The Legacy of Angels
FOUNDATION

2022 ANNUAL REPORT

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FOUNDATION

FROM THE DESK OF THE CO- FOUNDER

Those of you who know me, know that I am not a mushy guy, I say it like it is.
You also know, my faith guides me in everything I do, including my 2022 decision announced at the KTRN meeting that I would be stepping back from my role with the foundation. The time has come for me to enjoy family and friends without the juggle of working, raising a family or running a foundation. Over the course of 2022, we began transitioning staff roles and preparing for me to shift my involvement to an advisory level.The time has come for TLOAF's capable staff to lead the way.

As I reflect back on the last fifteen years, my now late wife, Sue, and I never thought we could make a significant impact on the disease that took our young granddaughter's life. Five years after our grandaughter's death, we won the lottery on the very same date. Given the odds of winning the lottery, we believe God answered our prayers for finding a way to impact the quest for finding treatments and therapies for those affected by Krabbe Disease.

When a disease affects one person, it affects their entire family. When it is a rare genetic disease, that impact is taken to a new level. After learning of our granddaughter's Krabbe disease diagnosis, our entire family was tested. It was then we learned of another rare genetic disease, Cystic Fibrosis, which also runs in our family. Showing us it also needed to be included in our foundation's mission.

While we lost Sue to ovarian and uterine cancer a number of years ago, the foundation and finding a cure for Krabbe disease was her passion and will remain her legacy. She was the ultimate champion and the primary reason the foundation exists. While she is no longer with us, TLOAF remains committed to moving her legacy forward. Sue gets the credit for what we've started, and my role is to ensure her legacy lives on through this foundation's work.

We are now part of a thriving community of researchers, nonprofit organizations, and pharmaceutical companies, all rallying around a newly imagined future for families with a child diagnosed with Krabbe Disease an/or Cystic Fibrosis. We have accomplished much, but we are far from done. As the landscape around us shifts and TLOAF continues to grow, you may notice some changes in the people, approaches, and structure of TLOAF, but our commitment to finding a cure for Krabbe Disease and Cystic Fibrosis remains steadfast.

The foundation is now being run by Executive Director, Dr. Gabriel Cohn, who comes with a strong medical and research background and his ethics are beyond reproach. I have full confidence in his leadership and ability to guide TLOAF into its next stage of growth. My youngest daughter, Heather Techmeier, continues to hold the organization accountable in her role as Director of Finance and as a director on the TLOAF board. My oldest daughter, Stacy Pike Langenfeld, left her role with the foundation this year to serve full time as the executive director of Krabbe Connect, a nonprofit she co-founded to provide family support, disease awareness, and connect families and caregivers to the medical community and clinical trials. TLOAF continues to seek a diversity of professionals to serve on the Scientific Advisory Committee which reviews all grant applications and the Board of Directors who provide financial and strategic guidance of TLOAF into the future.

With the loss of my young grandchild to Krabbe Disease and the loss of my wife to cancer just a few short years later, some might say I have faced many hardships. I don't see it that way. What I see are the blessings bestowed upon me. One of those blessings is the opportunity to love another and share my later years with my new wife, Tammy. God has blessed me with much, and for that I am grateful. I am eternally grateful for being part of this community's effort toward finding treatments and eventually, a cure! God Bless and until next time.

Paul Rosenau

Paul Rosenau
President/Co-Founder

Contact Us

info@tloaf.org
www.tloaf.org

The Legacy of Angels
FOUNDATION

ABOUT TLOAF

Paul and Susan Rosenau established The Legacy of Angels Foundation (TLOAF), a 501 (c)(3), private family foundation, after winning the Powerball on May 4, 2008. The surprising win felt more like a message from God than it did luck. That same date coincided with the death of their two-year old granddaughter, Makayla Lynn Pike, just five years earlier. Makayla lost her battle with Krabbe Disease, a rare-genetic disorder which the family had never heard of until her diagnosis. The Rosenau family had genetic testing after learning of Makayla's genetic disease. Tests revealed another genetic disease, Cystic Fibrosis, also runs in the Rosenau family which is why TLOAF includes both diseases in their mission.

