DDC clinic
Center for Special Needs Children

Fall 2023
Chronicle

Enhancing the quality of life for people with special needs caused by rare genetic disorders.

COMING SOON –

DDC Clinic Family Heart Center

DDC Clinic is pleased to announce that our highly anticipated Family Heart Center will open in early 2024.

The new DDC Clinic Family Heart Center will be dedicated to the diagnosis and treatment of genetic cardiac conditions in children and adults. Offering specialized care, the center will bring much-needed cardiology services to families in our area, as well as focus on education and research related to genetically-based heart diseases.

"This is a significant step forward in the growth of DDC Clinic and the scope of medical services we provide," said Dr. Wang, DDC Clinic Medical Director. "Heart disease is a leading cause of death in our country, and the incidence of cardiogenetic disorders in the Amish community is very high. Many cardiogenetic diseases go undetected, putting lives at risk. Our new Family Heart Center will not only improve the health of our community; our research efforts will also benefit families and health professionals around the world."

The new center will provide affordable testing, early diagnoses and onsite treatment for heart diseases such as cardiomyopathy and long QT syndrome. Patients will receive the same high level of compassionate, comprehensive care for which our clinic is known. If needed, an entire family can be seen at the same appointment, and multiple members of a family can be tested on the same day.

Patients diagnosed with cardiogenetic disorders will receive a highly personalized care plan to meet their unique medical needs. In addition, patients will benefit from having access to pediatric and adult cardiologists at DDC Clinic, providing them with the convenience of highly specialized care close to home.

> PAGE 4

BETHANNE'S STORY

This story was written by Bethanne's mother, Lena.

This is our family's story. We are Aden and Lena Troyer, and we had two daughters, Karen and Bethanne (deceased).

On November 23, 2016, we were blessed with a little girl, who we named Bethanne. She weighed 6 lbs. 7 oz., and was 19 ½" long. She was born at the Care Center in Middlefield, Ohio, and the doctor there told us she had a heart murmur.

We tested Bethanne right away for Troyer syndrome, as our first daughter Karen has the disorder. Bethanne's results came back, and to our relief, she didn't have Troyer syndrome. What we didn't know at the time was that Bethanne had cardiomyopathy.

For the most part, Bethanne was a happy baby, but she still had her fussy times. A week before we took her to the hospital, she started not eating well. On the last night she was at home with us, which was a Sunday, she cried almost every hour. We were with family that day, and Bethanne just kept on not wanting to eat and crying. We thought we'd take her to the doctor on Monday.

> PAGE 6

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 over 1,600 patient families in 35 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 160 different rare conditions.

Our in-house certified clinical genetics laboratory provides rapid, high quality and affordable testing. 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.

Executive Director's Corner

We Are Blessed

And God is able to bless you abundantly, so that in all things at all times, having all that you need will abound in every good work. — ***2 Corinthians 9:8***

Families with special needs children need compassion, understanding and support. They face daily challenges caring for loved ones. These moms are often full-time nurse and full-time mom. Are you willing to sacrifice a day here or there to help them? They'll greatly appreciate it. Please bless them with compassion and understanding to let them know you care about their burden.

2023 brought incredible blessings. Our fundraising events were above and beyond what we hoped. Many helped in numerous ways to make these events successful, and folks from different states supported our raffles and came to our auctions. Witnessing their generosity is truly humbling, making us realize how fortunate we are for the communities we live in. To all who generously supported us, we're grateful and blessed to have you as neighbors and friends. Thank you!

We've been very busy this year. New patients are coming from different communities, and we now have close to 1,700 patients. Newborn screening testing continues to grow. More young adults are coming in for carrier testing before getting married to learn if they're at risk of having children born with genetic conditions. GAP (Genetic Awareness Panel) is the preferred testing method and has proven to be everything we expected.

Our outreach location near Spartansburg, Pennsylvania will open soon and our Family Heart Center is set to open in early 2024. These two projects have generated much excitement from patient families. We're grateful for the incredible support we've received.

Thank you to our community, funders, volunteers, donors, board, and staff. You are all greatly needed and appreciated. Each of you is a blessing to us and the special children, families, and people we serve.

May you all be blessed,

Eli Miller

Eli Miller, Executive Director

Understanding Genetics

WHAT IS CARDIOGENETICS?

In recent years, there has been rapid growth in understanding the genetic basis of a wide variety of heart diseases. More and more research indicates that the majority of **sudden cardiac deaths (SCD)** at a young age are caused by an inherited cardiac disease, and many deaths can be prevented by timely recognition and preventative treatments.

