Fighting for Fiona & Friends

ND-NKH News Today

Volume 1, Issue 1
November 2018

A Bi-Annual Newsletter for the Non-Ketotic Hyperglycinemia Rare Disease Community & Beyond

INSIDE THIS ISSUE:

UPCOMING EVENTS

- **WORLD RARE DISEASE DAY**
  February 28, 2019
- **RARE DISEASE DAY 2019 Conference at Notre Dame**
  March 1-3, 2019
- **NOTRE DAME DAY 2019 Matching Fundraiser**
  April 2019 (Date TBD)
- **NKH AWARENESS DAY**
  May 2, 2019

Alone We Are Rare, Together We Are Strong!

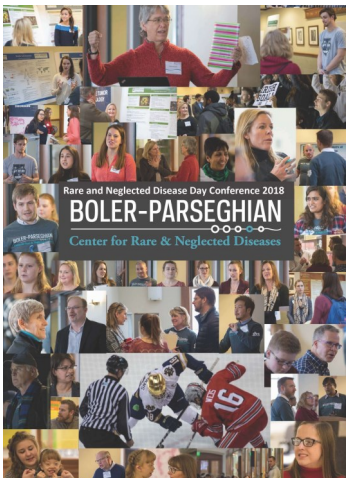
By Kerry Molina & Sean Nohelty

Welcome to the inaugural issue of ***"Fighting for Fiona & Friends / ND-NKH News Today"***, a bi-annual newsletter for the NKH (Non-Ketotic Hyperglycinemia) rare disease community and beyond. Our goal is three-fold, to: 1) share information, 2) increase awareness, and 3) together, accelerate progress in the fight against NKH.

Here you will find the latest updates on NKH research, profiles on NKH families across the globe, calendar of upcoming events, and ways you and your friends can get involved. In this first issue, we are pleased to highlight Fiona Fitzpatrick and Owen Sarb. Hear their stories and how their families helped found the NKH research initiative at Notre Dame.

Get updated on the latest research by Dr. Kasturi Haldar and her team at the Boler-Paresghian Center for Rare & Neglected Diseases at Notre Dame, and the importance of Patient Histories and how you can get involved by sharing your family's patient history with Barb Calhoun, Outreach Coordinator.

Lastly, be sure to Save-The-Date for the annual **Rare Disease Day 2019 Conference at Notre Dame** in South Bend, IN on **March 1-3, 2019**, where families fighting NKH and other rare diseases will gather with lead researchers to share, learn and be inspired. More details and registration info coming soon!



Rare Disease Day 2018 at Notre

Fiona Fitzpatrick's Story

By Mary Fitzpatrick

Our family became familiar with NKH (Non-Ketotic Hyperglycinemia) soon after the arrival of our third child, Fiona. She was born April 19, 2006. The pregnancy, labor and delivery were all normal and there was no reason for us to suspect that our lives were about to turn upside down.

She was diagnosed at 9 days old with the most severe version of NKH. My husband John and I had never heard of NKH – who has really? Unless you know someone whose life it has affected.

(see Fiona, continued on page 4)

Latest in NKH Research at Notre Dame

By Dr. Kasturi Haldar, Ph.D.

Our major goals are to develop (i) therapy to treat NKH and (ii) precision-medicine based tools to predict severity of the disease and guide appropriate therapies for each patient. We are looking for treatments using multiple strategies.

Dr. Kasturi Haldar, Ph.D.,
James Parson and Carrie Quinn
Director, BP-CRND

Earlier this year we reported using CRISPR-Cas9 methodology to create a mouse model with mutations in GLDC/P protein that shows severe disease. Mutational defect in GLDC/P protein is a major cause of NKH. This mutation severely affects survival of infant mice. To understand severe NKH disease we are utilizing nutritional supplements as well as developing gene therapy vectors to rescue severe disease. We are also creating new mouse models predicted to show less severe disease, in order to study NKH disease as a function of age.

We have made strong progress towards developing a zebrafish model of NKH disease. This model will help us understand early developmental defects caused by NKH disease and how they can be treated. The zebrafish model will also help screen a large number of drugs against whole organisms with NKH.