Because newborn screening is critical for the early diagnosis of both diseases, support of newborn screening completes the philanthropic focus of The Legacy of Angels' Foundation. As a private grantmaking organization, with a preference for leveraged strategic funding, TLOAF remains focused on funding innovative approaches to research in the rare disease space. Grant applications are by invitation only.

Learn about our grantmaking process at https://www.tloaf.org/our-grant-program.

Paul and the late Sue Rosenau

VISION

The Legacy of Angels FOUNDATION

Living a life undefined by
Krabbe disease & Cystic Fibrosis.

MISSION

Improving the lives of people impacted by Krabbe disease & Cystic Fibrosis through research funding & disease advocacy.

PRIORITIES

Research Funding

Krabbe disease – a rare, inherited degenerative disorder of the central and peripheral nervous systems. Krabbe disease is one of a group of genetic disorders called leukodystrophies.

Cystic Fibrosis – a genetic disease that causes a thick, sticky mucus to build up in the lungs, digestive tract, and other areas of the body. It is one of the most common chronic lung diseases in children and young adults.

Disease Advocacy

Krabbe Disease

Cystic Fibrosis

Newborn Screening
NS is a vital public health program that's utilized Internationally to identify genetic disorders in infants.

VALUES

Collaboration ● **Ethical Decision-making** ● **Science-Driven**

BOARD OF DIRECTORS

The Legacy of Angels FOUNDATION

Executive Committee

Paul Rosenau
Chair

Chair-Elect
open

Past-Chair
open

Gillian Hauboldt
Treasurer

Mariah Stone
Secretary

Directors

Julie McCarrier
Academia - Health Services

Marci Sontag
CF Bench Science & Grant Writer

Phil Christenson
CEO of CA Medical Evaluators

Karlita Blackwell
Caregiver

Li Ou
Pharma

Heather Techmeier
Rosenau Family Member

Dr. Gabriel Cohn
Ex-officio

Director-open

NEW TO THE BOARD

The Legacy of Angels FOUNDATION

Marci Sontag

Marci Sontag is the Director of the Center for Public Health Innovation at CI International. She has a Ph.D. in Epidemiology and an M.S. in Biometrics from the University of Colorado Health Sciences Center. Dr. Sontag has studied pediatric clinical outcomes and newborn screening systems since 1995, with a special focus in cystic fibrosis newborn screening and more recently in sickle cell disease. Her passion is to help improve the public health field by applying innovative solutions to common problems, partnering with public health stakeholders at the local, regional, and national levels.

Karlita Blackwell

Karlita holds a master's degree in counseling and has spent over nine years working in the social work field. Today, she acts as the Community Engagement Associate for a non-profit that provides support, services and resources for caregivers of children with medically complex, neurological conditions. Karlita and her husband are also parents to a six year old boy with Krabbe Disease, which spurred her passion to become involved in newborn screening and rare disease advocacy over the past five years. In her free time, Karlita enjoys spending time with friends and family, traveling and listening to true crime podcasts.