Cardiogenetics is a new area of medicine that determines the genetic cause of heart disease. It often requires a team effort from primary care physicians such as pediatricians, internists or family doctors, along with the expertise of pediatric and adult cardiologists, clinical geneticists and genetic counselors.

Cardiogenetic disorders are generally inherited in families, meaning they're passed down from generation to generation. In contrast to many autosomal recessive disorders in the Plain community, the majority of cardiogenetic diseases are inherited in **an autosomal dominant manner**. This means that individuals with a mutation in one copy of a gene have the disease and all first-degree relatives of a patient have a 50% risk of inheriting that disease.

However, the matter is more complicated. For reasons we don't completely understand, some individuals have only mild or no symptoms from a disease, although they carry the same mutation their relatives have. *Variable expressivity, partial penetrance* and *incomplete penetrance* are medical terms doctors use to refer to these situations. We're studying these phenomena in the hope that one day we can help more people to "escape" these types of diseases.

Unfortunately, most cardiogenetic conditions are often severe, even lethal, and may go undetected before a heart attack or tragic event happens. Therefore, it's very important to learn more about these cardiogenetic diseases, as well as to raise awareness in our community by empowering individuals with better knowledge and understanding.

There are four groups of cardiogenetic conditions we usually deal with:

Inherited Cardiomyopathy

Cardiomyopathy is a disease of the heart muscle. The heart muscle can dilate, thicken, stiffen or not form completely. **Hypertrophic cardiomyopathy, dilated cardiomyopathy** and **restrictive cardiomyopathy** are common cardiogenetic disorders in our community. So far, we've identified several mutations related to cardiomyopathy in the genes *MYBPC3, DSP* and *TTN* in the Plain community.

Inherited Cardiac Arrhythmia

Those with inherited arrhythmias often have an abnormal heart rhythm that beats too fast or too slow, or irregularly. These many types of arrhythmias can increase the risk of a life-threatening arrhythmia and therefore require highly specialized care. The *KCNQ1* gene related **long QT syndrome (LQTS)** is one of the most common arrhythmic conditions in our community.

Connective Tissue Disorders

This includes **Marfan syndrome, Ehlers-Danlos syndrome** and several other genetic conditions. Connective tissues provide support and structure to other tissue and organs, thus these disorders may cause weakening of the arteries with some potentially life-threatening complications. Because connective tissue is in many different places in the body, the eyes, bones, joints and lungs can also be affected by these diseases.

Inherited Metabolic Disorders

In these conditions, an enzyme is not produced by the body or is produced in a form that doesn't work. The missing enzyme means that toxic chemicals build up in the body or an essential product may not be produced at all causing symptoms of heart disease. The common metabolic disorders causing heart problems in our community include **familial hypercholesterolemia, sitosterolemia, hereditary haemochromatosis, propionic acidemia and many mitochondrial disorders.**

With the presence of all of these cardiogenetic disorders, it's extremely important to have an early and accurate diagnosis and learn about possible treatments as soon as possible. It's also critical to have a comprehensive evaluation of all family members to assess each individual's risk, provide advanced genetic testing and cardiac assessments, and come up with personalized treatment plans which are often very valuable and even lifesaving.

The advanced genetic tests developed at DDC Clinic, which target specific mutations in our community and screen for a broad range of cardiogenetic disorders, have made early diagnosis and treatment very feasible, even before any signs and symptoms appear. Personalized medicine is in practice right here in Northeast Ohio.

Thanks for Supporting Our Auctions

Our community benefit auctions offer an enjoyable family outing, providing a day of food, fun and fellowship. But more importantly, our auctions provide the funds we need to sustain our clinic's mission and help special needs children get the medical care they need.

"Our auctions are our biggest fundraisers of the year." said Eli Miller, DDC Clinic Executive Director. "Proceeds from our auctions bring in as much as 25% of our annual budget. The success of these auctions is due in large part to the caring community members who host and support these events."

This year's auction season was a resounding success. We thank our hardworking friends in Shiloh, Spartansburg, PA and Middlefield for holding these benefit auctions and for their generous donations of goods, time and labor. We're truly blessed by the continued support of so many.

Patchwork Benefit Breaks Record

Thanks to our generous friends and supporters, this year's Patchwork Benefit was a record-breaker, raising more money than any previous year.

"We were pleased to see many friends this year – from longtime donors to new supporters. It's heartwarming to know that so many good people believe in our clinic," said Patti Gallagher, DDC Clinic Operations Director.

A celebratory gathering of 210 guests joined us in giving thanks, sharing our successes, and remembering the special children and families we've helped.