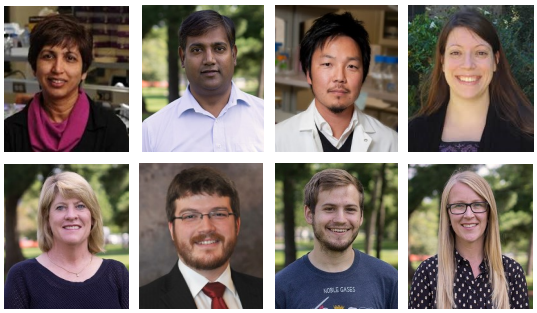
We have made strong progress on a cell model of NKH which has had GLDC genetically removed. This model is helping us to understand the metabolic role of GLDC by looking at how protein and metabolite levels change when GLDC is removed. An in depth understanding of GLDC metabolism will greatly assist in therapeutic design for NKH, and our cell model will be an essential tool for drug screening as well as testing patient mutations and their responsiveness to drugs.

Our computational predictive tool shows that genetic mutations that give higher scores in our model have worse clinical measures of NKH disease, such as number of drugs needed to control NKH-based symptoms, and overall severity of disease symptoms. We are grateful to all patients who participate in our natural history studies (with both medical records and cells) to help develop precision-medicine tools that will be used to guide patient therapies.

> "The Zebrafish model will also help screen a large number of drugs against whole organisms with NKH."
> *- Dr. Kasturi Haldar*

The research is being undertaken by the Haldar Lab, Lee Lab and Wingert Lab at the University of Notre Dame. Barb Calhoun, MSN, RN, PNP is our Outreach Coordinator.

We are grateful for support from ND families (Nohelty, Fitzpatrick & Sarb) through Fighting for Fiona & Friends and the ND-NKH funds, the Drake Rayden Foundation and NKH Crusaders. We also thank the Almany Family, Judy Alvarez and BEE-lievers and all of the many members of NKH community for helping us fund raise on ND-Day 2018 to raise ~ $40,000 in 29 hours!



Boler–Parseghian Center for Rare & Neglected Diseases NKH Research Team

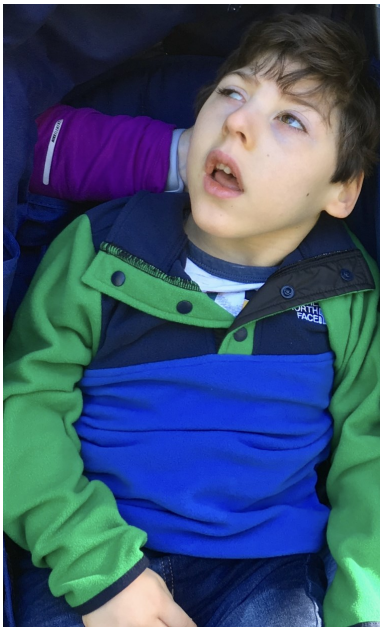
Dr. Kasturi Haldar, Ph.D.	Barb Calhoun, Outreach Coordinator
Dr. Suhail Alam, Ph.D.	Stefan Freed, Graduate Student
Dr. Shaun Lee, Ph.D.	Joe Farris, Graduate Student
Dr. Rebecca Wingert, Ph.D.	Corriane Kellems, Admin. Asst.

… and all the NKH Families & Friends like YOU!! …

Owen Sarb's Story

By Michelle Sarb

Our family's journey with NKH started the same as so many others, unexpected and chaotic. Owen Charles Sarb was born on September 22, 2011. When he did not respond as a typical newborn, and no cause could be found at our local hospital, Owen was transported to the University of Iowa Children's hospital. At 8 lbs. 13 oz., he was one of the largest babies in the NICU. Owen had countless tests and saw every specialty discipline. After about 3 weeks we had a tentative diagnosis. When we started doses of dextromethorphan and sodium benzoate and Owen opened his eyes and woke up for the first time for more than a few minutes, we were pretty confident it was NKH. Official genetic reports came about a month later confirming non-ketotic hyperglycinemia.



Owen Sarb

Owen's first few months included a couple life flights back to the University of Iowa, an hour away from our home in Davenport, Iowa. It quickly became apparent that we had to be advocates and educators to the doctors for our boy with his rare diagnosis. When he was hospitalized, I stayed with him and Joe commuted back and forth daily so he could work and take care of our dogs. There was more than one occasion that I needed to speak up to prevent him from getting medications that he shouldn't have, or make sure that his medications were given in a timely fashion. Owen just turned 7. He is in 1st grade at the local public school where he spends most of his day in the special education classroom. His nurse goes to school with him and he rides the bus in his new wheelchair. Owen has a little sister, Aubrey, who just turned 2. She is a big helper and likes to help carry his syringes and bring out diapers for him.