Gillian Hauboldt

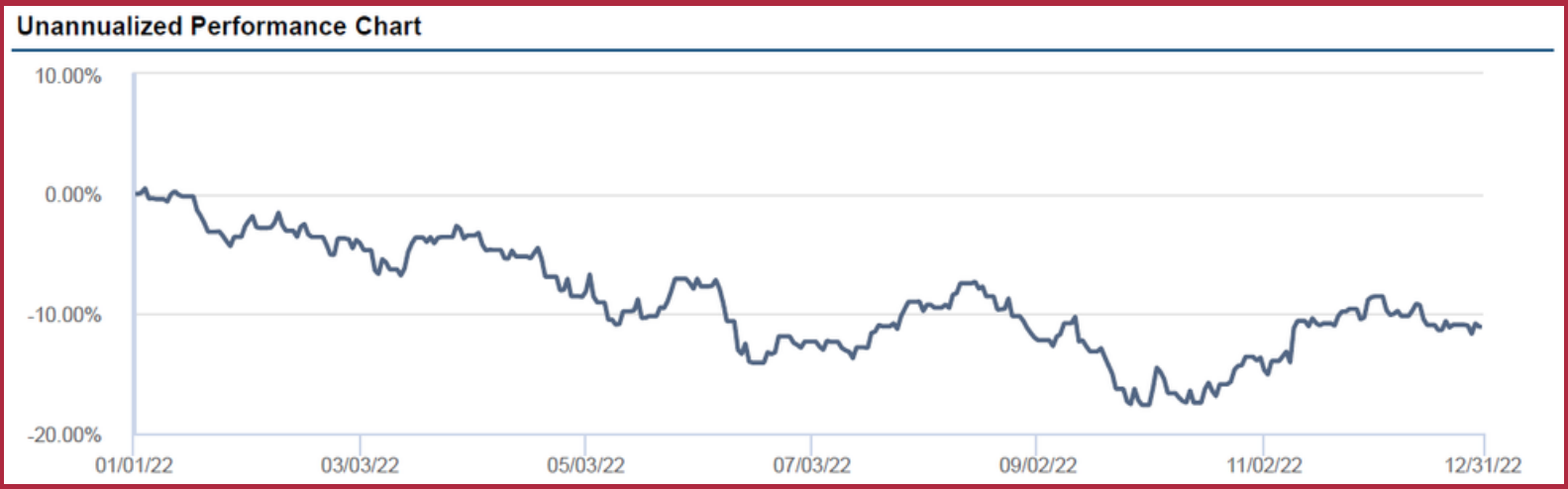
In May 1996, Gillian Hauboldt graduated from UW Milwaukee with a B.S. in Accounting. In the fall of 2019, she passed the Uniform CPA Exam and has been working in public accounting with non-profits for over 25 years. Her specialty is tax and accounting. In working with non-profits, she has also dabbled in grant writing. Gillian sits on several boards of various non-profit organizations and is excited to take on the new role of Board Treasurer for the Legacy of Angels Foundation. When she is not working, she enjoys spending time with her six children ranging from ages 8-20.

FINANCIAL REPORT

Sticking To The Plan

It's important to find an investment company who puts your need first. However, not all investment companies are held to the same standards. As a fiduciary, Foster Group holds themselves to the highest of standards of conduct and trust. They have a fee only pricing structure, which enables them to focus on the Foundation's best interests.

By aligning our Foundation with the Foster Group, we can feel confident and assured of the impact our grants are making for patients. Knowing Foster Group is committed to managing our investments, allows the Foundation to extend its investments long into the future so, we can achieve our vision of living a life undefined by Krabbe disease and Cystic Fibrosis.



As a result of the market performance in 2022, The Legacy of Angels Foundation's investment portfolio was down 11.7 % as of December 31, 2022.

2022 GRANTS

The Legacy of Angels FOUNDATION

The Legacy of Angels Foundation's grant program is vital to the foundation's mission of finding better treatments and a cure for Krabbe disease and Cystic Fibrosis.

$29,506	Improving the Family Experience Through Communication and Promoting Resilience; A Pilot Project. -Adang, Laura
$128,030	Evaluation of Immunomodulatory Therapy for the Treatment of Krabbe disease in a Mouse Model. -Crocker, Stephen
$124,756	Psychosine Profiling and Evaluation of 1-Deoxgalactonojirimycin as a Therapeutic for Krabbe disease. -Lee, Chris
$200,000	Caregiver and Clinician AwaREness for Early Cystic Fibrosis Awareness (CARE-CF) -McColley, Suzanna
$142,423	Vesicular Delivery of GALC for ERT of Krabbe's disease -Givogri, Maria I.
$75,000	Generation of a Krabbe Mouse Model to Enable Regulated Expression of Therapeutic GALC Enzyme -Bongarzone, Ernesto
$183,012	Support for the Infrastructure of Krabbe disease and Myelin Research at the University at Buffalo -Feltri, Laura M.
$199,974	Innovative Model Systems to Study and Boost Innate Immunity in Krabbe disease -Feltri, Laura M.

