

The Story of Marcus, Anna & Luke

Spastic Ataxia is an exceptionally rare, progressive, neurodegenerative condition. To date, the medical research literature states no known treatment.

We want to share a personal story that reflects our clinic's daily work, the journeys our patient families take and the journeys we take with them.

Marcus was one of the very first patients of DDC Clinic. We saw him first in 2002. We didn't have a building at the time so Dr. Wang and JoAnn Brace, an early intervention specialist and a founding board member, did a house call together. Marcus was then three years old. His parents explained that he was fairly normal for the first year or two of his life but was beginning to experience tremors, speech difficulties and increasing difficulty walking. We evaluated Marcus, acknowledging his developmental delays and progressing symptoms, but we did not have an answer for the family.

Over the next ten years, we continued to search for answers, reviewing the medical literature and consulting with multiple other specialists including a pediatric neurologist and three different geneticists. Together the geneticists had more than 100 years combined experience. But they too were stumped.



Dr. Wang and Marcus

Though ten years of effort had yet to produce a diagnosis, we began to suspect a more specific set of gene mutations. We reached out to Dr. Craig Blackstone, a section chief with the National Institutes of Health in Washington, DC. Dr. Blackstone had some experience with similar conditions. We asked him to travel to Middlefield and he agreed. He even joined us on a house call to evaluate Marcus.

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Molecular Diagnostics Laboratory Leads the Region

Since receiving a clinical license two years ago, DDC Clinic's *Molecular Diagnostics Laboratory* has grown to be one of the top laboratories in Ohio and the region. The lab currently offers 189 tests for more than 470 genetic conditions and was the first in the state to have both next generation sequencing (NGS) and high definition genotyping platforms installed. These assets have been well-leveraged. The lab's test offerings have grown significantly of late to include 40 targeted mutations via Sanger sequencing, 98 whole gene sequences, nearly 50 custom NGS panels and chromosomal microarrays.

"DDC Clinic's board made a key strategic decision in committing to grow the capabilities of our lab and we have been most fortunate to have a number of individuals and area foundations provide support to help us grow the depth, breadth and sustainability of laboratory services." – Blake Andres, Executive Director.

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About DDC Clinic



DDC Clinic - Center for Special Needs Children is a non-profit primary care and research facility serving patients with complex medical needs. Located in Middlefield, Ohio, we have been recognized internationally for our state-of-the-art genetic research impacting broad-based health concerns such as heart disease, cancer and neurological disorders.

Our mission is to enhance the quality of life for people with special needs caused by rare genetic disorders. Founded in 1998 by five local Amish families committed to helping tomorrow's special children, we now serve more than 750 patient families in 30 U.S. states and several foreign countries.

Our clinic is a unique collaboration of the Amish and non-Amish communities, dedicated doctors and researchers all working together to find answers for parents and treatments for children. The Clinic was built on the 'medical home' concept defined by the American Academy of Pediatrics. We provide comprehensive and personalized medical care for special children with over 70 different rare conditions.

Our in-house certified clinical genetics laboratory provides rapid, high quality and affordable testing and we conduct patient centered research – always seeking faster diagnoses, better understanding and improved treatments for our children.

We offer personalized education and support services for patient families. No family is ever turned away based on ability to pay.

DDC Clinic is a gathering place; a place of love, compassion and caring; a place where people take the time to listen and share; a place of faith and hope.

DDC Clinic Partners with MSI to Provide Adult Day Services

For just over a year now, our clinic has been working with MSI (Metzenbaum Sheltered Industries) to host an Integrated Day Program for special need adults in our community.

MSI provides highly valued services for adults who may no longer wish to participate in structured work programs, but still benefit from services that allow them to socialize and participate in recreational activities. We're very pleased to be able to host the MSI adult program in two of our center's community rooms.

A typical day for clients includes a variety of activity choices. Talented and committed staff follow daily, weekly and monthly schedules of events geared toward community integration, creative choices and sensory opportunities.