We still follow up at the University of Iowa for most of his appointments. He sees orthopedics, gastrointestinal, neurology, and genetics specialists there. Owen has physical and occupational therapy weekly at a local facility. He has intermittent appointments with a speech therapist and works with a vision specialist at school. He has an adaptive tricycle and has done therapeutic horseback riding. He uses AFOs, a TLSO, wrist splints, a wheelchair, standing frame, gait trainer, and bath chair. Owen has mixed tone and is not able to sit independently. He is able to activate a switch to play with some toys and reaches to an iPad in therapy. He wears glasses for his nearsightedness and just got botox injections in his hip adductors for his high tone.

His medications include sodium benzoate, Delsym, CBD oil, baclofen, lansoprazole, carnitor, and cyproheptadine. He requires meds around the clock and the longest gap between doses is 4 hours. His history outside of NKH includes pyloric stenosis, chylous ascites, a hip infection that required surgery, bilateral hip dysplasia, and cyclical vomiting. Owen does have some residual ability to break down glycine, but to what extent is unclear. We find that he gets very tense and irritable when his levels get too low and we try to keep him in the upper 200s or lower 300s.

Owen's diet consists of a blended formula which we make every night (or morning when we get too tired to do it before bed) and was designed by his nutritionist to carefully avoid too much additional glycine. He does have some oral skills and enjoys eating baby food on most days. Though he can't chew his food, sometimes he'll have special sweets like suckers and he loves the taste of bacon!

> "It is my hope that in sharing Owen's story, we can help others who struggle to find answers ..." - *Michelle Sarb*

Our stories all have similarities, but our kids all present so differently. It is our hope with this newsletter to share our stories and create a unified discussion to help our common quest of finding a cure. Every time we read a story or question in the Facebook groups, we try to offer suggestions and share our experiences. It is my hope in sharing Owen's story, we can help others who struggle to find answers or that we may find commonalities that may teach our researchers something relevant as well.

(see Owen, continued on page 6)

Fiona

(continued from page 1)

At birth, Fiona was healthy in every way except she did not cry, open her eyes or move much at all. The next day, she continued to be very sleepy, did not cry and they started doing some tests including an MRI. The EEG of her brain showed seizure activity and she was started on phenobarbital. As the hours went on, Fiona was unresponsive, and started having periods of apnea where she would stop breathing. On day three, Fiona was in a coma and on a ventilator. Her diagnosis was confirmed by Dr. Van Hove (he was the only doctor in the USA at the time researching NKH), indicating the abnormal high levels of glycine in her blood and spinal fluid.

We were told that Fiona would have severe developmental delays and not be able to do anything for herself. She would have difficult-to-treat seizures all her life, would not be able to eat and would have low muscle tone and not be able to sit up, crawl or walk. They suggested taking her off the ventilator and let nature take its course. We chose to start treatments for NKH which consisted of giving her Sodium Benzoate, Dextromethoraphan, anti-seizure medications and an antacid to combat the harsh effects of the SB on her stomach. We understood that there was no cure but we had to give our daughter a chance. It took 28 days in NICU (and a surgically inserted stomach tube) before Fiona was "well enough" to go home, with hospice care. Her doctors didn't believe she would live to see her 1st birthday. We spent every day thankful for our little girl, and endless hours with doctor appointments, administering medications, hospice visits, social workers and various types of therapists (art, music, PT, OT and speech) and caring for our two older children, Maggie (then 3 ½) and Karter, (then 5).

Mary, Maggie, John, Fiona & Karter Fitzpatrick

Life was exhausting. We were fortunate to find NKH International Family Network online. This amazing network of families provided so much support, encouragement and advice. Attending the NKH Conference in 2007 gave us the opportunity to meet Dr. Van Hove and so many of the families we'd met online – it gave us hope and inspiration to not give up! We would never stop fighting for our little girl!

Fiona Fitzpatrick

Fiona was a fighter too. She amazed us all and endured so much (seizures, illnesses, multiple hospital stays and way too many doctor visits). She lost her fight just before her 3rd birthday on February 17, 2009. We miss her every day…..and she is our inspiration. We've not lost touch with the many NKH friends and families we've met since Fiona's birth. And our commitment to continue support the fight against NKH is always present.

> "After meeting Joe's parents, Pat and Lynda, a forever bond was born between our families and our fight against NKH was strengthened!"
> *- Mary Fitzpatrick*

I "met" Joe and Michelle Sarb on the NKH Family Network via Facebook, their son, Owen has NKH. One day, Joe posted on FB that there was a very good possibility Notre Dame would be researching NKH. After reaching out to Joe to learn more, I learned we had another shared connection beyond NKH, Notre Dame. My family has a long history and connection with Notre Dame, my Dad ('57) and brother, Sean ('97) are both ND graduates. The Sarb family has a very strong bond with ND as well (that's another story! - see page 6). After meeting Joe's parents, Pat and Lynda, a forever bond was born between our families and our fight against NKH was strengthened!