Grant Total for 2022: $ 1,082,701

Grant Funding Total since inception: $20,801,545

FOCUS AREA: Krabbe Disease

Krabbe disease and Stem Cell Transplantation

Dr. Anthony Steyermark

Krabbe disease (KD) is a fatal, inherited lysosomal storage disorder caused by deficiency of β-galactocerebrosidase (GALC) that leads to the buildup of psychosine in the brain and peripheral nervous system. The high levels of psychosine result in the destruction of neuronal myelinin in the brain and throughout the nervous system. KD affects about 1 in 100,000 people in the United States.The disease is most severe in the infantile form, IKD (Infantile Krabbe Disease). In patients with IKD, the disease usually results in death by age two. Low GALC activity combined with a high psychosine level supports a neonatal diagnosis of IKD.

Hematopoietic stem cell transplantation (HSCT) performed, ideally before 30 days of age, has been shown to improve survival and neural function in pre-symptomatic infants with EIKD (Early Infantile Krabbe Disease). In short, HSCT introduces cells from a donor individual that can produce the functional GALC enzyme. The GALC enzyme then acts to reduce the levels of psychosine, decreasing the amount of demyelination.

HSCT has the best outcomes in pre-symptomatic neonates; thus, it is imperative that infants are identified early through newborn screening (NBS).

New York State began NBS for Krabbe disease in 2006. Since then, an additional eight states have added Krabbe disease to their NBS programs, and an additional state is piloting KD NBS.

Page et al (2022) reported the treatment outcomes of six infants with EIKD detected by NBS and referred for HSCT. All infants underwent HSCT between 24-40 days of age, successfully engrafted, and were alive 30-58 months later. All were gaining developmental milestones, though at a slower rate than unaffected age-matched peers. The survival and developmental outcomes were all improved over affected peers who did not undergo HSCT. Thus, while HSCT is not a cure, advances in the procedure are resulting in survival and developmental improvements in infants with EIKD detected via NBS.

Yoon et al (2021) evaluated the efficacy of HSCT for late-infantile KD patients. Nineteen late-infantile patients underwent HSCT between 1997 and 2020. Compared with untreated patients, transplanted infants had a longer survival probability and improved developmental outcomes. Asymptomatic patients benefitted the most from transplantation, with normal to near-normal development and some gross motor delays. Among symptomatic patients, those with disease onset at >12 months of age had better cognitive outcomes than untreated patients.

The Future is Bright

In addition to advances in Hematopoietic cell transplantation procedures and two exciting gene therapy clinical trials, significant advances have been made in better understanding the natural history of Krabbe disease. Spurring research into enzyme replacement therapy and substrate reduction therapy. New hope for infants, juveniles, and adults with Krabbe disease is truly around the corner.

FOCUS AREA: CYSTIC FIBROSIS

The Legacy of Angels FOUNDATION

MARCI SONTAG

Newborn screening (NBS) is universally offered in the United States, making it one of the most equitable public health services. While almost every newborn in the country receives testing for a panel of disorders that requires early diagnosis and treatment, there are some potential inequities within the system. For example, cystic fibrosis (CF) is one of the disorders tested in every state, and yet there are disparities in health outcomes among different racial and ethnic groups. While most individuals diagnosed with CF are non-Hispanic White, there is a growing proportion of diagnoses among minority groups, including Black and Hispanic populations.

One key metric for the success of NBS programs is timeliness. Two indicators of timeliness are the number of days elapsed from birth to diagnosis and birth to treatment. Aggregate data from infants with CF reported to the Association of Public Health Laboratories NewSTEPs program demonstrate that White infants have a shorter period to diagnosis (29 days) and intervention (18 days) compared to Black infants (diagnosis: 50 days and intervention: 29 days, $p<0.05$). (Singh ACHDNC Meeting). Further, differences in clinical outcomes have been described, with almost twice as many minority infants presenting with respiratory symptoms compared to non-Hispanic White infants (4.6% vs. 2.5%). Minority infants with CF are also more likely to experience failure to thrive or malnutrition in infancy (8.8% minority, 4.7% non-Hispanic White). (McColley poster)

The source of the inequities may stem from a couple of areas. First, the CF newborn screening algorithm includes a DNA test. Each infant's sample is tested to determine if the baby has one or two copies of a variant in the gene responsible for CF, compared to a standard panel of variants. If two variants are present, the baby is likely to have CF and is referred for diagnostic testing. If one variant is present, there is a risk for the infant to have CF, but the likelihood is much lower. Regardless, the infant should be referred for follow-up testing. CF variant panels are typically developed with variants that have been seen in the White population, as those variants are more common, and more research has been done in that population. Infants with CF from minority populations may have variants that are not on the state panel and therefore may not be referred for diagnostic testing.

