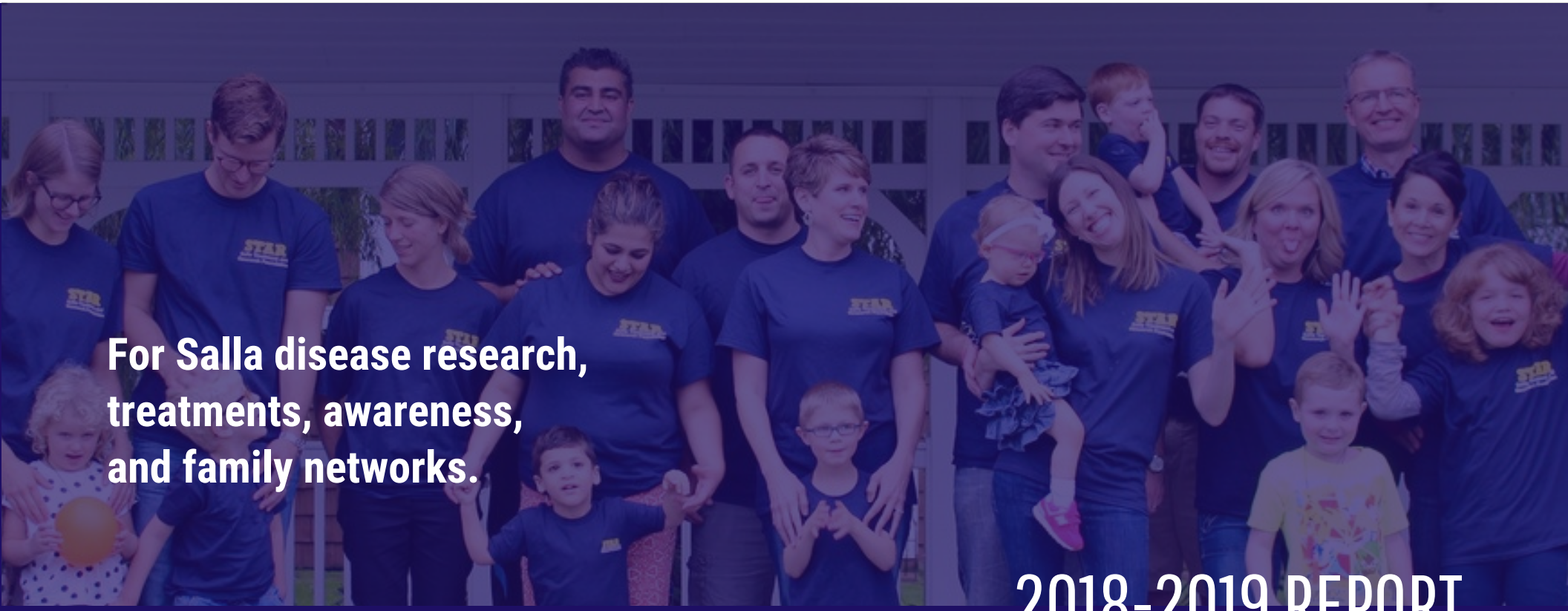
Salla Treatment And Research
FOUNDATION

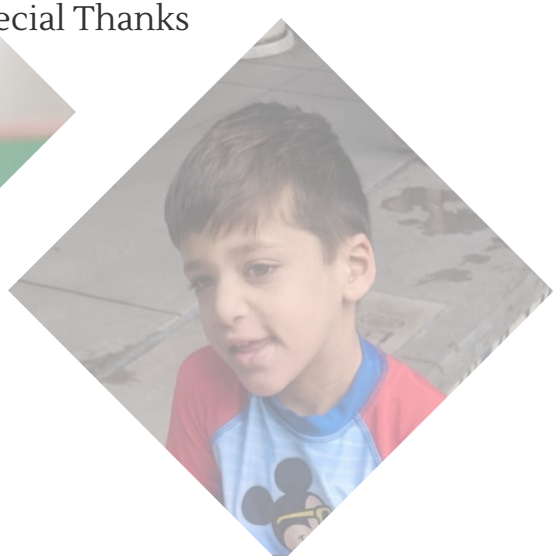


2018-2019 REPORT

ABOUT

The Salla Treatment and Research Foundation was established in 2018 as the first-ever organization dedicated to promoting Salla disease research, treatments, awareness, and family networks. The Foundation supports collaborative scientific research in order to accelerate the prospects for effective medical treatments for those affected with Salla.

The Salla Treatment and Research Foundation is driven by an unwavering belief that no disease is too rare to fight, and that with sufficient support, hope, and faith, a small team of committed researchers, families, supporters, and advocates can create meaningful solutions for those impacted by this disease.



