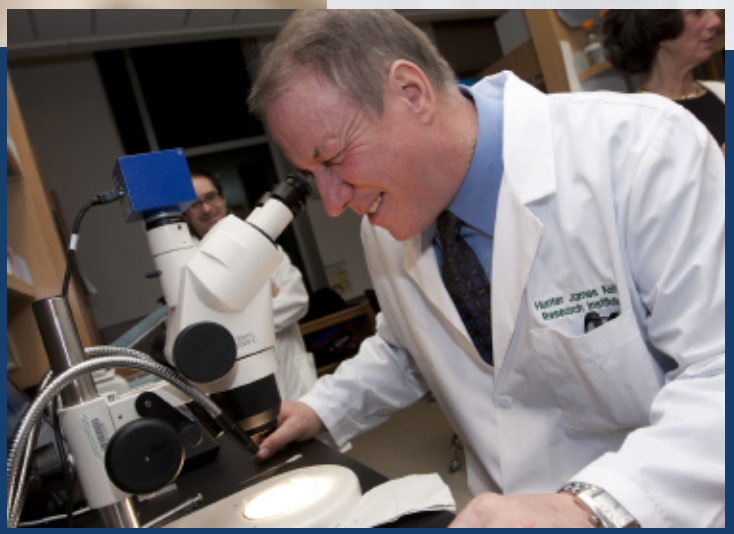


The HopeSpot ...get connected

Hunter James Kelly Research Institute

When Co-Founders Jim and Jill Kelly created Hunter's Hope in 1997, one of their primary goals was funding research to find treatments and ultimately a cure for Krabbe and other Leukodystrophies. As time progressed it became clear that a central location exclusively devoted to Krabbe and similar diseases was the best way to advance research.

Accordingly, in 2008, Hunter's Hope joined the University at Buffalo to create the Hunter James Kelly Research Institute (HJKRI). To maximize its effectiveness, the HJKRI, led by Lawrence Wrabetz, MD, approaches research from two primary perspectives — Basic Science, which involves laboratory based research exploring the animal and cellular models of the disease, and Clinical Research, which studies the disease in affected patients. This comprehensive and translational method facilitates new insight into Krabbe and other Leukodystrophies, paving the way to new treatments and a cure in the most efficient manner possible.

Welcome to The HopeSpot ...get connected

Hunter's Hope will be sending periodic updates about the exciting work being accomplished through the Foundation. Each HopeSpot will highlight a different program: Research, Family Support, and Education & Awareness, giving you the inside scoop on what we've been working on and how you can become more involved.

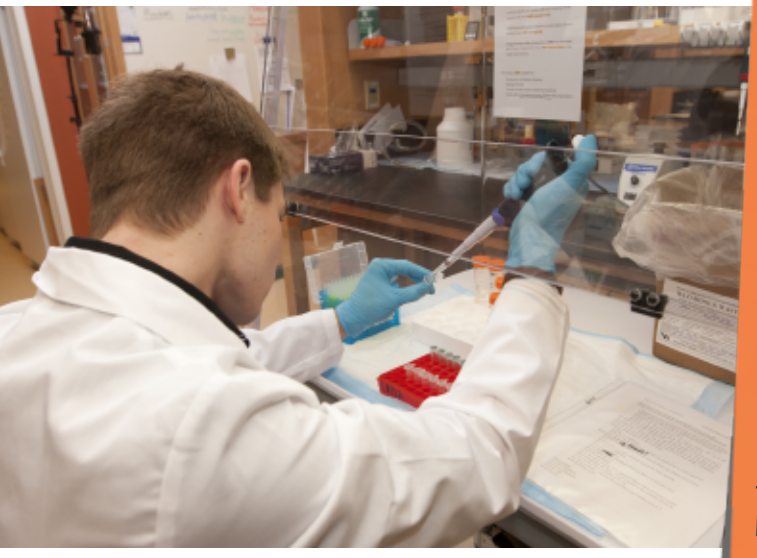
Hunter James Kelly Research Institute

Basic Science

The Basic Science Research at the HJKRI is comprised of six state-of-the-art laboratories devoted to studying the cause, effects, and potential therapies of Krabbe disease and other myelin disorders. The researchers at the HJKRI create cellular and animal models to analyze the complex details of the disease, to progress research from the animal model, to clinical trials, and ultimately better treatments and a cure.