Program themes guide a wide variety of weekly activities including reading, art lessons, crafts, food preparation and community outings. The group can regularly be seen in the community in area parks, restaurants, stores, businesses and other social service organizations. Participating clients and staff have been busy volunteering at Briar Hill Nursing Facility, Middlefield Library, First Methodist Church Food Pantry, Middlefield Senior Center and Destination Geauga.

The DDC Clinic hosted program is supported by three full-time staff and several therapists. Program participants also receive regular visits from activity staff at the Geauga County Board of Developmental Disabilities (Metzenbaum Center), therapy dogs and family and friends from the Middlefield community. To date, the program is running close to capacity.

For more information about this program or other MSI services, please call (440) 729-1919.



Several times over the years of working with Marcus, we felt we were very close to making the correct diagnosis. However, in each instance, confirmational testing proved us wrong – we had yet to identify the disorder. We were now convinced that this was a new condition, one never before described in the medical literature. We explained to Marcus' parents that we had yet to find an answer, but were narrowing the possibilities. At one point Dr. Wang promised them: "I'm not going to retire before I have an answer for you!"

Another year passed and then one day Dr. Bao Xin, our Research and Technical Director, walked quietly into Dr. Wang's office, handed him a small scrap of paper and then walked away. This is Dr. Xin's traditional way of telling us about a big breakthrough. There were five letters on this piece of paper – MTPAP. The name of the gene that caused the condition is MTPAP. The mutation causes a defect in mitochondrial messenger RNA maturation resulting in a new condition we now call spastic ataxia.

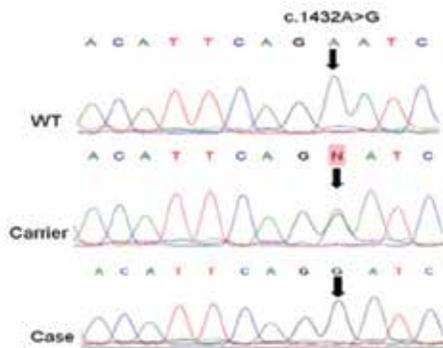
We finally had the long-sought diagnosis but yet another challenge – the medical literature states "no known treatment."

Patients affected by spastic ataxia have conditions that include abnormal constriction of the muscles (spasticity), and difficulty coordinating movements (ataxia). They can also be affected by increased tone of some muscle groups and hyper-reflexes of some joints. The disorder is insidious, with slow but increasing disability each passing year. Affected children tend to first show symptoms at 18 to 24 months. Left untreated, most patients will end up in wheelchairs in adulthood.

Over time, affected patients suffer from muscle wasting and nerve degeneration resulting in further loss of coordination and the risk for frequent falls. This was indeed the case with Marcus. He was continuing to lose motor control and fell often, requiring the use of a helmet to prevent head injuries. We needed to find a treatment for Marcus and quickly!

With no treatment options offered in medical literature, we began to review treatment possibilities we've used with

Dr. Wang promised them: "I'm not going to retire before I have an answer for you!"



Dr. Xin's Discovery – MTPAP Gene Mutation

other related conditions. Some years ago, in collaboration with other physicians, we used the drug Sinemet to treat a patient with dopa responsive dystonia, a related neurodegenerative disorder that affects a patient's muscles. The drug Sinemet was originally designed to help relieve some symptoms associated with Parkinson's disease. We thought Sinemet might be an option for Marcus and began treatment. In a few short months, we had reason for hope – Marcus regained significant motor control and no longer had to wear a helmet. But we knew we also had a challenge. Using this drug for spastic ataxia only treats the symptoms, not the cause. Marcus gradually developed resistance to the drug and was losing the earlier progress made. We needed to come up with some new treatment!