The second source of inequities in timely diagnosis is the misconception among the broader community that CF only occurs in White populations. Clinical care providers and families may not recognize the importance of timely follow-up, believing that a Black or Hispanic child will not have CF (Sontag, NACFC abstract). Infants from minority groups, who have only one identified variant from the NBS panel may experience delayed diagnostic testing. Thus increasing the elapsed time to intervention, resulting in poor growth and pulmonary infections among minority patients.

Tackling health inequities is never simple, yet concrete steps are underway to change the CF NBS field. For example, many state NBS programs are expanding their CF variant panels to include variants typically seen in minority populations. Further, educational initiatives are being developed to help care providers and families understand the risks of CF in minority populations. These approaches can help reduce the inequities seen in CF diagnosis and treatment, allowing all children the same opportunities for healthy outcomes.

References:

Singh 02/2022 ACHDNC meeting

BLACK RACE IS ASSOCIATED WITH LATER AGE AT INITIAL CF CENTER EVALUATION ANDDECREASED 1-YEAR WEIGHT FOR AGE Z-SCORE. N Fisher; L Balmert; A Elbert ; PM Farrell ; SL Martiniano; CL Ren, MD, ; K Rychlik, MS,; M Sontag, PhD,;; R Wu, MS; SA McColley. Poster Presented at the North American Cystic Fibrosis Conference.

Cystic fibrosis newborn screening: barriers and facilitators identified from 10 years of universal screening in the U.S. Marci K. Sontag, PhD, Sarah McKasson, MPH, Stacey L. Martiniano, M.D.,, Joshua I. Miller, MPH ., Rhonda West, , Clement Ren, MD, MBA, ,, Phillip Farrell, MD. PhD, Susanna A. McColley, MD,, Yvonne Kellar-Guenther. Poster Presented at the North American Cystic Fibrosis Conference, November 2021

The Legacy of Angels FOUNDATION

The Evolution and Crossroads

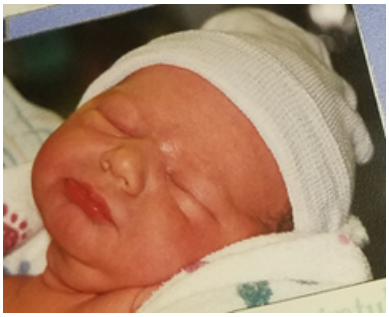
Amy Gaviglio, MS, CGC

It has been nearly 60-years since the first newborn screening test for phenylketonuria was implemented in the United States. Not surprisingly, since that time, newborn screening programs have seen significant growth – not only in the number of diseases now being screened for, but also in the complexity of the technologies being employed by screening programs. And while the evolution of this public health program over six decades is certainly expected; today, newborn screening programs are finding themselves at more of a crossroads than ever before.

The addition of diseases to newborn screening panels still relies heavily on criteria originally outlined in a World Health Organization report on the principles of preventative screening programs. These measures, known as the Wilson and Jungner criteria, include ten key tenants of a disease that makes it suitable for population screening. Briefly, these criteria include: the condition should be an important health problem, there should be some understanding of the natural history of the disease, a suitable test, an agreed upon policy on whom to treat, and there should be an accepted and effective treatment. Though these criteria were developed in 1968, they very much remain the basis for the addition of diseases to the Federal Recommended Uniform Screening Panel (RUSP) today.

While, historically, the availability of a suitable test in the newborn period was the limiting factor for the addition of diseases to newborn screening panels, more recently, owing to the availability of technologies like tandem mass spectrometry and genetic sequencing, the limiting factor is the availability of effective therapeutic intervention. However, this, too, is changing. Today, the FDA receives more than 200 investigational new drug applications each year for cell and gene therapies and has stated it expects to approve at least 10-20 new cell and gene therapies each year.