Contents

Letter from STAR President

Jessica Klein Foglio

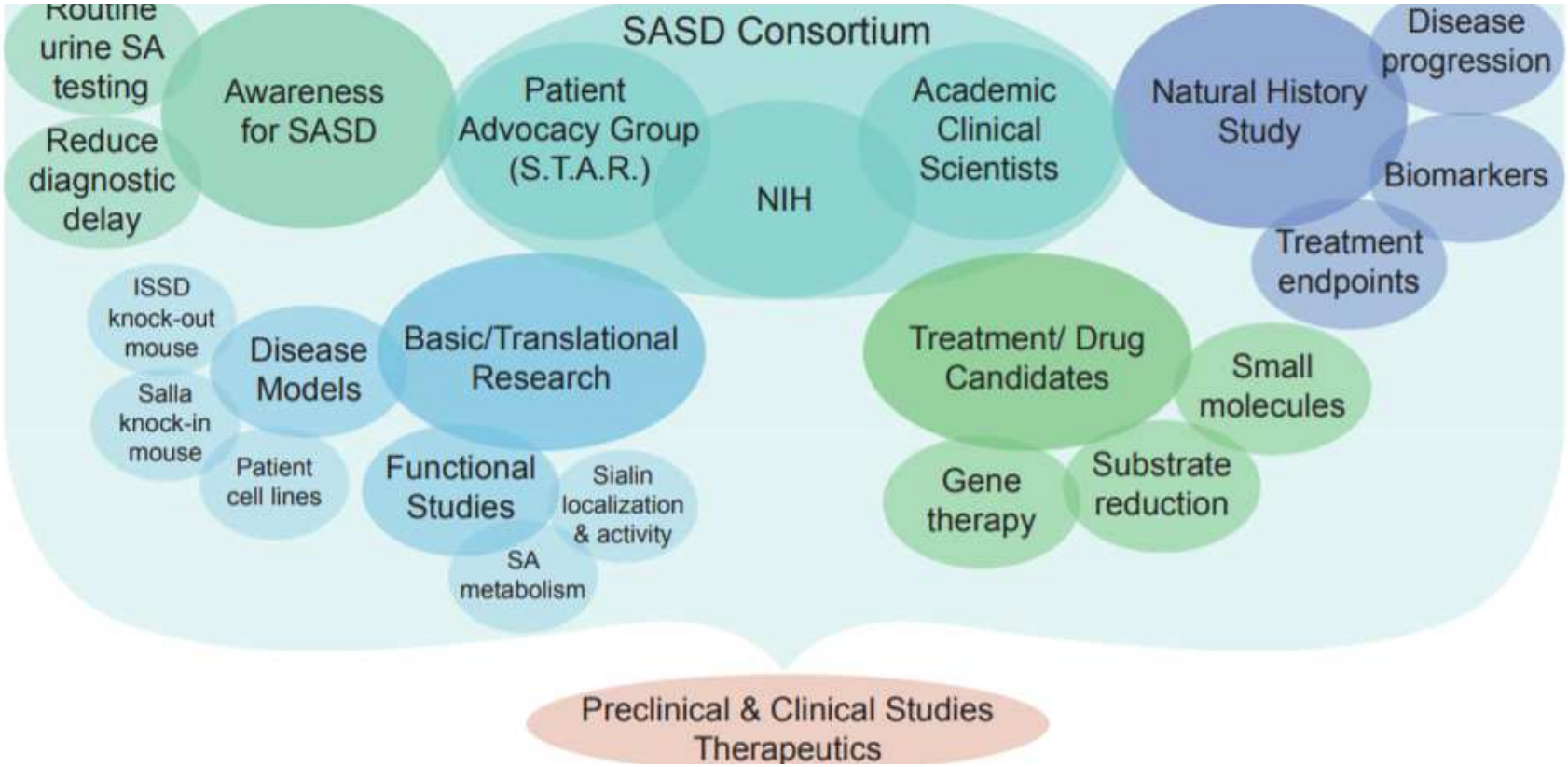
On behalf of the entire Board of Directors of the Salla Treatment and Research ("STAR") Foundation, I am delighted to present our 2018-2019 report. This document has been carefully prepared by the Board to inform our researchers, friends, and families of the remarkable progress and status of our fledgling organization, and what remains for us to accomplish.

We want to share with you our mission, our goals, and the significant impact that all of our stakeholders have had on our organization - every dollar has resulted in direct impacts to our progress in establishing more baseline research regarding Salla. Our foundation is the direct result of passion - the passion of mothers and fathers who chose not to accept a diagnosis of an orphan disease for which there is minimal research, little outlook, and no treatment or cure. We are families that have pooled our resources and our talents to start something from nothing; we endeavor to sponsor the research and effort that yields treatments and cures for any person in the world that is affected by Salla. Despite the challenges and tribulations many of our families have faced, we remain optimistic and humbled - this foundation has been supported by an outpouring of moral and financial support by families and friends.

Hundreds of hours of time and effort have been donated to this organization and cause, many by families with no direct ties to the disease. We personally thank you all for your generosity and empathy to those of us who face this disease daily. "STAR families" - those represented on our Board and all who have dealt with Salla - have felt the hopelessness and loneliness of this diagnosis; we have cried tears from frustration over the seeming unfairness of our circumstances and have also wept in joy in seeing our children progress, meet, and exceed seemingly impossible milestones. It is from these moments and memories that drive us - to make the change we want that no one should have to experience those moments again. We hope you share in our optimism that the journey to a world without Salla has begun and we thank you for every person's part in beginning - and completing - this journey.