Since MTPAP is a mitochondrial-related gene, we consulted a world expert in disorders of mitochondrial genes, Dr. Richard Kelly of Johns Hopkins. Dr. Kelly had developed a mitochondrial "cocktail" and suggested we approach a company in California who makes a product called MitoSpectra, a nutritional supplement sometimes used to treat autism. Based on what we had learned about the natural history of this disorder over the years, we felt the product might help Marcus. After some significant coordination, the company agreed to support our effort and provided the supplement free of charge.

Marcus has now been on the mitochondrial supplement for two years and his motor function and coordination have improved significantly. He has a more stable gait and, when prompted, enthusiastically runs down our clinic's hallways!

Now let us share with you the story of Anna, Marcus' cousin. If you were to watch Anna run through our halls, you would not be able to distinguish her from any other healthy eight-year-old. She appears completely normal with the exception that she has the diagnosis of spastic ataxia. Anna earns all A's in school and has no signs of developmental delay. The difference with Anna is we had a much earlier diagnosis and were able to pursue earlier treatment. We monitor Anna closely and, to date, she demonstrates no symptoms associated with this rare condition.

Just six months ago we met Luke for the very first time. Luke is just two years old and not related to Marcus or Anna. He too has been diagnosed with spastic ataxia. Now that we know more about the genetics, biochemistry and natural history of this disorder, there will likely be other children diagnosed in years to come.

Each of these children and their families face a different journey. At DDC Clinic, we have the privilege of being able to work with these families, searching for diagnoses, effective treatments and, sometimes, even a cure. These journeys we take with them are often fruitful. What we learn from working with today's families can indeed help tomorrow's children.

We trust that Marcus, Anna & Luke will continue to progress, to grow up as all other children with productive lives. This is the hope we hold for them and all the world's special children, each and every day.

Many Thanks to...

DDC Clinic is grateful for the support from the following friends:

Ohio Developmental Disabilities Council

For the \$20,000 grant award in continued support of the "Amish Community Project" for targeted research and community outreach services. Matching funds are provided by Holmes County Association for Handicapped Citizens and Holmes County Board of Developmental Disabilities.

Susan and John Turben Foundation

For the pledge of \$20,000 for general operating support. We appreciate Dr. Susan and John Turben for their ongoing support of our programs.

Bessie Benner Metzenbaum Fund

We are grateful for the fund's ongoing commitment to our mission and program services. Thank you for the general operating support award of \$10,000.

United Way Services of Geauga County

Thank you for your continued partnership. We also wish to recognize the Youth Fund Distribution Committee for a grant of \$3,500 for our Patient Assistance Program.

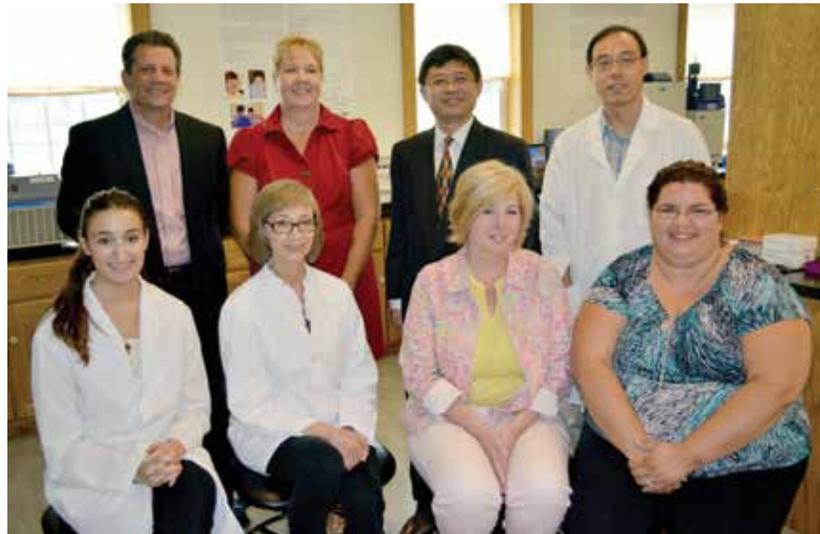
Char and Chuck Fowler Family Foundation

For the two-year, \$250,000 Grant Award in support of marketing, promoting and growing the professional capacities of our Molecular Diagnostics Laboratory. We appreciate your ongoing commitment to the clinic and our laboratory, and for this timely capacity-building gift.