The evening included a presentation by Dr. Heng Wang, DDC Clinic Medical Director, who spoke about our clinic's achievements and our road to a bright future. Executive Director Eli Miller and board member Tom Stone also spoke about our clinic and why supporting our mission is so critical.

As a special thank you, each guest received a commemorative book celebrating our clinic's 20th anniversary entitled "Our Journey of Hope and Healing."

DDC Clinic Family Heart Center > from page 1

Located in the lower level of DDC Clinic, our Family Heart Center will house a waiting room and examination rooms. Equipped with new diagnostic medical equipment, the center will perform tests to detect heart disease such as EKG (electrocardiogram) tests and echocardiograms.

During its first year of operation, our center plans to develop a new diagnostic tool for the detection of cardiogenetic diseases. Known as the cardiogenetic awareness panel, or C-GAP, the panel will leverage the same technology as our genetic awareness panel (GAP) which is currently used to test for 220 genetic diseases found in the Amish community.

"CGAP will be an integral part of our new Family Heart Center," said Dr. Baozhong Xin, DDC Clinic Research and Technical Director. "No family should be unaware of their risk. With CGAP, we'll be able to use a patient's blood sample to screen for a large number of cardiogenetic diseases all at the same time, leading to faster diagnoses, earlier treatments and better outcomes."

Patient-oriented research has always been a major focus of DDC Clinic's work, and it will also play a significant role at the Family Heart Center. Our in-house team will work with our pharmaceutical and academic research partners toward developing new treatments for heart disease. What we discover from our research efforts will be integrated into our patient care and shared with physicians and scientists around the world.

The DDC Clinic Family Heart Center has been funded in part by grants from the Elisabeth Severance Prentiss Foundation and the Cleveland Foundation. The Prentiss Foundation awarded $900,000 to be disbursed over a 5-year period, while the Cleveland Foundation gave $75,000 toward support of the center's first year.

"We're so grateful to these foundations for their generous support and their investment in our future," said Eli Miller, Executive Director of DDC Clinic. "They've made it possible for us to bring this new heart center to our community and provide lifesaving diagnostic services and medical care to at-risk families."

Our clinic welcomes donations to support our Family Heart Center. To make a gift, please use the donation envelope in this newsletter.

Educating Families About Genetic Diseases

At DDC Clinic, we're committed to furthering personalized medicine and creating deeper understanding of genetic diseases within the Plain community. Our efforts help to "close the gap" by building bridges between families and the healthcare system.

One of the ways we've helped to close the gap is through our Genetic Awareness Panel (or GAP) which can simultaneously test for 220 rare genetic conditions found in the Amish population. Knowing their risk factors or having a diagnosis can be empowering to families.

We've also worked to narrow the gap through collaborations with major medical centers and pharmaceutical companies, such as Tenaya Therapeutics. Our clinic is currently participating in Tenaya's ongoing natural history study on the impact of *MYBPC3* genetic mutations on heart disease, including hypertrophic cardiomyopathy, in children.

"Cardiomyopathy is one the most common causes of sudden death," said Dr. Wang, DDC Clinic Medical Director. "A number of our patients are affected by cardiomyopathy, so it's very important to educate our families about the disorder. Being part of this large study enables us to better understand cardiomyopathy and share the knowledge we gain with our patient families. One of the meaningful ways we do this is through planned family gatherings, such as the one we had this summer."

Cardiomyopathy Family Gathering

On August 19, DDC Clinic hosted our second annual Hypertrophic Cardiomyopathy Family Gathering. The event brought together Amish families who lost children or had a child with a heart transplant due to *MYBPC3* gene-related cardiomyopathy. Adults who are affected by the disorder were also invited.

A total of 89 people came to the day-long educational program which provided families with an opportunity to learn about cardiomyopathy, share their stories and support one another in a comfortable, familiar setting.

Families gained an understanding of the genetics of cardiomyopathy and its diagnosis, treatment options and gene therapy. They also learned about living with cardiomyopathy and personalized care for children with the disorder. Updates on our clinic's participation in Tenaya's cardiomyopathy natural history study were also shared.

The Mast family with Dr. Wang at our Cardiomyopathy Family Gathering. Their older son had a life-saving heart transplant when he was a baby thanks to Dr. Wang's timely intervention.

"This gathering was an important program for families affected by cardiomyopathy. Not only did they learn more about this disorder, but hopefully, they walked away with a sense of hope and optimism," said Bea Torres-Fults, Clinical Nurse at DDC Clinic.

The day's agenda featured discussions, Q&A sessions and presentations by DDC Clinic doctors and staff, including Eli Miller, Executive Director; Dr. Heng Wang, Medical Director; and Dr. Vince Cruz, Geneticist and Internist.