(see Fiona, continued on page 5)

Fiona

(continued from page 4)

A small yet passionate team led by Dr. Kasturi Haldar was researching NKH at Notre Dame as part of the Center for Rare and Neglected Diseases (CRND) at the university. After meeting the team, it was so encouraging to hear about their research, future plans, and equally fulfilling to see their deep personal commitment .

Our families created the **FIGHTING FOR FIONA & FRIENDS** fund at Notre Dame in memory of our dear, sweet Fiona, to pay it forward to those families who have come after us, whose lives have been dramatically impacted by NKH (as ours was). 100% of all donations go exclusively towards NKH research at Notre Dame's BP-CRND: giving.nd.edu/fionafund

The excitement over the progress made by Dr. Kasturi and her team is so inspiring! With continued efforts and support from donors, progress can continue to help patients with NKH, providing hope and invaluable resources for their families, too.

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.*

Patient Histories and their Importance in Research

By Barb Calhoun, MSN, RN, PNP

Barb Calhoun, MSN, RN, PNP

As the Outreach Coordinator for the Boler-Parseghian Center for Rare and Neglected Diseases at the University of Notre Dame, my overall goal is to support rare disease patients and their families. This is accomplished through a variety of educational, research and community focused programs.

Through courses (BIOS 40450/60565) co-taught by Kasturi Haldar, Ph.D. and myself, students become adept in the study of natural history of rare diseases. Patient families provide medical records that are reviewed for information to better understand the pertinent rare disease symptoms and their progression. In addition, the center provides opportunities for patient/student interactions that enhance learning and provides families a platform to raise awareness about their disease.

The Haldar Lab is currently conducting research on five different rare diseases, one being Non-Ketotic Hyperglycinemia (NKH). In addition to medical records, researchers request skin biopsies and plasma from patients to evaluate the molecular and cellular factors contributing to disease. This data is then used to develop targeted therapies for the disease.

> "The data is then used to develop targeted therapies for the disease."
> *- Barb Calhoun, MSN, RN, PNP*

If you are interested in participating in our NKH studies, please contact the Boler-Parseghian Center for Rare and Neglected Diseases at 574-631-3372 or bcalhoun@nd.edu.

Owen

(continued from page 3)

OWEN'S DAILY SCHEDULE

12:00am	Sodium Benzoate, Lansaprozole, Delsym
4:00am	Sodium Benzoate, Baclofen
6:00am	Delsym, Carnitor, Cyproheptadine
6:30am	Breakfast
7:00am	CBD Oil
8:00am	Sodium Benzoate
8:15am	Bus to School
11:00am	Lunch
12:00pm	Sodium Benzoate, Delsym, Baclofen
3:00pm	Bus home
3:30pm	Snack
4:00pm	Sodium Benzoate
5-5:30pm	Dinner
6:00pm	Delsym, Carnitor
7:00pm	CBD Oil
7:30pm	Bedtime
8:00pm	Sodium Benzoate, Baclofen, Melatonin

Joe, Aubrey, Michelle & Owen Sarb

The Sarb Family: Pat, Joe, Michelle, Dean & Mona Gartello, Karen Hickey, Linda & Owen

Learn more about the Sarb /Notre Dame Connection HERE

NKH Researcher Profiles: Joe Farris & Dr. Suhail Alam

Joe Farris

Graduate Student

Year of Graduation: 2020, Ph.D. in Integrated Biomedical Sciences

Special interest: Metabolism of NKH

My passion to work on NKH: I'm passionate about working on NKH because I believe that there is a scarcity of researchers in the fight against rare diseases. Working with families in the NKH community has inspired me to do what I can to understand the metabolism of NKH in hopes of making the process of developing therapies and treatments more effective and efficient.

Dr. Suhail Alam, Ph.D.

Year of graduation: Ph.D. 2008

Special interest: Investigating molecular basis and developing therapies to treat rare diseases, particularly the ones that occur due to changes in DNA.

My passion to work on NKH: I am passionate to understand how genetic changes in NKH associated genes alter the fundamental property and function of a cell. I hope to utilize these scientific findings to develop strategies for treating NKH and save the lives of many kids. Perseverance of NKH community drives my scientific curiosity.

