show neurological disease.

Based on our strong progress in the mouse model and other areas for 2019-2020 we also plan work in the following three areas.

1. Develop computational models to predict functional deficiency associated for all patient mutations. This combined with natural history data will translate into an on line portal that both physicians and patients can use to help understand and manage disease.

2. Understand the nutritional status of human cells with defect in P protein to design nutritional therapies that will be tested first in mutant mouse models. Studies on cinnamon will be done in collaboration with Dr. Pahan, Rush University.

3. Use new zebrafish models to study NKH mutations affecting brain and kidney development that remain unknown and develop screens for new drugs.

Our NKH research could not have been done without support from the Drake Rayden Foundation, Fighting For Fiona and Friends, ND-NKH and the NKH Crusaders. We are very grateful to them. We also thank the Almany Family, Judy Alvarez and BEE-lievers and all of the many members of the NKH community for their contributions to ND Day 2018. We look forward to scaling even new heights with you on ND Day 2019 on April 28-29!
Rare Disease Day 2019 Recap
By Barb Calhoun & Kasturi Haldar

The Boler-Parseghian Center for Rare and Neglected Diseases is deeply grateful for an extraordinary weekend celebrating our 10th Annual Conference Advancing Rare Disease Research, Therapy and Patient Advocacy on March 1-2 2019!

It was our largest meeting with over 200 in attendance. Thanks to our illustrious alumni, outstanding faculty, students, staff, patient families, clinical partners and other community partners for making it a great success!

The Friday March 1 dinner, was introduced by Dr. Kasturi Haldar (Director, CRND) and Mrs. Barbara Calhoun (Outreach Coordinator CRND). Dean Mary Galvin (Dean, College of Science-COS) spoke to the commitment of the COS and the University to Rare and Neglected Diseases and led with the invocation. The keynote speaker Mr. Matt Boler, Chairman of the Board, President and CEO Boler Company inspired us with sharing his family’s pledge to this area of high unmet need and potential for research discoveries.

We were also excited to establish two new awards for our exceptional undergraduates. The first was the Megan K. Crowley Award for Patient Advocacy, whose recipient Megan Crowley, ND ’19 is a tireless patient advocate and President of the Notre Dame Chapter of Make a Wish Foundation that aims to grant a wish of every child diagnosed with a life threatening condition. CRND is honored Megan came to study at Notre Dame.

The second award was the John M. and Mary Jo Boler Rare Disease Research Award in honor of the parents of Matt Boler and Jill McCormack and the resonance of their generous philanthropy with rare diseases.

The recipient Gabrielle O’Dougherty ND ’19 in partnership with a local patient family and their neurosurgeon developed a unique case report on Shprintzen Goldberg Syndrome (SGS) that is currently under revision for publication. O’Dougherty et al, Case Report: Complications of Insufficient Dura and Blood Loss during Surgical Intervention in Shrintzen-Goldberg Syndrome.

Jill McCormack, Trustee Boler Family Foundation, presented both awards.

We completed Friday evening with a rousing hockey game honoring patients and families. Notre Dame came from behind to beat Penn State 5-4!

"It was our largest meeting with over 200 in attendance... alumni, outstanding faculty, students, staff, patient families, clinical partners and other community partners..." - Barb

Saturday March 2 morning began with a dazzling Glee Club performance of the Rare Disease Fight Song and gracious welcome Deputy Chief of Staff Suzanna Fitzberg, South Bend Mayor’s Office. Dr. Xin Lu, John M and Mary Jo Boler Assistant Professor, Boler- Parseghian Center delivered the keynote lecture on preclinical models that help move research findings from the laboratory to treatments in the clinic for rare tumors and cancers.

This was followed by three panel discussions with active audience participation! In the first panel on ‘Rare Disease Research and Therapy’, John Crowley (CEO Amicus), Steve Aselage (Board Member Retrophin), Dr. Diana Wetmore (V.P. and Director Harrington Institute), Dr. Elizabeth Berry-Kravis (Rush Medical Center) joined Drs. Brian Blagg (Director Warren Center, Notre Dame) and Kasturi Haldar (Director CRND) to discuss the promises of partnerships between pharmaceutical industry and academic researchers and the importance of patient advocates to accelerate new treatments for rare diseases. They also reviewed challenges and how to bridge them with new models of research and development in the 21st century.