Guest speakers from regional medical centers and Tenaya Therapeutics also spoke at the gathering. Physician speakers included Dr. John Tumbush, doctor of family medicine at University Hospitals Evans Medical Center; Dr. Jeffrey Bennett, pediatric cardiologist at Cleveland Clinic; and Dr. Wai Hong Wilson Tang, doctor of cardiovascular medicine at Cleveland Clinic. Speakers from Tenaya Therapeutics included Dr. Bardha Varfaj, Senior Director of Clinical Development and Wendy Borsari, Patient Advocate.

One of the day's memorable highlights was a personal story shared by the Mast family who have been friends of our clinic for many years. Two of Maria and Leland Mast's children have been affected by cardiomyopathy. The family traveled from Mississippi to speak about their family's story of battling cardiomyopathy and living through the pain of loss but also of joy.

"It's important to present educational programs such as this," said Eli Miller. "Bringing together medical professionals, researchers and patient families was a huge part of our founder's vision. We're privileged to present such an awesome gift to the rest of the world."

Recent Publications

DDC Clinic contributed to these prestigious scientific journals and online resources in 2022 – 2023.

Human Molecular Genetics
"Hemizygous variants in protein phosphatase 1 regulatory subunit 3F (PPP1R3F) are associated with a neurodevelopmental disorder characterized by developmental delay, intellectual disability and autistic features" (2023)

Neurobiology of Disease
"Characterization of Vps13b-mutant mice reveals neuroanatomical and behavioral phenotypes with females less affected" (2023)

GeneReviews
"GM3 Synthase Deficiency" (2023)

The American Journal of Human Genetics
"Bi-allelic variants in neuronal cell adhesion molecule cause a neurodevelopmental disorder characterized by developmental delay, hypotonia, neuropathy/spasticity" (2022)

Journal of Hepatology
"Genotype-phenotype relationships of truncating mutations, p.E297G and p.D482G in bile salt export pump deficiency" (2022)

Blood Advances
"Health-related quality of life and fatigue in children and adults with pyruvate kinase deficiency" (2022)

GeneReviews
"Prolidase Deficiency" (2022)

View more at ddcclinic.org/selected-publications/

BETHANNE'S STORY > from page 1

Bethanne's four cousins had passed away from hypertrophic cardiomyopathy. The cousins' mom, who was with us that Sunday, listened to Bethanne's breathing and said that she thought Bethanne acted like her babies who had cardiomyopathy. We decided to take Bethanne to University Hospitals Rainbow Babies and Children's Hospital in Cleveland. Once there, we told the doctors about Bethanne's cousins.

Bethanne was put into the pediatric intensive care unit. After the doctors checked her out, they told us her kidneys were shutting down, and they thought she had cardiomyopathy. We were with Bethanne at the hospital for a week. The first evening, they put her on a breathing machine, and then a couple of days later, they put a feeding tube in. One night they gave her more blood, and her coloring got better. The doctors told us that they could test for cardiomyopathy to see if it was genetic, but it would take some time to get the results.

I called Dr. Wang at DDC Clinic and told him what was happening. He said he still had some of Bethanne's blood from when she was tested for Troyer syndrome, and he told us the clinic's lab could check right into it. I didn't tell the doctors at Rainbow that we had called Dr. Wang.

The next day, Dr. Wang called us and said Bethanne had cardiomyopathy. When we told the doctors at Rainbow, they were very surprised to hear that Dr. Wang had tested for this and had the results so quickly.

The doctors and nurses at Rainbow gave Bethanne excellent care, but her condition grew worse. On Saturday evening, the doctors removed the machines from Bethanne. She passed away Sunday morning, March 19, 2017 at 9 a.m. We had three months and 24 days with our sweet daughter.

My husband and I are both carriers of the cardiomyopathy gene. Some of my family and my husband's family are also carriers. We thank Dr. Wang and his team for everything they did for us and still do for us.

Today, our daughter Karen is the sunshine of our lives. We miss our Bethanne, but we hope to meet again someday.

God's blessing to everyone,
Aden, Lena, and Karen Troyer

Visiting Professor Comes to DDC Clinic

Dr. André Bachmann joined us this summer as a visiting professor from Michigan State University (MSU). Currently on a six-month sabbatical, he's working on a research project with Dr. Wang, Dr. Cruz and Dr. Xin.

A tenured Full Professor of Pediatrics and Associate Chair for Research at MSU, Dr. Bachmann is also the Scientific Director and co-founder of the International Center for Polyamine Disorders in Grand Rapids, Michigan.