Clinical Research

The Clinical Research Center, led by Thomas J. Langan, MD, works to improve understanding of the natural history of Krabbe disease, what factors and tests best predict its onset and severity, and which treatment options are most effective. At the center of this research is the World Wide Registry for Krabbe disease (WWR). See below for more information on the WWR.



Krabbe World Wide Registry (WWR)

Shortly after Hunter's Hope was founded in 1997, the Foundation began gathering medical information from affected families. In 2008, this registry officially became the Krabbe World Wide Registry and is now the center of all clinical research at the HJKRI.

The information catalogued in the WWR provides vital insight into diagnosis, outcomes, symptom management, and treatment. The WWR and its research are completely dependent upon family participation. If you are an affected family and are not yet participating in the WWR, we urge you to contact Kathleen Scott at kathleen@huntershope.org and enroll your family.

In 2014, Hunter's Hope and the HJKRI partnered with the Newborn Screening Translational Research Network, which is funded by the National Institutes of Health, to begin utilizing their Longitudinal Pediatric Data Resource. This database provides a secure and protected infrastructure for data collection, analysis, and sharing with other researchers, and is the optimal platform for storing data gathered through the WWR. We are excited to utilize this resource to further advance Krabbe and Leukodystrophy research.

Understanding Krabbe Disease

Pathology of Krabbe Disease

The team at the HJKRI is working tirelessly to determine how Krabbe disease is caused and its specific effect on the brain, peripheral nerves, and the body as a whole. They are using cellular and animal models to understand the effect of low GALC in each of the different cell types. Additionally, they are studying the effect of low GALC on myelin and the overall degeneration of the nervous system, and identifying other toxic substances (including the known toxin, psychosine) that contribute to the damaging effects of the disease.

Whole Genome Sequencing in Krabbe Disease

HJKRI researchers in collaboration with James Lupski, MD, PhD, from Baylor College of Medicine, plan to use whole genome sequencing to study the entire genetic code of Krabbe affected patients. They are hoping to determine whether there is additional genetic information that can help predict disease outcome alongside GALC levels.

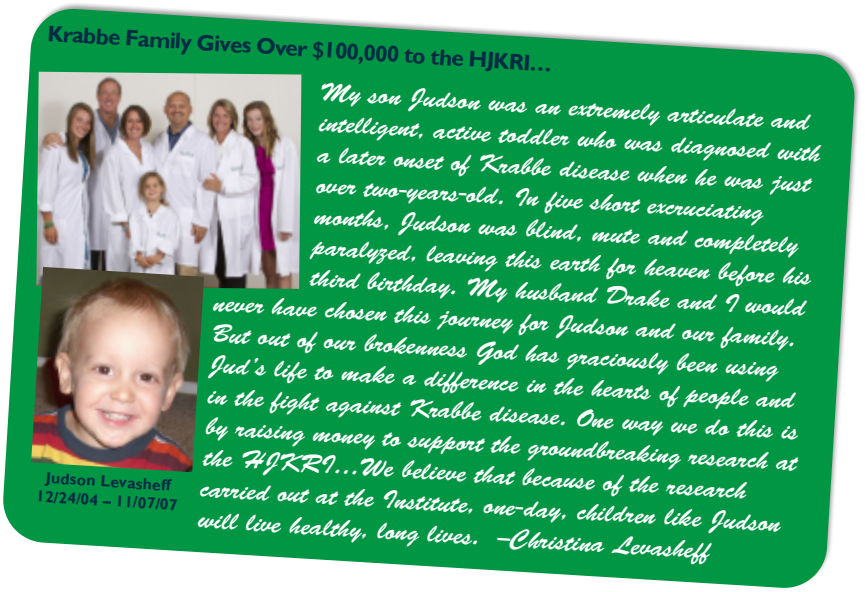
Predicting Onset

Predicting disease onset, or when symptoms will occur, is crucial to ensuring all Krabbe patients receive treatment at the optimal time. This is especially important for children identified through newborn screening. The HJKRI researchers are exploring how different mutations of the GALC gene cause more benign or more severe variations of Krabbe, and how the most common GALC mutation, the 30-kb deletion, causes a different pathology than other mutations of Krabbe.