(see Rare Disease Day, page 6)
It was every parent’s worst nightmare when the doctors told Eric and Tarah their son, Drake, was very sick. He was diagnosed with a terminal, rare disease called Non-Ketotic Hyperglycinemia (NKH). The medical community could do very little to help, because there is currently NO CURE...there is very little treatment options on top of that. Trusting that God would carry the family through this tragedy, Eric and Tarah took their one-month old son home on hospice to pass surrounded by his sisters and brother. Drake turned two in October, and God has shown them that He is not finished with Drake just yet.

Read on to follow the O’Sullivan’s story from a recent post shared earlier this month.

Drake is doing well right now. He is continuing to grow and become more chunky. We all smile when we rub his little pudgy legs or squish his chubby cheeks. We are still juicing his food to maximize the amount of veggies and fruits he gets in a day. We normally buy a week’s worth of food on a Friday or Saturday, and spend the weekend cleaning, cutting, and juicing so we can freeze it for the next week. It is quiet time consuming, but we know how much he has benefited from the added nutrition, so it makes it worth it.

Drake’s seizures have been very calm these past few weeks. He is still on his antibiotic as we continue to pursue what mechanisms are being calmed in his brain. We are awaiting a report now from a research facility that studies Drake to submit a new supplement/pathway to try. We are working together to use published data for different cases, and the clinical reactions we see with Drake, to try to test some of the pathways being affected. Our goal is if we can find another supplement that works in the same way as the antibiotic, he will be able to transition and come off the antibiotic. Also, it could give us great insight to why the antibiotics are working to calm his brain. There is always a delicate balance between trying to move forward, and not putting Drake through unnecessary things. We are thankful the team goes through many steps before they ever refer anything to our doctors. God has really put some phenomenal people in our lives.

We are also expecting another child later this year (it’s a girl!). The children are very excited, and we are trying to prepare them for different situations, without stealing their sweet joy. Having a baby after having a child as sick as Drake … it is hard. We were not planning for a baby at this point in our journey… We are very excited about the new little feet kicking in my tummy, but the conversations are much different now, and the excitement quickly fades from people/doctors’ faces as the hard reality hits the conversations…..“Will she be sick” …. “Are you going to test her while you are pregnant”….. “how will you manage with two sick children?”…..

(see O’Sullivan’s, continued on page 5)
O’Sullivan’s
(continued from page 4)

Honestly, we don’t have all the answers…. and I would be lying if I said fear never crept in. And, we have to trust that if God saw fit to bless us with another child, then He will give us the strength and stamina to handle the next step, and then the next step after that. We will love and cherish her with the same love and admiration we have for all our children. And if our baby is sick…. then we will fight just as hard for her life, as we fight for Drake’s, everyday God gives us with him.

That is the hard truth with genetic diseases… it is no longer planning paint colors or fluffy bows… it is genetic counseling, abortion pressure, and having a plan on what hospital to transport her to if she starts declining.

And if Drake’s life ends tomorrow…. this disease will not just go away…. It lives in our genes. Just like our families’ genes that have passed if for generations, unknowingly, down to us. That is why we have to step out on faith in every direction God calls us to, if we are ever going to give Drake, or children like him coming in the future, hope. Hope that one day this disease will not be so horrific…. one day, their mommy and daddy will be able to think about their future with excitement and love…not gut-wrenching heart ache and loss.

One day, these children will have a better future, because God reminds us every day that even though this is going to be the hardest thing we have ever faced … He is going to send an army of people to stand up, and join us in our fight to save Drake’s life… up! We would never stop fighting for our little girl!

Patient Advocacy at BP–CRND
By Barb Calhoun, MSN, RN, PNP

At BP-CRND, students assess Rare Disease patient medical records to identify pertinent symptoms of the disease. Records are summarized into concise 2-3 page Clinical Summaries that are used by patient families for future physician visits. It provides a detailed history that includes past office visits, hospitalizations, tests, procedures and treatments.