Our Strategy: Collaboration

- ☑ Build Awareness
- ☑ Initiate and Support Scientific Research
- ☑ Identify Effective and Viable Treatments



Report from STAR Researchers

Dr. Steven U. Walkley, DVM, PhD

Dr. Melissa Wasserstein, MD

Just over 2 years ago on November 9, 2017, the Foglio family came to the Rose F. Kennedy Intellectual and Developmental Disabilities Research Center (IDDRC) at the Albert Einstein College of Medicine in New York and met with a team of scientists led by Dr. Steven Walkley and their son's Montefiore physician, Dr. Melissa Wasserstein. This was a new program at Einstein-Montefiore, Operation IDD Gene Team, whose goal was to help parents more fully understand the nature of the genetic diagnosis underlying their child's intellectual disability and to let them know they were not alone in their quest for answers.

Here the Foglio's heard a lay tutorial addressing the science behind their son's diagnosis. They learned that Salla disease is an ultrarare type of lysosomal storage disorder – genetic diseases which themselves are uncommon – and one for which little research was underway in the U.S. or Europe. There was even a lack of knowledge as to whether any other families in the US might be affected. They also learned that while there was no treatment known for Salla disease, a closely related lysosomal disease (cystinosis) did have a treatment, developed at the National Institutes of Health (NIH) some years earlier. More research might lead to a therapy for Salla as well. As a result, within 6 weeks of the tutorial the Foglio's announced that they would create a foundation dedicated to Salla disease families and to finding a treatment for this disease.

Since that fateful decision, a S.T.A.R. was born, and was buoyed by numerous collaborations with other affected families in the U.S. and Europe, by successful fundraisers and by a first "think tank" meeting held in Tarrytown, New York in the fall of 2018. Organized by Drs. Walkley and Wasserstein, this intense one-day meeting represented a "first" for Salla disease, where a dozen top notch scientists from the U.S. and Europe came together with an equal number of families affected by this condition. As a result, a Sialic Acid Storage Disease (SASD) Research Collaborative was established and projects initiated in labs at Einstein and the NIH.

A summary of current work and their advances is provided on the following page.

Salla Research Progress Report

A summary of current research being conducted as a result of the support from the Salla Treatment and Research Foundation

A knockout mouse model of Salla disease has been established at Einstein.
-The CNS disease in this mouse model is being fully characterized.
-A therapy examining substrate reduction directed at glycosphingolipid storage is being tested.

A new Salla disease knockin mouse model is being generated at NIH.
-A CRISPR SLC17A5 knock-in Finnish mutation (Arg39Cys) mouse is being created, with efforts currently in progress focused on a targeted mutation screen.
-This new model, which is anticipated to show a more chronic disease progression than the rapidly fatal KO model (and thus better reflect human disease), will be used in future phenotyping/drug treatment studies.

SLC17A5/Sialin mutation analysis allowing for research confirmation of diagnosis has been established at NIH.
-Genetic screening for SLC17A5 gene defects on gDNA has been set up (research base).
-Optimized sequencing of mRNA to show effects of specific mutations on gene expression has been established.
-All currently published SLC17A5 mutations are being compiled for a publication.

Salla disease cell lines are being established at NIH for research/sharing purpose (fibroblasts + lymphoblastoid cells).
-Fibroblasts (skin cells) and Lymphoblastoid (blood) cells now being established will allow us to look at the disease state in a controllable cell model.
-Coriell repository cell lines: Mutations in these commercially available SALLA cell lines are being determined, informative for other research groups that purchase these lines.
-NIH SALLA patient cell lines are being characterized.

The Salla disease intracellular phenotype is being characterized at NIH for use in drug screening/testing + purpose.
-Immunofluorescent (IF) lysosomal staining on SALLA fibroblast cultures were started to establish lysosomal size, cellular distribution and intracellular movement - not previously described for SALLA.
- Other cellular markers will be tested by IF + confocal microscopy imaging.

NIH investigators are establishing/characterizing SIALIN antibodies for use by all research groups.
-Testing commercially available Sialin/SLC17A5 antibodies for Western Blotting and immunofluorescence on human cells is underway.

Efforts toward collecting Natural History data for Salla disease are in place.
-Knowledge of the natural history of a disorder is valuable to the FDA when comparing the results of treated and untreated patients. Dr. Wasserstein at Montefiore has experience with Free Sialic Acid Storage Diseases (FSASDs) and other lysosomal storage diseases. In addition, a limited natural history study of FSASD can be conducted under a clinical protocol that already exists at the NIH. Up to 6 affected individuals would be evaluated with medical consultations, imaging, and SLC17A5 mutation analysis, and a skin biopsy would be obtained to grow fibroblasts for laboratory investigations. Those can include studies of what drugs might reduce the sialic acid content of the cells' lysosomes, in a screen for candidate therapies.