And here is where newborn screening programs are finding themselves at a critical inflection point. As explained above, the demand for disease addition to newborn screening is likely to only increase, at an exponential rate, but the resources to accomplish this screening and the health system infrastructure to diagnose, treat, and care for these patients are not keeping pace. What does this mean for newborn screening as we know it? How must this system evolve and what is the best path forward?



Acknowledging this dilemma calls for modernization of the newborn screening system, highlighted in recent publications by Don Bailey, et al and Andrews, et al. These papers discuss five domains needed for modernization of the system and call for innovative solutions to meeting the anticipated needs of the array of stakeholders involved in the screening system.

In summary, these five domains include:

· Domain 1: Revise and improve timeliness of the RUSP review process
· Domain 2: Create mechanisms to offer screening for diseases in addition to those on the RUSP
· Domain 3: Accelerate and expand data collection to inform policy decisions and implementation
· Domain 4: Help states expedite comprehensive implementation of NBS for new diseases
· Doman 5: Evaluate emerging methods of screening and their consequences

These five domains represent a call to action for newborn screening. Just as it has over the past 60 years, the newborn screening system will need to evolve in novel and disruptive ways as it continues its efforts in providing life-changing early diagnosis and treatment to newborns with rare diseases.

MEET THE TEAM

The Legacy of Angels FOUNDATION

Paul Rosenau
President & Co-founder

Dr. Gabriel Cohn
Executive Director

Heather Techmeier
Finance Director

Mariah Stone
Administrative Assistant

Mary Kay Delvo
Strategy, Talent & Board Development

COMINGS & GOINGS AT TLOAF...

The Legacy of Angels FOUNDATION

2022 was a year of good byes and hellos. While change and transitions are hard and disruptive, they also make room for new ideas to emerge.

In late 2021, TLOAF brought on its first medical director, Dr. Anthony Steyermark. In just a short-time, Tony helped find and develop a grants management platform. Something we know our grantees are looking forward to using to make the work of reporting less time-consuming. Tony left us in September and we wish him all the best in his next endeavor.

Stacy Pike Langenfeld, had been with TLOAF since 2016 as a program director and then executive director. Stacy also co-founded KrabbeConnect, a nonprofit working to help families navigate medical services, support, and connect them to clinical trials when their child is diagnosed with Krabbe disease. Stacy made the difficult decision to resign from TLOAF in October, so she could spend more time with her children and family. Ultimately allowing for more focus where she serves as President of KrabbeConnect.

Heather and Paul had their work cut out for them with both executive and medical director positions open in October. Paul had his faith with him at the helm, so it is no surprise that Dr. Gabriel Cohn found his way to TLOAF's door step with interest in the medical director position. TLOAF's hiring team was so impressed with Dr. Cohn that they offered to combine the medical director and executive director positions so they could hire him as the new Executive Director of the organization.

Welcoming Dr. Gabriel Cohn

With more than 30-years of combined medical leadership and research experience in academic medicine, and in the bio-tech industry, Dr. Cohn has the combined skills and experience to serve the foundation's medical and executive director needs.

Dr. Cohn's industry experience has spanned rare and genetic disorders, as well as investigational biologics, including cellular and gene therapy and enzyme replacement therapy. He has led clinical teams in the IND clearance and the initiation of several first-in-human gene therapy and infertility clinical trials. Dr. Cohn's medical and research experience, along with navigation of multi-plex, systems, will be valuable for taking TLOAF's mission to the next level.

As the Executive Director, Dr. Cohn will be the public voice and face of the foundation. He will serve as a liaison between researchers, partner agencies, TLOAF staff, and the TLOAF Board of Directors. His background allows him to put a scientific and patient-centered lens around the science of new and existing developments in the areas of Krabbe disease, Cystic Fibrosis, and Newborn Screening. TLOAF is looking to Dr. Cohn to cultivate a collaborative organizational culture with staff, board, and stakeholders and to provide a medical perspective in layperson's terms so TLOAF staff and Board of Directors are able to make decisions in alignment with the foundation's mission.