Gabrielle O’Dougherty is a Senior undergraduate at the Boler-Parseghian Center for Rare and Neglected Diseases. She is currently conducting clinical research on Shprintzen-Goldberg Syndrome. This involves developing a natural history of the disease by delineating the disease progression over time and comparing various patients. She is currently working with a patient family and their medical professionals on creating a case report that will bring attention to newfound unique risks and symptoms in Shprintzen-Goldberg Syndrome. She has done similar work with Nieman Pick Type C and Non-Ketotic Hyperglycinemia.

If you are interested in participating in our NKH studies, please contact Barb Calhoun at the Boler-Parseghian Center for Rare & Neglected Diseases at (574) 631-3372 or bcalhoun@nd.edu.
The second panel on ‘Resources and Empowerment’ comprised of ND faculty Drs. Suhail Alam, Rebecca Wingert, John Koren and Siyuan Zhang, as well as Kunigunda Szentes from the IDEA Center at ND. The panel also included patient advocates Gillian Shaw (Enfocus) and Nicole Boyce (Founder Global Genes). Drs. Alam and Wingert presented on strengths of murine neurological disorders and zebrafish genetic models available at the Freimann Life Sciences Center.

Dr. Koren has newly established a Biological Screening Core at the Warren Center for Drug Discovery. Dr. Zhang emphasized the importance of computational training to understand a complex target or drugs directed to it, to fully understand the properties of new medicines, while Ms. Szentes outlined funding mechanisms made available to move them to market. Gillian Shaw and Nicole Boyce are key community stakeholders who broadly empower patients in activities that range from home-based technology-assisted disease management to building patient services organizations (PSO’s) that effectively fund-raise for research and treatment in rare diseases.

The third panel on Saturday morning was on ‘Patient Health & Advocacy’. Dr. Mary Alice Reid, (Beacon Pediatrics), Karen Quandt, R.N., (NPC Patient Family & Advocate), Tarah O’Sullivan & Mary Fitzgerald (NKH Patient Advocates), Dr. Daniel Fulkerson, (Beacon Health), Francis Fitzgerald (ND’18) and Rob Long, (Uplifting Athletes), spoke to how they as clinicians and patients came to be advocates and address daunting tasks of satisfactory and timely diagnosis and care for rare disease patients. The panel concluded there may be need for post baccalaureate training in patient advocacy to support families to access technology-driven treatments and services as these become increasingly available in many rare diseases. Last and most importantly were presentations by patient families on their personal natural histories of Spinal Muscular Atrophy with Respiratory Distress, Angelman Syndrome, Von Hippel Lindau Disease, Leber’s Hereditary Optic Neuropathy, Coats Disease, Rett Syndrome, Neurofibromatosis Type 1, Mast Cell Activation Syndrome/ Eosinophilic Esophagitis, Sickle Cell Disease, Shprintzen Goldberg Syndrome and Non-ketotic Hyperglycinemia. We were transfixed by their courage, grace and tenacity to fight and raise awareness that rare diseases are not strange afflictions but rather part of our common genetic heritage and at an overall prevalence of 1 in 10, a forefront of human wellness.
Rare Disease Day
(continued from page 6)

Once again, we thank all the participants for their invaluable contributions. We thank Corianne Kellem for organizational support and Matt Frazier for photography.

A special shout out goes to Haldar lab members, Niraja Suresh, Arpitha MysoreRajashekara, Innocent Safeukui, Suhail Alam, Joe Farris, Katharyn Lee, Morgan Hiller, Abhishek Trivedi, Maisha Khair Nima and Fang Liu for their many hands and team spirit to bind the weekend.

How You Can Help

Donate to the NKH research funds at Notre Dame supporting Dr. Haldar and her research team:

FIGHTING FOR FIONA & FRIENDS
giving.nd.edu/fionafund

- and -

NKH-ND
supporting.nd.edu/NKHResearchFund

100% of all donations to both funds are directed exclusively to NKH research.
Archibald Family & NKH Crusaders

by Kristin Archibald

NKH Crusaders was formed in 2009 when our son Thomas was diagnosed with atypical NKH at Boston Children’s Hospital. After his diagnosis we were frustrated to learn how little research was being done for this devastating disease. We began raising funds for NKH research and it grew to include holding conferences with Doctors from Boston Children’s and NKH researchers and to bringing families together to learn more about NKH.