Outreach/awareness of SALLA research has been expanded.
-An abstract and poster entitled "Collaborative Development of Therapeutics for Sialic Acid Storage Disease" authored by NIH and Einstein scientists will be presented by Mary Hackbarth at the following meetings. {American Society of Human Genetics annual meeting (Oct 15-19, 2019; Houston, TX); 2019 NHGRI Symposium (Nov 25-26, 2019, NIH Campus, Bethesda, MD); ASCB/EMBO annual meeting (Dec 7-11, 2019, Washington, DC).
-A second Salla disease Think Tank meeting is being scheduled for September, 2020, to be held at the NIH. Like the first think tank, scientists and clinicians with focus on Salla disease from the US and Europe will be invited to attend.

What is Salla?

An ultra-orphan rare lysosomal storage diserase

Salla disease, intermediate severe Salla disease, and infantile free sialic acid storage disease (ISSD) are neurodegenerative disorders resulting from increased lysosomal storage of free sialic acid. The mildest phenotype is Salla disease, which is characterized by normal appearance and neurologic findings at birth followed by slowly progressive neurologic deterioration resulting in mild to moderate psychomotor retardation, spasticity, athetosis, and epileptic seizures. The most severe phenotype is ISSD, characterized by severe developmental delay, coarse facial features, hepatosplenomegaly, and cardiomegaly; death usually occurs in early childhood.

Free sialic acid storage disorders result from defective free sialic acid transport out of lysosomes caused by pathogenic variants in SLC17A5, encoding the lysosomal transport protein sialin. The diagnosis of a free sialic acid storage disorder is suggested by significantly elevated free (i.e., unconjugated) sialic acid (referred to as N- acetylneuraminic acid, a negatively charged sugar) in urine and/or cerebrospinal fluid using the fluorimetric thiobarbituric acid assay, thin-layer chromatography, or mass spectrometry. The diagnosis is established either by demonstrating lysosomal (rather than cytoplasmic) localization of elevated free sialic acid or by identifying pathogenic variants in SLC17A5.

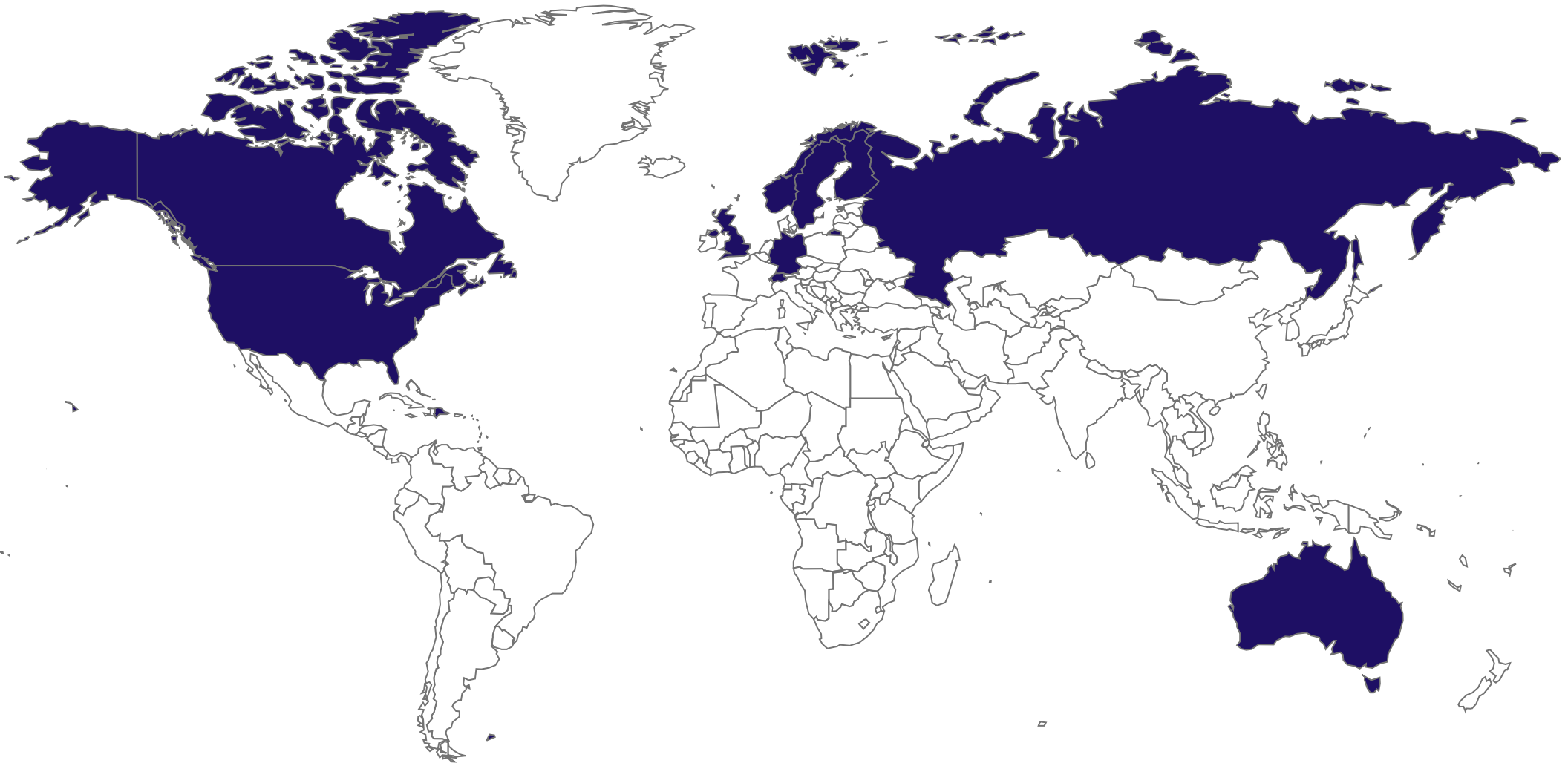
There are no consensus clinical diagnostic criteria for Salla disease. The diagnosis of Salla disease is suspected in individuals who manifest truncal ataxia and hypotonia at age approximately one year, developmental delays and growth retardation in early childhood, and severe cognitive and motor impairment or intellectual disability in adulthood. The association of intellectual disability, spasticity, ataxia, myelination defects, and facial coarsening in adulthood is suggestive of Salla disease. The diagnosis of infantile free sialic acid storage disease (ISSD) is suspected in individuals with early multisystemic involvement including: hydrops fetalis, hepatosplenomegaly, failure to thrive, increasingly coarse facial features, neurologic deterioration typical of a lysosomal storage disease, dysostosis, and early death.