DDC Clinic Craft Club for Community Women

Each month 15 to 20 women from the local Amish community come together for fellowship and to craft various items including quilts, pillows, wall hangings and dolls. We appreciate the donations they provide for our benefit auctions and for other worthy causes in the community.

Molecular Genetics Laboratory Leads the Region > from page 1



The CLIA certification (Clinical Laboratory Improvement Amendments – CMS), has allowed the lab to offer physicians, clinics and hospitals high-quality, competitively-priced testing services. We are currently providing testing for medical clinics focused on rare disorders in Indiana, Wisconsin, Central Ohio, and Central Pennsylvania. The lab is also receiving inquiries and testing samples from hospital systems in Ohio, New York, Florida and Canada, to name a few.

DDC Clinic remains committed to serving self-pay patient families with lab services through the *Love, Faith and Family Assistance Program*. In keeping with our mission of serving all patients regardless of ability to pay, enrolled families receive targeted diagnostic tests for just \$75 – tests that would cost many hundreds and sometimes thousands of dollars elsewhere.

To grow clinical capabilities and meet increased sample volume, the lab has added several staff in recent years including a lab supervisor, technician and, most recently, a licensed genetic counselor (see story page 5). "We're grateful to have such a committed and efficient lab team dedicated to serving patient families and growing and leveraging our unique capabilities. For example, the lab recently added NGS panels for *Galloway Mowat Syndrome*, *Congenital Cataracts*, *Overgrowth with Intellectual Disability*, and *Early-Onset Parkinson's Disease*. These four panels are not currently offered by any other laboratory in the country." – Dr. Bao Xin, Research & Technical Director.

For additional information about our Molecular Diagnostics Laboratory offerings, please see complete listings at the following links on the National Institutes of Health and DDC Clinic websites:

- <http://www.ncbi.nlm.nih.gov/gtr/labs/505371/>
- <http://www.ddclinic.org/laboratory/>

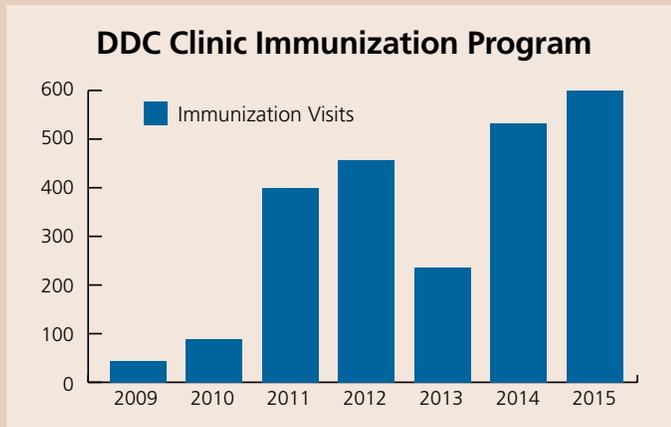
DDC Clinic wishes to thank the following contributors for their generous support of this project:

*The Char and Chuck Fowler Family Foundation
The Fred A. Lennon Charitable Trust
The Reinberger Foundation
Lake-Geauga Fund of The Cleveland Foundation*

Immunization Program Continues to Grow

DDC Clinic has been an active participant in the Vaccines for Children (VFC) program since 2009. The program provides vaccines to children whose parents or guardians may not be able to afford them. This helps ensure that all children have a better chance of getting their recommended vaccinations on schedule. Vaccines available through the VFC program are those recommended by the Advisory Committee on Immunization Practices (ACIP). These vaccines protect babies, young children, and adolescents from 16 diseases.