This exciting area of research holds tremendous promise, as HJKRI scientists Daesung Shin, PhD, and Laura Feltri, MD, have found that some mutant GALC proteins never arrive to the right part of the cell. Dr. Shin is now exploring whether GALC activity is more important in specific parts of the cell. This line of research could improve the reliability of predicting the onset of disease and if a mutation will actually cause disease.

Role of Psychosine in Krabbe Disease

Through a collaborative effort with Dr. Langan at the HJKRI, Joseph Orsini, PhD, from New York State's Newborn Screening Wadsworth Laboratory, and Dieter Matern, MD, PhD, from the Mayo Clinic, are investigating the role of psychosine in Krabbe disease to determine if increased levels are associated with the onset of disease in patients identified through newborn screening (NBS). Preliminary results suggest that measuring psychosine in newborn dried blood spots could serve as a second tier test in NBS for early infantile Krabbe disease. Future studies will determine whether psychosine levels in the blood predict disease progression or response to treatment following transplant.



What is Krabbe Leukodystrophy?

Krabbe disease is a fatal hereditary disorder affecting the central and peripheral nervous systems. Those who inherit the illness cannot produce an important enzyme called *GALC*, which is needed to make myelin in the nervous system. Myelin is the fatty material that creates a protective layer around nerves and acts like insulation surrounding an electric wire. When too little GALC enzyme is produced, it causes toxicity in the brain leading to myelin loss, changing brain cells, and irreversible neurological damage. Children with the early onset form of Krabbe disease rapidly lose all voluntary movement including the ability to smile, speak, walk, and swallow. If not promptly treated, these babies have an average life expectancy of just 14 months. Later onset forms of the disease result in similar medical outcomes, although they present later in life, at any age, and symptoms usually progress more slowly.

Using MRIs to Help Diagnose Different forms of Krabbe Disease

A recent study conducted through the HJKRI shows promise for improving the prediction of symptom onset in Krabbe disease. By looking at 64 MRI results from the Hunter's Hope Krabbe World Wide Registry, research indicates that distinct differences appear on MRI scans among different types of Krabbe — early infantile, later onset, and adolescent/adult. Currently, New York State Consortium members and researchers at the HJKRI are sending MRI discs from Krabbe patients for review by Mount Sinai School of Medicine's Thomas Naidich, MD, in an effort to correlate neuroradiological findings with onset, severity, and disease course.

Long-Term Follow Up for Krabbe

Hunter's Hope and the HJKRI joined forces with Chet Whitley, MD, and the Lysosomal Disease Network. Through a collaborative application to the Rare Disease Clinical Research Network (NIH Funded), the HJKRI proposes to follow the developmental and functional outcomes of children identified through Krabbe newborn screening.

Mutation Analysis for Individuals with Positive Screens for Krabbe

The team of researchers at New York State's Newborn Screening Wadsworth Laboratory is working with the HJKRI to analyze genotypes of known Krabbe patients. Through newborn screening and the expansion of the Krabbe WWR, many more patient genotype/phenotype correlations are helping physicians more accurately predict the onset and severity of a patient's specific form of Krabbe. After conducting mutation analysis on saliva and newborn blood spots, results are compared with the clinical course of the disease to provide genotype/phenotype correlations. In this phase of research, Dr. Langan of the HJKRI, collaborates with Drs. Denise Kay, Carlos Saavedra and Michele Caggana of the Wadsworth Laboratory.