Salla disease is the mildest phenotype, characterized by a normal appearance and normal neurologic findings at birth followed by slowly progressive neurologic deterioration resulting in mild-to- moderate psychomotor retardation. Muscular hypotonia is often first recognized at approximately age six months. One third of affected children learn to walk. Speech can be limited to single words but understanding of speech is good. Slow developmental progress often continues until the third decade, after which regression can occur. Some individuals with Salla disease present later in life with spasticity, athetosis, and epileptic seizures, becoming nonambulatory and nonverbal. Affected individuals are characterized as good-humored and sociable. Abnormal myelination of the basal ganglia and hypoplasia of the corpus callosum are constant and early findings. MRI reveals these predominant white matter changes. Cerebellar white matter changes are also present and can explain the ataxia. In addition to the central dysmyelination, a peripheral dysmyelination with the clinical picture of a polyneuropathy occurs with variable neurologic presentations. Affected individuals do not have organomegaly, skeletal dysostosis, or abnormal eye findings. In a single individual, growth hormone and gonadotropin deficiencies were observed. Life expectancy appears to be shortened, although affected individuals up to age 72 years have been observed.

ISSD, the most severe phenotype, is characterized by severe developmental delays, coarse facial features, hepatosplenomegaly, and cardiomegaly. ISSD can present prenatally and in the neonatal period with nonimmune hydrops fetalis [Lemyre et al 1999, Stone & Sidransky 1999, Froissart et al 2005]. Some affected infants are born prematurely. Other affected infants appear normal at birth but deteriorate and lose milestones during infancy [Kleta et al 2003, Kleta et al 2004]. Seizures are common. Some infants with ISSD develop proteinuria and nephrotic syndrome [Lemyre et al 1999, Ishiwari et al 2004]. Skeletal changes may include irregular metaphyses, diffuse hypomineralization, club feet, short femurs, enlarged metaphyses, fractures, hip dysplasia, anterior beaking of the dorsal vertebrae, and hypoplasia of the distal phalanges [Froissart et al 2005]. Death usually occurs in early childhood, typically from respiratory infections.

Salla disease is believed to have been reported in approximately 150 individuals, mainly from Finland and Sweden. Individuals with molecularly proven Salla disease have been identified outside of Finland and Sweden.

From "Free Sialic Acid Storage Disorders" (2013) by David Adams, MD, PhD and William A Gahl, MD, PhD



STAR Foundation has connected with Salla families in 7 U.S. states and 12 countries.

SEPTEMBER 2018

THINK TANK & FAMILY CAMP

Organized by Drs. Walkley and Wasserstein, this intense one-day meeting represented a “first” for Salla disease, where a dozen top notch scientists from the U.S. and Europe came together with an equal number of families affected by this condition.

As a result, a Sialic Acid Storage Disease (SASD) Research Collaborative was established and projects initiated in labs at Einstein and the NIH.

Among the participating researchers:

Dr. David Adams, M.D., Ph.D.
Dr. Kostantin Dobrenis, Ph.D.
Dr. William A. Gahl, M.D., Ph.D.
Dr. Bruno Gasnier, Ph.D.
Dr. Marjan Huizing, Ph.D.
Dr. Marc C. Patterson, M.D.
Dr. Richard J. Reimer, M.D.
Dr. Steven U. Walkley, DVM, Ph.D.
Dr. Melissa Wasserstein, M.D.
Dr. Roberto Zoncu, Ph.D.