This has been a highly valued and growing service for the community. In 2015, we will provide an estimated 600 immunization visits. Immunizations are offered to all patients of DDC Clinic and to qualified non-patient families in surrounding communities.



Valerie Sency, RN

DDC Clinic Enhances Laboratory Services with Genetic Counseling

In March 2015, DDC Clinic welcomed Christine Wensel, a licensed genetic counselor with both clinical and laboratory experience.

With a growing number of clinicians utilizing our Molecular Diagnostics Laboratory, having an in-house licensed genetic counselor is key in helping doctors navigate the maze of genetic testing.

Prior to joining us, Chris worked at University Hospitals Case Medical Center in Cleveland and at Tod Children's Hospital in Youngstown. More than 10 years ago, while working at Tod Children's, Chris had some early involvement with DDC Clinic having participated in several subspecialty clinics that were held in our first facility. We're glad to have her on board in a much expanded capacity!

Chris has been working to increase awareness of our Molecular Diagnostics Laboratory as a provider of molecular genetic testing. This involves including our CLIA certified laboratory on several national registries that are routinely used by clinicians to locate a laboratory that provides the needed testing. Our inclusion on the Genetic Testing Registry (GTR at the NIH) and GeneTests has resulted in broader use of our services. The clinic's early



Christine Wensel

investment in next generation sequencing technology has given us the ability to provide physicians worldwide with a broad range of custom gene test panels. For example, Autosomal Recessive Congenital Cataract NGS Panel and Early Onset Parkinson Disease NGS Panel are two gene panels that are not available at any other laboratory in the U.S. We have had multiple inquiries and are already receiving samples for these tests.

As a genetic counselor licensed by the State of Ohio, Chris will work with clinicians to help them through the genetic testing process – from start to finish. She serves as a liaison between the ordering physician and our Molecular Diagnostics Laboratory assisting with test utilization, reporting and interpretation of results.

Recent Publications

International Journal of Rheumatic Diseases: *Prolidase deficiency breaks tolerance to lupus-associated antigens*

Analytical Biochemistry: *A new liquid chromatography tandem mass spectrometry method for quantification of gangliosides in human plasma*

Gene Reviews: *Prolidase Deficiency*

Brain: *Recessive nephrocerebellar syndrome on the Galloway-Mowat syndrome spectrum is caused by homozygous protein-truncating mutations of WDR73*

BioMed Research International: *SAMHD1 Gene Mutations Are Associated with Cerebral Large-Artery Atherosclerosis*

Journal of the American Academy of Dermatology: *Aggressive CD8+ epidermotropic cutaneous T-cell lymphoma associated with homozygous mutation in SAMHD1*

Virology Journal: *Central memory CD4+ T-cells are preferential targets of double infection by HIV-1*

To view the full manuscripts go to www.ddcclinic.org

Community Volunteer Days

We were the beneficiaries over the last year of a dozen full-days of community service. Board members, staff, families and many clinic friends volunteered to spruce up our facility and grounds.

The results include a power-washed and now sparkling building exterior, a planting of perennial beds at our patient entrance, weeding and pruning of the family garden, and a top-to-bottom deep cleaning of the interior of our building.

Additionally, a new outdoor patio and activity space was created on the north side of our building. Thanks go to a local scouting group and their family and friends for installing the new patio and for building the picnic tables and benches. The new patio benefits participants in the adult-day program that's offered by Metzenbaum Sheltered Industries (MSI) in DDC Clinic's community rooms.

We are grateful for the many hands that came together in service that left a very visible impact on our building and grounds.



Patchwork Live Auction

Patchwork 2015 Benefit

To all supporters of the April 18th benefit, including co-chairs Beth Ballee and Patti Gallagher, thank you for a terrific event. Thanks to the efforts of our table sponsors, guests and corporate sponsors, proceeds totaled more than \$76,000. We hope to see you at our event next year. Save the date for **April 16, 2016** at The Family Life Center of the Federated Church in Bainbridge Township.