Accelerating Academic Rare Disease Research & Innovation

Excerpt from article by Ellen Crowe Finan and Deanna Csomo McCool

Medicine and patient care for those who have rare diseases is undergoing a revolution, according to John Crowley, Chairman and Chief Executive Officer of Amicus Therapeutics and founding board member of Global Genes.

And the first question he posed to researchers, drug companies, and patient advocate groups who gathered in a working session at the University of Notre Dame in October was simple: "What role can Notre Dame and universities play in this revolution?"

A rare disease, by National Institutes of Health standards, is one that affects fewer than 200,000 people in the United States at any given time. Such diseases run the gamut from certain cancers to lysosomal storage disorders including Niemann Pick Disease Type C, which took the lives of three grandchildren of the late Notre Dame Football Coach Ara Parseghian. Patients with rare diseases often experience long roads before diagnosis, and are faced with limited therapeutic options.

The collaborative session, "Accelerating Academic Rare Disease Research and Innovation," was sponsored by Amicus Therapeutics and drew stakeholders from across the country who discussed strategies for advancing research, bringing new drugs to market, advocating for patients, and disseminating information about rare diseases, among other topics. It was co-chaired by Crowley and Dr. Marshall Summar, division chief and genetics metabolism director of the Rare Disease Institute at Children's National Health System in Washington D.C., as well as chairman of National Organization for Rare Disorders.

Dr. Kasturi Haldar & John Crowley among the panel

Keynote speaker Dr. James Wilson, director of the Orphan Disease Center and the Gene Therapy Program at the University of Pennsylvania, described how the development of gene therapies disrupted and displaced traditional methods of delivering treatments to patients. "These therapies were hatched and fermented in academic centers outside of traditional business centers," he said.

Instead of treating diseases with drugs or surgery, gene therapy delivers a gene into a cell with the goal of reprogramming it and treating the disease. When academic researchers were able to overcome the challenge of transferring genes to metabolic cells for degenerative neurological diseases around 2001, the gene therapy industry bloomed. "They are 'one and done therapies. No pills are necessary," Wilson explained, adding that gene therapies to treat hemophilia and muscular dystrophy have had some good results.

> "Notre Dame has an opportunity to improve the delivery system and work with the legal systems and the FDA to create more flexible systems for clinical trials and to bring treatments for rare diseases forward."
>
> *- Dr. Kasturi Haldar, Ph.D.*

"The complicated part is disrupting traditional markets and getting it to patients," he said. But this is where he believes Notre Dame can emerge as a leader, helping bring new technologies to patients by leveraging its strong relationships with politicians and legal institutions.

"There is not the same evidence base for rare diseases as there is for cancer or other more widespread diseases," said panelist Diana Wetmore, vice president of therapeutic development for the Harrington Discovery Institute, at University Hospitals Cleveland Medical Center. "More research is needed."

(see Accelerating, continued on page 8)

Accelerating...

(continued from page 7)

A stakeholder panel moderated by Crowley and Summar discussed the challenges of getting treatments for rare diseases approved by the Federal Drug Administration (FDA). Traditional FDA protocols for clinical trials are not practical for rare diseases, and make it hard to get treatments approved. The small number of patients, the progressive nature of the diseases, and the wide variations in disease were reasons noted by the panelists that make it hard to conduct clinical trials for new treatments.

Those on the panel agreed that research universities like Notre Dame can invest in models that support short-term, moderate, and long-term ideas and research, noting there can be more collaboration between researchers and pharmaceutical companies. "Notre Dame has an opportunity to improve the delivery system and work with the legal systems and the FDA to create more flexible systems for clinical trials and to bring treatments for rare diseases forward," said Kasturi Haldar.

READ THE FULL ARTICLE HERE

Other NKH Related Organizations

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

ND NKH

NKH INTERNATIONAL FAMILY NETWORK

NKH HOPE CURE CRUSADERS

DRAKE RAYDEN Foundation

Joseph's Goal

NKH AWARENESS DAY MAY 2 Hope for NKH

NKH AWARENESS DAY MAY 2nd

The Foundation for NONKETOTIC HYPERGLYCINEMIA

Volume 1, Issue 1
November 2018

Fighting For Fiona & Friends
ND-NKH News Today

UNIVERSITY OF NOTRE DAME

BOLER-PARSEGHIAN
Center for Rare & Neglected Diseases

**Alone We Are Rare,
Together We Are Strong!**

Share your story, ask a question, and/or submit ideas for future articles to:

kerry@fourcloversconsulting.com

Publisher: Kerry Molina
Editor: Sean Nohelty

Apply Required Postage Here