DECEMBER 2018

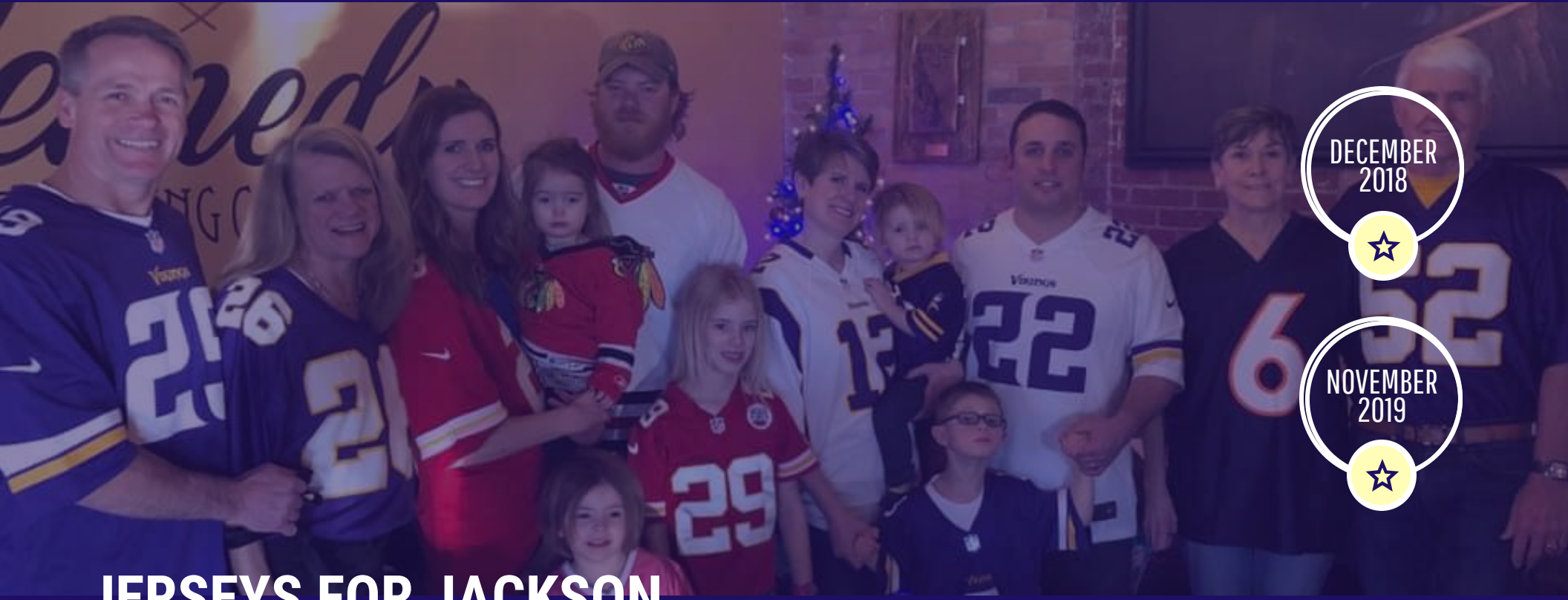
NEW YORK HOLIDAY AUCTION

The first-ever community-wide fundraiser for the Salla Treatment and Research Foundation took place in Riverdale, NY, attracting local television and print media coverage and raising awareness of Salla disease and the new effort to fund dedicated research at the National Institutes of Health.

Riverdale couple raises funds for 3-year-old son with 'extraordinarily rare disease'

NEWS12 THE BRONX

The RIVERDALE PRESS



DECEMBER 2018

NOVEMBER 2019

JERSEYS FOR JACKSON

For two years in a row, the community in Sioux Falls, South Dakota has come together for the "Jerseys for Jackson" event. Organized by the Horsted family, the event has been covered by local media, expanding awareness of Salla and raising funds for Salla research.

"Jerseys for Jackson" to help fund research of rare genetic disease

KELO 1320 AM · 107.9 FM

KDLT NEWS

FEBRUARY 2019

A STAR FOR JADA CONCERT

Organized by Shawn Merriman, the "Star for Jada" concert in Manitoba, Canada was the first international event for Salla disease, gaining local media attention and raising thousands of dollars for Salla research.

laronge NOW
La Ronge. RIGHT NOW!

It was a big night for Jada Halkett who was the center of attention Thursday. (submitted photo/Sheldon Merriman)

SALLA FUNDRAISER

By Derek Cornet

Residents raise $7,600 at Salla research benefit

Mar 01, 2019

GEORGIA STAR GALA

The LeBlanc family brought together family, friends and local businesses for a remarkable gala event near Atlanta, Georgia, in what was the most successful fundraiser yet in support of the Salla Treatment and Research Foundation.

INTERNATIONAL STAR WALK

SEPTEMBER 2019

$39,000 raised

5 countries

In our most ambitious event since the creation of the Salla Treatment and Research Foundation, the first annual "International STAR Walk" took place in 5 countries worldwide with numerous communities coming together to support family and friends, raising significant awareness and support for the Foundation and the research ahead.

'Kori's First Annual Walk and Roll Family Fest' brings community together CBS7

A WORLDWIDE EFFORT

Feature news articles and chocalate sales in Switzerland, lemonade stands in New York, wine events in Georgia, bake sales in California, speaking opportunities at scientific conferences, and more... in two short years, efforts to raise awareness and resources has been taking place across the world, led by a network of Salla families and friends who together are building momentum to advance Salla treatment and research.