2015 Community Benefit Auctions

Each year, friends in several Amish and Mennonite communities hold benefit auctions in support of our work with special children. This year, these three benefit auctions had combined proceeds of \$193,000. Many hundreds of local community members show up with donations of goods, time and labor, all in support of our work at DDC Clinic. The Shiloh, Spartansburg and Middlefield communities' commitment to our mission and the families we serve is truly humbling.



Shiloh Auction

This marks the eighth year that our clinic has shared in the proceeds from the Shiloh Mennonite Community Benefit Auction. We're grateful for the record number of participants at the July 11th event. The bidding started promptly at 9:00 AM and, even with extended hours in the second auction ring, bidding continued till 4:30 PM. In 2008, the first year DDC Clinic was named as a beneficiary, the Shiloh community raised \$10,000 to help us help special children. And in just eight years, the benefit's proceeds have grown 400%. This annual auction benefits both DDC Clinic and the Clinic for Special Children in Lancaster, Pennsylvania. This year's proceeds for DDC Clinic were \$40,395. Many thanks to our many friends in Shiloh.

Spartansburg Auction

On September 1st, the 3rd Annual Spartansburg Auction benefit was held. Located in Crawford County in Western Pennsylvania, a number of families from the region travel to our clinic for their children's care. Several years ago the community came together and held this benefit to support our mission. Our friends in "Sparty" were grateful this year for our board of directors' donation of one of the auction horses. Many other items, from handmade quilts and furnishings and local produce, were featured at the benefit. In just three years, proceeds from this annual evening benefit have already grown to \$34,000.

Geauga Auction

Thanks to the generosity of 1700+ in attendance and the auction committee's hard work and careful planning, the October 9th, 15th Annual Geauga Benefit Auction was an unprecedented success! At the end of the night, more than \$120,000 was raised for DDC Clinic!

A 40-foot addition to the auction barn allowed plenty of room for the large crowd as well as new spaces for silent and Chinese auction items and multiple areas for food sales. This year's live auction featured a wide variety of household goods and furnishings. Highlights included a custom two-car garage built on the successful bidder's site and handcrafted quilts donated by the Ladies Quilting Group that meets monthly in DDC Clinic's community room.

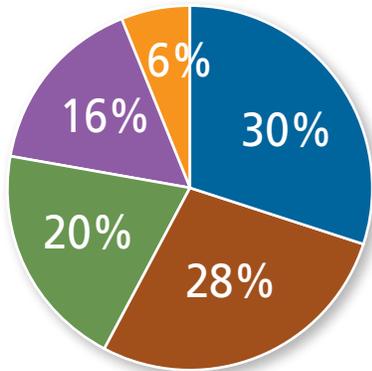
A very special thank you to our guest, Dr. Holmes Morton, co-founder of the Clinic for Special Children in Lancaster, PA. His inspiring words and stories reminded everyone in attendance of the importance of supporting our most privileged work with special children and their families. A few fortunate bidders were even able to win a one-of-a-kind item signed by both Dr. Morton and Dr. Wang!

If you've yet to make it to one of our traditional Amish auctions, please consider doing so in 2016 and bring your family and friends.

2014 Annual Report

Revenue

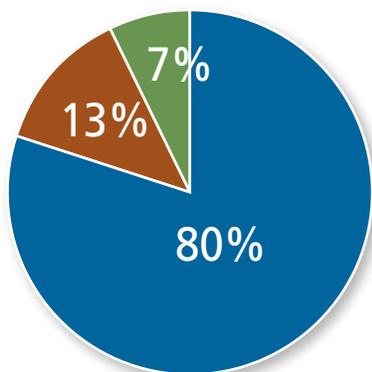
Total Revenue for 2014 – \$1,012,113



| | |
|------------------------|------------|
| ■ Grants and Research | \$ 302,452 |
| ■ Benefit Auctions | \$ 279,659 |
| ■ Clinical Services | \$ 204,403 |
| ■ Individual giving | \$ 162,800 |
| ■ Miscellaneous Income | \$ 62,799 |

Expenses*

Total Expenses for 2014 – \$1,015,649



| | |
|------------------------|------------|
| ■ Program Services | \$ 815,838 |
| ■ Fundraising | \$ 130,815 |
| ■ Management & General | \$ 68,996 |

*Reported less \$92,478 depreciation.