Screening for Krabbe and Similiar Disorders in Multiple Sclerosis Patients

Hunter's Hope is supporting the research of James Weisfeld-Adams, MD, and his colleagues at the University of Colorado School of Medicine and Icahn School of Medicine at Mount Sinai. Their research hypothesizes that some patients diagnosed with the Primary Progressive form of Multiple Sclerosis (PPMS) are suffering from later onset forms of Krabbe or similar disorders. Although less studied than PPMS, later onset of Krabbe disease may have similar MRIs to PPMS. The investigators hope this study will enhance understanding of how individual rare disease genes are related to progressive MS, assist neurologists in differentiating between MS and rarer neurologic diseases, and shed light on the spectrum of disease severity in Krabbe disease and other Leukodystrophies.

Multistate Krabbe Newborn Screening Consortium

The Krabbe Consortium was established in 2006 when New York became the first state to screen for Krabbe disease. The purpose of the Consortium is to ensure that children identified through newborn screening receive the best possible immediate and long-term follow-up and clinical care. Clinicians and doctors from the state meet regularly to discuss new insights gained from their patients and to continuously improve and carry out a superior standard of care. As additional states begin screening for Krabbe, their physicians are also included in the Consortium meetings. This timely and all-inclusive collaboration is essential to ensure all children, in every state, are followed with professionalism, excellence, and the highest possible standard of care.

Improving Cord Blood Transplant & Discovering Additional Therapies

Better Treatments and a Cure for Krabbe and other Leukodystrophies

Currently, the only successful treatment proven to halt the progression of Krabbe disease is cord blood transplant. Unfortunately, it is available only to those diagnosed before the onset of symptoms, emphasizing how critical it is for each state to add Krabbe to its newborn screening panel. Through their efforts to find better ways to diagnose in time for effective treatment, researchers now believe combining treatments may offer more promise.

Through the use of cellular and animal models, the HJKRI researchers are investigating how to compensate for the known limitations of cord blood transplants and gene therapy by improving these methods and unearthing alternative treatments. They are also exploring the reason psychosine levels are elevated in Krabbe disease and determining if inhibition of psychosine decreases the severity of disease in the animal model. The HJKRI is working together with other researchers to find new combinations of treatments for Krabbe disease that will work faster and better than they do alone.

A Mother Visits HJKRI for the First Time…

My first opportunity to tour the HJKRI was an overwhelmingly emotional and bittersweet experience. Simultaneously, I was filled with HOPE at the promise for new treatments and ultimately a cure for the horrible disease that afflicted my beautiful Jacque throughout her life and at the same time, I felt great sorrow my daughter wasn't here to benefit from these advancements…I'm so grateful for the work of the HJKRI and what it means for future children affected by these truly devastating diseases. –Kathleen Scott

Jacquelyn Scott
07/10/02 – 02/10/07

Gene Therapy

Steven Gray, PhD, at the University of North Carolina's Gene Therapy Center, is another researcher whose work is supported by Hunter's Hope. Dr. Gray is investigating the means to globally deliver a gene to the nervous system, bridging the gap between earlier encouraging laboratory studies in animal models and a possible human treatment. This approach uses a modified virus called AAV, which has been designed to carry a therapeutic gene, essentially serving as a molecular delivery truck or "vector" that is injected into the spinal fluid. This is a routine outpatient procedure with minimal risk.

Hunter's Hope Annual Family & Medical Symposium

Since 1998, Hunter's Hope has hosted an annual Family and Medical Symposium. More than sixty of the world's leading researchers and disease experts gather for a two-day round table discussion. Together, these individuals share the outcomes of the past year's research efforts and gain insight from their contemporaries as to the best options available to move their research forward. Topics discussed at the Symposium include Basic Science and Clinical Research for Krabbe and other Leukodystrophies, as well as Newborn Screening. The Symposium continues to offer researchers and clinicians the opportunity to collaborate and build momentum in the advancement of research and medical innovation for Krabbe and other Leukodystrophy patients.