For most of his career, he focused on ODC/polyamines and drug development in oncology. He also worked in the field of genetics with Dr. Caleb Bupp. Together, they discovered a new ODC1 gene-linked neurodevelopmental disorder, known as Bachmann-Bupp Syndrome.

Although he came to DDC Clinic to do research, Dr. Bachmann was also interested in the Amish culture, having grown up in the German-speaking part of Switzerland.

Referring to DDC Clinic, Dr. Bachmann said, "I love how close the doctors' offices are and how they're able to share ideas daily, leading to more impactful translational science."

Reflections on 2022

As we look back at another year, we're filled with gratitude and awe that we're able to do such privileged work. We remember the special children we cared for and the generous friends who supported us throughout the year. They have all touched our hearts.

2022 was a major milestone – DDC Clinic's 20th anniversary. What an incredible journey it has been. What started as a modest medical practice, with its humble beginnings, has grown into a respected, world class medical and research facility. Along the way, we've made a difference in the lives of many special children here in our community and around the world.

In 2022, Eli Miller began his second year as our executive director. Under his leadership, our ties to the Plain community grew even stronger, and their trust in our work and belief in our mission grew deeper.

It was a year in which we saw growth in the area of patient care. We had 1,030 total patient visits, and of that number, 137 were new patient visits. Families traveled from out of state and across the country to bring their children to our clinic.

Our Patient Assistance Program also grew, saving our community $4,500,000 by providing 275 families in need with free or reduced-cost prescription medicines, specialized baby formula and medical supplies.

On another front, Dr. Wang and Dr. Xin continued to make important strides in 2022, diagnosing patients with previously undiagnosed conditions, working on major research studies, and sharing their findings in four scientific publications and online resources.

We also hosted educational programs related to rare genetic diseases, including our first Cardiomyopathy Family Gathering which was attended by families who lost children or had a child with a heart transplant due to MYBPC3 gene-related cardiomyopathy.

In staffing news, nurse Valerie Sency was promoted to Clinical Charge Nurse, and we welcomed Bea Torres-Fults to our nursing team. Together, they provide compassionate care to all of our patients, from infants to adults.

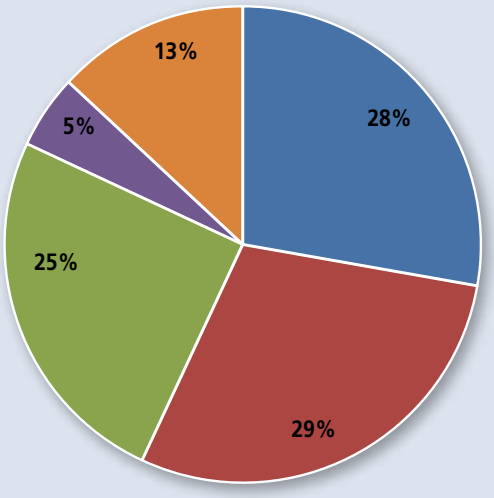
2022 was also the year that we eagerly looked toward our future, laying the groundwork for our new Family Heart Center and our much-needed satellite clinic in Pennsylvania.

Our advances in patient care, research and education were possible because people like you were there to help. With your support, we were able to provide hope to parents and life-changing care to their special needs children.

Thank you for putting your faith and trust in us. We're truly grateful to all of you.

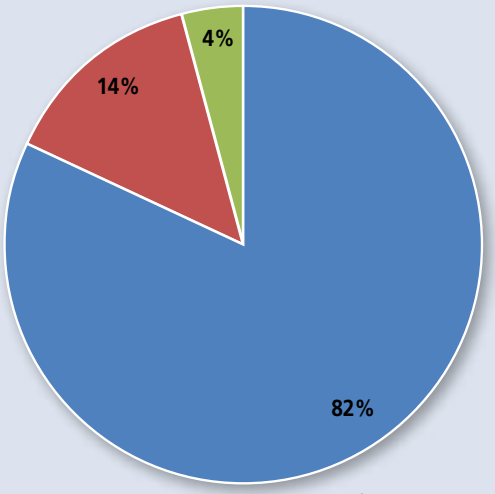
2022 Financial Report

Total Revenue $2,321,797



Corporate, Foundation and Group Contributions	$652,470
Fundraisers	$665,104
Clinical and Laboratory Services	$568,894
Research Collaborations	$123,089
Individual Giving	$312,240

Total Expenses $1,687,962



Program Services	$1,385,687
Fundraisers	$234,904
Management & General	$67,371

DDC clinic
Center for Special Needs Children

14567 Madison Road
Middlefield, Ohio 44062

440-632-1668
ddcclinic.org

Enhancing the quality of life for people with special needs caused by rare genetic disorders.