Statement of Financial Position

Assets

2014

| | |
|------------------------------|--------------|
| Cash and Cash Equivalents | \$ 580,266 |
| Accounts Receivable | \$ 46,711 |
| Pledges Receivable | \$ 10,860 |
| Grants Receivable | \$ 70,839 |
| Prepaid Insurance | \$ 22,795 |
| CLIA lab inventory | \$ 10,665 |
| Property and Equipment | \$ 1,868,173 |
| Investments | \$ 114,718 |
| Cash restricted to Endowment | \$ 256,500 |

Total Assets

\$ 2,981,527

Liabilities and Net Assets

| | |
|------------------------|--------------|
| Accounts payable | \$ 6,232 |
| Other liabilities | \$ 71 |
| Total liabilities | \$ 6,303 |
| Net Assets | |
| Unrestricted | \$ 2,486,389 |
| Board designated | \$ 134,718 |
| Total unrestricted | \$ 2,621,107 |
| Temporarily restricted | \$ 87,617 |
| Permanently restricted | \$ 266,500 |
| Total net assets | \$ 2,975,224 |

Total Liabilities and Net Assets \$ 2,981,527

Thank you for your support!



Back, L-R: Julia Szekely, Karen Cechner, Patti Gallagher, Valerie Sency, RN, Erica Stewart
Front, L-R: Blake Andres, Heng Wang, MD, PhD, Baozhong Xin, PhD
Not pictured: Christine Wensel, MS, LCGC

OUR STAFF

Blake Andres
Executive Director

Karen Cechner
Lab General Supervisor

Patti Gallagher
Business Manager

Valerie Sency, RN
Registered Nurse

Erica Stewart
Admin. Assistant

Julia Szekely
Lab Technician

Heng Wang, MD, PhD
CEO/Medical Director

Christine Wensel, MS, LCGC
Genetic Counselor

Baozhong Xin, PhD
Research and Technical Director

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Crist Yoder

Robert Yoder

Thank You to our **2014** Donors

Donor Recognition report from 1/1/2014 - 12/31/2014



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\$25,000 AND UP

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Development Center
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The Fred A. Lennon Charitable Trust
The Reinberger Foundation
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Shiloh Mennonite Community
Benefit Auction
Spartansburg Community Benefit
Auction
United Way Services of Geauga Co.
Ms. Frann R. Zverina

PACESETTER

\$10,000 – \$24,999

Anonymous
Affymetrix
Geauga Amish Loan Fund
Bessie Benner Metzenbaum Fund
of The Cleveland Foundation
Ohio Developmental Disabilities
Council
The Ortino Family Foundation
Susan & John Turben Foundation

HUMANITARIAN

\$5,000 – \$9,999

Boston Children's Hospital
Case Western Reserve University
Drs. Vichai and Patra Duangjak
Holmes County Association for
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Ms. Lea Kelly Rankin
Dr. & Mrs. Heng Wang

SAMARITAN

\$2,500 – \$4,999

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\$1,000 – \$2,499

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Western Reserve Farm Cooperative
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LPA
Mrs. Anna L. Zverina