At our last event in March 2018 we had 19 NKH families attend from across the globe a 2-day conference with Dr. Johan Van Hove from the University of Colorado and Dr. Kasturi Haldar of Notre Dame. The conference featured research updates from these two amazing doctors, one on ones with families and ended with a fundraiser event hosting over 300 people and raising just over $40,000.

In the past all funds had been donated to the University of Colorado, however, with Notre Dame now doing NKH research we were able to establish the NKH Crusaders fund at Notre Dame after this event. To date we have raised and donated over $300,000 for NKH research and we are hopeful to surpass our $350,000 goal this year. In 2018 alone we sent $46,667 to Colorado and $12,500 to Notre Dame. We plan to increase the amount we support Notre Dame with each year.

We are happy to announce we have set the dates for our next NKH Conference and Fundraiser. It will be held in the Boston area on October 2,3 and 4th. We are looking forward to bringing families together as we hear updates from both Notre Dame and the University of Colorado. If you have questions about the upcoming conference please email: nkhcrusaders@yahoo.com  Thank you for your continued support of NKH.

NKH Researcher Profile: Dr. Rebecca Wingert, Ph.D.

Dr. Rebecca Wingert, Ph.D.: Director of Graduate Studies, Department of Biological Sciences

Year of Graduation: 2005, Ph.D. in Cell & Developmental Biology, Harvard University

Special interest: Working with zebrafish models of NKH to tackle the question of how this disease affects organ development. Zebrafish are a small, tropical freshwater species belonging to the minnow family, and named for the appearance of blue and white stripes on their body, making them look a bit like their “zebra” namesake. In the past 30 years, zebrafish have become a widely used animal model for biomedical research because they are actually quite similar to people—despite the very obvious differences in their appearance (they are very small fish!!) and residence in an aquatic habitat. Zebrafish are powerful because scientists can utilize these animals for genetics. Because zebrafish and humans have very similar GLDC and AMT genes, the fish can be used to study the question of HOW these genes function in the cells of our body.

My passion to work on NKH: When I first learned what NKH is, I was shocked and dumbfounded to learn how very little is known about this terrible and devastating disease. We know which genes cause this disease, but barely anything about HOW they cause disease. The need to advance this understanding was so apparent and important…and I knew my research team had expertise that could help to make progress.
Volu_me 1, Issue 2

Nor_te Dame Day 2019
(continued from page 1)

Follow these steps to support NKH Research at the Boler-Parseghian Center for Rare & Neglected Diseases:

1. Click https://notredameday.nd.edu/organizations/boler-parseghian-center-for-rare-and-neglected-diseases

2. Click on MAKE A GIFT

3. Donate $10 & Cast Your 5 Votes for

4. Select: Boler- Parseghian Center for Rare & Neglected Diseases (BP-CRND)

5. SHARE WITH ALL YOUR FAMILY, FRIENDS & BEYOND!
Fiona & Friends Walk
By Kerry Molina & Sean Nohelty

In celebration of the 5th anniversary of the founding of Fighting for Fiona & Friends by the Fitzpatrick and Nohelty families, and in the spirit of the “Walking for Fiona & Friends” campaign along the Notre Dame Trail in August 2017, plans are underway for an Inaugural Fiona & Friends Walk in South Bend, IN in late summer/early Fall 2019. Stayed tuned for details on how you can participate (either in person or remotely in your own neighborhood)! Alone We Are Rare, Together We Are Strong!

For more information on these organizations, click on their logos:

- Fighting For Fiona & Friends
- ND–NKH
- NKH International Family Network
- Drake Rayden Foundation
- Joseph’s Goal
- NKH Awareness Day May 2
- Hope for NKH
- The Foundation for Nonketotic Hyperglycinemia

Share your story, ask a question, and/or submit ideas for future articles to:
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Publisher: Kerry Molina
Editor: Sean Nohelty