Core components of his role include leading, managing, and recruiting for a robust and active scientific advisory committee. Additionally, working to improve the foundation's grant program, and by acting as a liaison between researchers, staff, and the board. As a liaison, Dr. Cohn will facilitate connections and conversations around the science of new and existing developments in the areas of Krabbe disease, Cystic Fibrosis, and Newborn Screening.

"Together, we can move mountains and conquer any challenge that comes our way."

Dietric Matern,MD,PhD.

Clinical Biochemical Geneticist & Co-Director
Biochemical Gåenetics & Genomics Laboratory
Mayo Clinic, Rochester, Minnesota

The Legacy of Angels FOUNDATION

The Sue Rosenau Legacy Award was created in honor of The Legacy of Angel's Foundation's co-founder, and rare disease advocate, Sue Rosenau. This award has been given in her memory since 2019 to keep her legacy alive within the foundation and community at large after losing her three-year battle with ovarian and serous endometrial cancer in July of 2018. The award recognizes individuals whose work in the areas of Krabbe disease or Cystic Fibrosis creates memorable and lasting change. The 2022 award was presented to Dietrich Matern, MD, PhD., of the Mayo Clinic.

Dr. Matern is a recognized leader in the development and improvement of laboratory assays for the biochemical diagnosis and follow-up of patients with inborn errors of metabolism. Dr. Matern's research has been funded by the NICHD, ACMG's Newborn Screening Translational Research Network (NBSTRN), industry, and The Legacy of Angels Foundation (TLOAF). His focus, in recent years, has been on newborn screening for lysosomal disorders, including Krabbe disease.

The work of Dr. Matern and his colleagues in the Biochemical Genetics Laboratory has also significantly reduced the number of families that have to go through unnecessary worries and tests because the result of their baby's screening test was a false positive.

To determine the best and most effective approach to screen for more than a dozen disorders, including Krabbe disease, Dr. Matern and his lab had received funding from the NICHD. This funding was a time-limited contract and due to unforeseen barriers, causing delays in the project, they were unable to complete the study before the contract expired. The team planned to do molecular testing at the end, as a confirmatory test of screen positive samples from de-identified newborn screening blood spots. To fill the gaps caused by the time limited funding to finish the study, The Legacy of Angels Foundation was able to provide grant funding to successfully complete the study. Dr. Matern's team had a paper, about the study, published after Sue Rosenau had passed and the publisher allowed them to dedicate it to her name.

"Sue received a good amount of care at Mayo Clinic in Rochester," said Dr. Matern. "Therefore, I had the opportunity to see her during some of her stays and get to know her a little better. I was always impressed by her selflessness, concern for others, and her ability to look beyond her own interests, which makes this award even more special. For example, while she was clearly eager to see newborn screening for Krabbe disease become universal, she appreciated that the initial screening tests created too much anxiety for families not affected by the disease, and therefore was willing to wait for improved screening procedures."

"This award means a lot to me and is particularly dear to my heart because it bears Sue's name."

Dr. Matern

2022 KTRN MEETING

The Legacy of Angels FOUNDATION

The Krabbe Translational Research Network (KTRN) focuses on specific aspects of research and topics integral to improving the lives of those impacted by Krabbe disease. 2022 marks the 10th collaborative gathering of this network. With each new meeting, the level of discussion and information shared becomes more complex, detailed and informative.

The KTRN meeting agenda is driven by a steering committee with expertise in biology, chemistry, gene therapy, newborn screening, and related technologies. The committee worked diligently to ensure the agenda allowed for a robust exchange of ideas, supports the examination of important research, and presents partnership opportunities. We appreciate the staff, supporters and participants combined that helped make this event a success. We are already looking forward to next year's meeting.

The following page outlines some of the key takeaways from the 2022 gathering. We hope you enjoy this brief summary.

The goal of this disease-specific meeting is to collectively bring together Krabbe disease researchers, clinicians, pharmaceutical companies, and the families impacted by Krabbe disease who live the reality of it every day.