PATRON

\$500 – \$999

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UP TO \$499

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Mr. & Mrs. Ronald Cechner



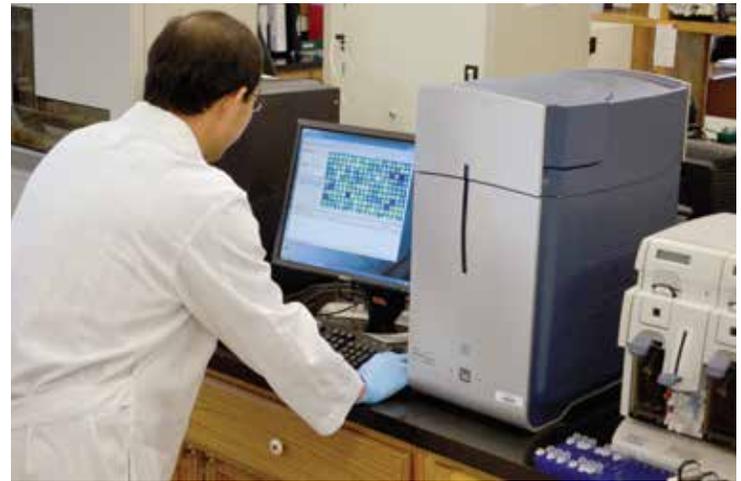


We are privileged to serve and learn from our special children and their families. Your help plays a big part in our continued ability to make a difference in their lives.

Thank you for your partnership!

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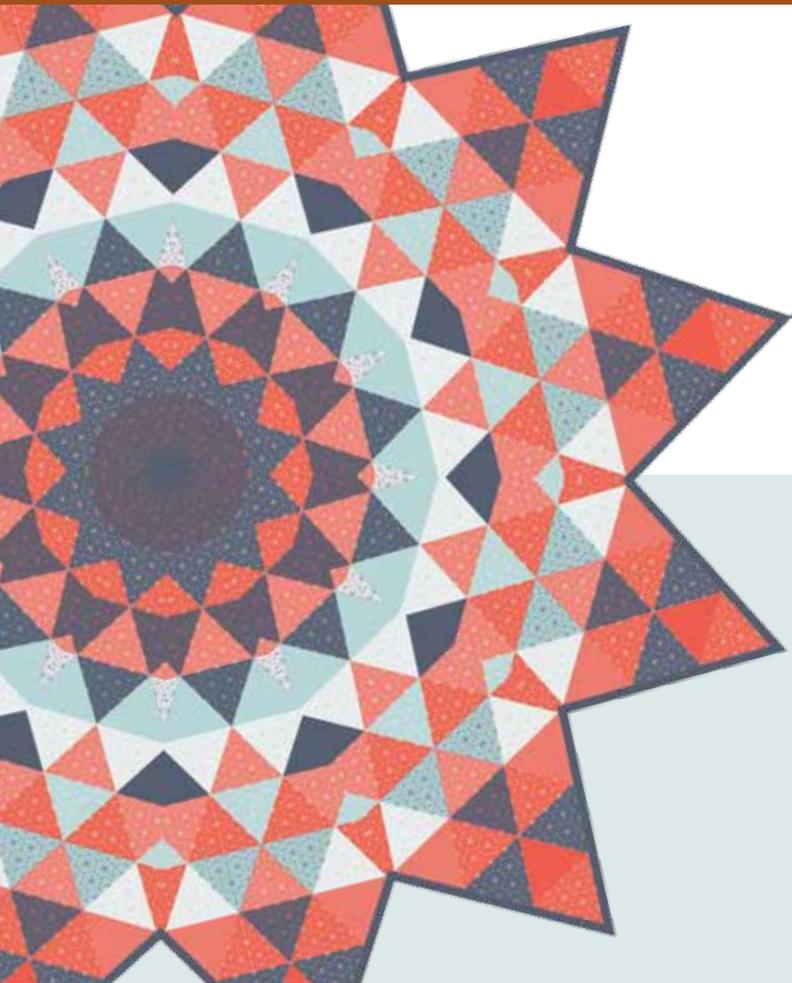


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