SUPPORT STAR

Dear friend,

It has been so inspiring to see our communities come together in support of Salla families since the founding of the Salla Treatment and Research Foundation. We are eternally grateful to you, our friends, family, and all our supporters.

The hope and progress that has been generated in the past two years is just the beginning. Together, we can make an enormous impact. Advancements in Salla research and treatments is within our reach. And we know it will happen with your help.

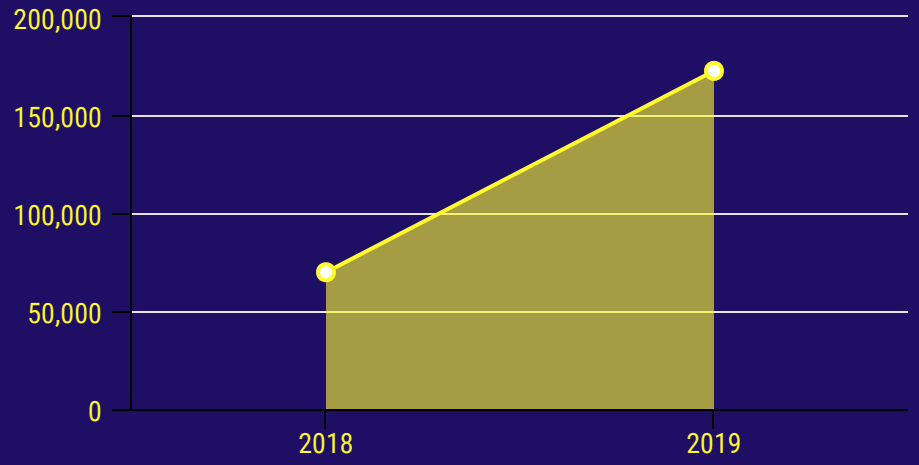
With all our gratitude,

Jessica Klein-Foglio

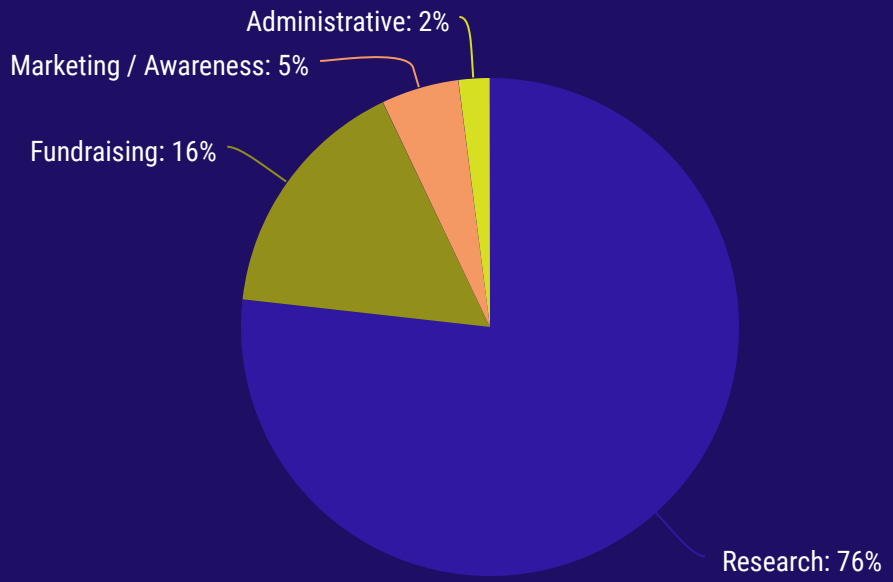
Jessica Klein-Foglio,
President, Salla Treatment And Research Foundation
(Mikey's and Ben's mom)

Financial Overview

Growing Resources Per Year 2018-2019



Financial Efficiency 2018 - 2019



SPECIAL THANKS

There are too many individuals, families, and businesses across the world for all of the Salla families to thank. Below is just a partial list of the many who have helped us to generate hope and progress. Thank you.

2 Square Feet Landscaping

A-1 Broadcasting, Chuck Edmundson

ABC Prooerties

Addeos Pizzeria

Albert Einstein College of Medicine/ Montefiore Medical Center.

All Around Gymnastics

American Haircuts (Roswell)

Amy Coggeshall

Amy Stone

Andretti

Ann Taylor

Anne & Randy Ward

Borgattis

Botanical Gardens

Brad Buffington

Cabernet Steakhouse

Café Intermezzo

Cakes by Darcy

Catch Air

Cherokee Drone Services

Children's Hospital at Montefiore

Chireen Hall & Latelier Hair Co.

Chris Morman

City of Odessa

Club Pilates (East Cobb)

Cora Housewares Hardware

Costco (Alpharetta)

Crystal Barbee Photography

Darlene Glenn

David and Shanit Halperin

Delta, Melissa Murphy

Dr. Bruno Gasnier, Ph.D.

Dr. David Adams, M.D., Ph.D.

Dr. Kostantin Dobrenis, Ph.D.

Dr. Marc C. Patterson, M.D.

Dr. Marjan Huizing, Ph.D.