Enzyme Replacement Therapy for Krabbe Disease

Hunter's Hope supports the research of Steven LeVine, PhD, from the University of Kansas Medical Center. Dr. LeVine is examining the potential of enzyme replacement therapy (ERT) as treatment for Krabbe disease. His innovative approach delivers the therapeutic enzyme (GALC) to the central nervous system through a non-invasive procedure. This work in the mouse model may lay the foundation for clinical trials and pave the way for new treatments for Krabbe and similar diseases.

Pharmacological Strategies for Preventing Damage that Occurs in Krabbe Disease

The Foundation also supports Mark Noble, PhD, of the University of Rochester, in his work to reduce, and potentially prevent, the damage that occurs in Krabbe disease. Dr. Noble is working to develop drug therapies that protect against toxicity formed as a result of disease, using preexisting, FDA approved pharmaceuticals.

In-Utero Transplants in Krabbe Patients

Joanne Kurtzberg, MD, at Duke Medical Hospital is conducting cord blood transplants before birth in Leukodystrophy patients with a family history of disease. The aim of this research is to provide treatment, while avoiding toxic preparations needed for transplant after birth. Therefore, a Phase I Clinical Trial will determine if it is safe to administer unrelated umbilical cord blood to pregnant mothers during their first trimester. This study includes Krabbe disease as well as other disorders including MLD, Tay Sachs, Sandhoff, and PMD.

Hunter's Hope Foundation

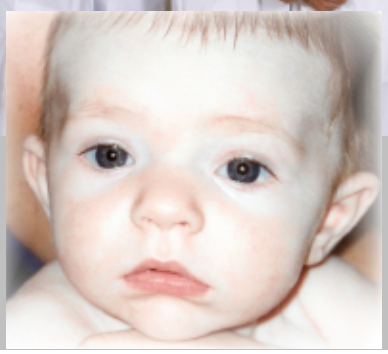
The Hunter's Hope Foundation was established to address the acute need for information and research with respect to Krabbe disease and related Leukodystrophies. In addition, we strive to support and encourage those afflicted and their families as they struggle to endure, adjust and cope with the demands of these fatal illnesses.

Among these essential goals, founders Jim and Jill Kelly seek to inspire an appreciation of all children and express a thankful heart towards God for these precious gifts of life. These bedrock values are categorically and vigilantly expressed throughout all of the Foundation's programs and activities.

From Our CEO (Hunter's Grandma)...

I realize we have shared a great deal of information here and it may be a little overwhelming, but that's our hope... That you are overwhelmed by the amazing and groundbreaking research taking place at the Hunter James Kelly Institute. With your help, this work will continue until one day a cure is found. You are a blessing!

With Hope and Prayers,
Jacque



Accordingly, the Hunter's Hope Foundation mission is four-fold:

- To broaden public awareness of Krabbe disease and other Leukodystrophies thus increasing the probabiliy of early detection and treatment.
- To gather and provide current, functional information and service linkages to families of children with Leukodystrophies.
- To fund research efforts that will identify new treatments, therapies and ultimately, a cure for Krabbe disease and other Leukodystrophies.
- To establish an alliance of hope that will nourish, affirm and confront the urgent need for medical, financial, and emotional support of family members and those afflicted with Leukodystrophies.

Upper photo from left to right: Erin & Jim Kelly, Jerry & Jacque Waggoner (Hunter's Grandparents), Jill & Camryn Kelly pose at the HJKRI in their white lab coats during a visit.

Lower Photo: Hunter James Kelly (02/14/97 - 08/05/05), photo taken on 06/30/97, the day Hunter was diagnosed with Krabbe disease.

12 EVERY SCORE
Every Child. Every Time. Everywhere.

Join Jim Kelly's Team & Make Every Point the Buffalo Bills Score Count!
HuntersHope.Org/EveryScore

every sister

Join Jill Kelly, Together We…
pray, advocate, give
EverySister.Org

Every Step

Lead or Join a Walk in Your Community
EveryStepWalk.Org

Every State

Take Action in Your State for Expanded & Universal Newborn Screening
HuntersHope.Org/EveryState

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