Key Take Aways:

Basic Science Research in Krabbe disease

There is emerging evidence, in Krabbe disease and related disorders, of the pivotal role of inflammation in the damage of the sheath (myelin) that protects nerves. Such damage causes nerve cell dysfunction and ultimately results in the loss of nerve cells. A reduction in such inflammation through various interventions was shown to improve outcomes in animal models of Krabbe disease. Furthermore, the replacement of older supporting cells (oligodendrocytes) which produce the myelin sheath, with newer oligodendrocytes, was shown to replace the damaged myelin sheaths more effectively.

Advances in Newborn Screening (NBS) for Krabbe disease.

Representatives from several state Newborn Screening (NBS) labs spoke of their approach to NBS for Krabbe disease. At the time of the meeting, a total of ten states were performing NBS for Krabbe. Each state has learned a great deal from the initial state of NY NBS experience, though approaches between states varied. Based on the discussion, there is a need for greater uniformity between states in how Krabbe disease is being screened.

A parent panel on NBS discussed their NBS experience, which highlighted the challenges they experienced around receiving and finding accurate information about NBS and Krabbe disease. They also expressed concerns related to timely referral to a center with appropriate expertise in this area.

Through the review of a single center's experience of NBS for Krabbe disease, we learned that many families were unaware that NBS was performed on their infant until they received a call about an abnormal result a week after the baby was discharged. This news was jarring.

The takeaway was the need for healthcare delivery systems to do a better job communicating with families and training physicians on how to discuss such results. Also discussed was the implementation of psychosine testing as a second-tier test to better identify infantile onset Krabbe disease.

Newborn Screening Produces Results

Dr. Joanne Kurtzberg presented the results from a multi-center observational study on the role of NBS and hematopoietic stem cell transplant (HSCT). Over the course of five years and across four states (IL, KT, OH, TN), six infants were identified with early infantile onset Krabbe disease (EIKD) through the state NBS programs. These infants had low GALC enzyme activity and elevated psychosine levels. Families were first contacted 7-14 days after birth and those infants underwent HSCT, after undergoing chemotherapy, in advance of stem cell treatment 14-28 days after birth. At the time of the KTRN meeting, all infants were alive (median age of 42 months (range of 28-64 months). Four of the six infants experienced transplant-related complications of some form which varied in severity. In general, neurodevelopment outcomes were improved compared to what is known of untreated children with EIKD but still slower than unaffected children. It was suggested that accelerating the time from initial diagnosis to transplant, such that HSCT is performed within 30 days of birth, might help further improve outcomes.

Additional presentations highlighted efforts to better understand the Krabbe disease experience and challenges (krabbeCURES research conducted by KrabbeConnect), as well as efforts to bring forth Krabbe disease NBS to all states (Hunter's Hope Foundation Update on Krabbe Disease RUSP Nomination).

Emerging and Ongoing Gene Therapy Trials

Other presentations focused on the preclinical advances in various Krabbe disease therapeutic modalities, emerging and ongoing gene therapy trials, study design, and eligibility criteria, and challenges in Spinal Muscular Atrophy gene therapy.

The meeting concluded with presentations from various nonprofit organizations. Kenneth Hobby, of CureSMA, spoke of their organization's challenges and efforts in bringing forth a gene therapy for the treatment of Spinal Muscular Atrophy.

LOOKING AHEAD

From the desk of the executive director

In my short time with TLOAF, I have come to learn two things: change is constant and opportunities are endless. This small but mighty organization is like the little engine that could. They keep chugging along regardless of things that could get in their way.

In 2021, the board created the foundation's first strategic plan. The process included space for imagining what could be possible and resulted in a focused vision for guiding the foundation's work moving forward. The board's intentionality and focus allowed me to step into my role as executive director the following year and focus on the future with some clarity. I have witnessed on a daily basis how the TLOAF team and board are keeping the vision and focus alive.

If you had regular interaction with TLOAF during 2022 you'll not be surprised to hear that it was a year filled with change and transitions. I have been impressed with the way the team and board have embraced this time, and latched onto the opportunity to dream, assess, reframe, and reflect.

As a stakeholder and partner in this work, thank you for hanging in there with us during these transitions and stay tuned for a big 2023.

Dr. Gabriel Cohn

THANK YOU

The Legacy of Angels FOUNDATION

Please visit our website for updates on our work throughout the year: tloaf.org

CONTACT US

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