Dr. Melissa Wasserstein, M.D.

Dr. Michael Papciak

Dr. Richard J. Reimer, M.D.

Dr. Roberto Zoncu, Ph.D.

Dr. Stephanie Grogan

Dr. Steven U. Walkley, DVM, Ph.D.

Dr. William A. Gahl, M.D., Ph.D.

Dry Bar

El Felix

Enchant a Party

Ennerations

EY

Family PowerSports of Odessa

Fifth Group

Gina's Happy Faces

Goldfish Swim School (Johns Creek)

Hal's

Hannah's Food Truck

HB Liquors

Hinzman Holdings

Hollywood Feed (Cumming)

Houcks

I Canita Cake

Imperial Fez

Ivy Lane

Jake's Steakhouse

Jennifer Klein

Jeremy Jutkowitz

John Patitucci

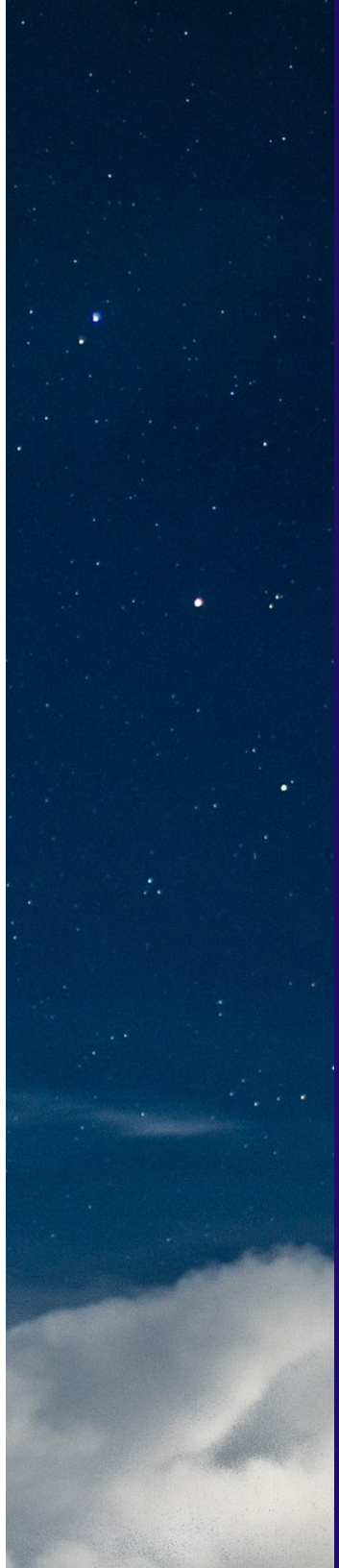
Joy Beider

Joy Langer

Just in Time Consign, Reggie Martin

JWO Jewelers

Kaiser family and friends
Katie Lester
Kilwins
Kimball House
L'atelier Hair Co, Chireen Hall
La Vida Massage
Laura Gill
Lee Chadwick
Leek Fire & Safety Supplies
Leigha Perkins
Lloyd's carrot cake
Madison's
Magic by Harlin
Magnolia Moon
Mandy's Hair Salon
Marcel
McCarty Equipment Co
Mekhal Anvaripour
Michelle Badour
Morgan Stanley
National Society of Colonial Dames In the State of New York
Noca
Novogrow LLC-Azriel Novogroder
Odessa Camera RC & Armory
Osteria Mattone
Pike Nurseries
Polo Golf and Country Club
Rebecca Huffman, Origami Owl
Rick and Mary Johnson
Riverdale Stables
Riverdale Yacht Club
Ruffle Butts
Sams Club (Roswell)
Scott Tarter
Seth Deitchman
Shine Speech
Skyview wine and liquors
Sno King
Sonya Chamberlain
Sukari Spirits
Sunbelt Rentals
Sweets by Sauer
Trader Joe's (Roswell)
Trish Anderson
Truffles Chocolate Factory
Twin Lakes Farm
T-Mobile Riverdale
The Alliance Theater
The Atlanta Hawks
The Atlanta Zoo
The Beaufort Bonnet Company
The Center for Puppetry Arts
The Cheese Guy
The Davis Book Club
The Garner Family
The Georgia Aquarium
The Metropolitan Club
The Pink Valise
The Roaden Family
The Seersucker Peach
The Shane Show
The Shaw Family
The Solid Bow
The University of Georgia Athletics Department
Therapy Stars & Strikes
Tom and Dawn McGee New Generation Realty of Georgia
Top Golf
Trader Joe's (Roswell)
Trish Anderson
Truffles Chocolate Factory
Twin Lakes Farm
Unique Nails
Unleashed
Vancortlandt Park House Museum
Vickie Jordan
West Elm
Whitney Panetta
Wild Birds Unlimited (Dawsonville)
William David Salon & Spa (Alpharetta)
Zach & Allie Pridgen
Zeke Moya, Car Freshies by Zeke's Peeps
Zulu Nyala Grop



BOARD

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Salla Treatment And Research Foundation is a 501 (c) 3 not-for-profit organization.

All contributions are tax-deductible.