Luanne Pinedo Madden, David Madden, and Holly Machado hosted the 2nd Fresno Dystonia Zoo Walk. Many thanks to Drs. Melvin Helm and Harrol Hutchison for providing remarks.

Sue Baron and family organized the Southern New England Dystonia Zoo Walk. Mandi Guilfoyle spoke about her experiences with dystonia and deep brain stimulation.

Hundreds gathered for the 2nd Twin Cities Dystonia Zoo Walk organized by Shanna and Brad Schmitt, Billy McLaughlin, and members of the Minnesota Dystonia Support Group. Speakers included St. Paul Mayor Chris Coleman and dystonia researcher Joshua Aman, PhD.

400+ people supported the 4th Detroit Dystonia Zoo Walk on July 16 organized by DMRF Community Leadership Council Member Rosemary Young. Families traveled from across the state to attend, and members of multiple Michigan dystonia support groups assembled teams. Guest speakers included Drs. William Dauer and Ellen Air.

The 2nd Portland Dystonia Zoo Walk was organized by Dee Linde and members of the Portland, Oregon & Southwest Washington Dystonia Support Group. Special guests included DMRF Leadership Chair Paula Schneider and Stacey Jochimsen from the office of Senator Jeff Merkley.

The 3rd St Louis Dystonia Zoo Walk organized by June Tritley took place August 26, promoting much-needed awareness in the metro area and raising funds for research.

On September 9, 500+ people gathered for the 5th Cincinnati Dystonia Zoo Walk organized by DMRF Community Leadership Council Member Melissa Phelps. DMRF Executive Director Janet Hieshetter presented Melissa with an award to commemorate the event’s milestone anniversary. The Zoo Walk was followed by “Go Blue for Dystonia Day” in Gallatin, Kentucky and surrounding counties on September 28.

DMRF Board Member Pamela Sloate organized the 3rd Dystonia Bronx Zoo Walk on September 10, attracting 500 people. Neurosurgeon Dr. Brian Kopell provided remarks.

The Flanagan Family, who created the original Dystonia Zoo Walk, continued their support of the DMRF with the 6th Cleveland Dystonia Zoo Walk on September 24. Many thanks to the organizing committee: DMRF Community Leadership Council Member Karen Flanagan, Jane Ann Flanagan, and Gale Flanagan.

The 4th Pittsburgh Dystonia Zoo Walk was a great success on September 23 thanks to Western Pennsylvania Dystonia Support Group co-leaders MaryRae Nee, Ed Cwalinski, and their supporters. Over 450 people participated. Chris Mack
of 93.7 The Fan/KDKA-FM Pittsburgh hosted and Dr. Mark Richardson provided remarks.

DMRF Community Leadership Council Member Jim Metherell organized the 5th Toss4Dystonia Cornhole Tournament in Buffalo on September 16 to raise awareness and research funds. Jim was presented with an award from the DMRF to commemorate the event’s milestone anniversary. Guest speakers included fellow Community Leadership Council Member Ginny Bryan.

Cards Against Dystonia Casino Night on September 9 in Minnesota invited participants to try their luck at cards and a sprawling silent auction in support of the DMRF. Many thanks to Ben Humphrey and Mike Erickson for organizing this event in honor of mother/aunt Donna Driscoll who serves on the DMRF’s volunteer Board of Directors.

The 3rd Putnam Dystance4Dystonia Walk organized by the Gardner Family took place September 23 in Connecticut. The event was spearheaded by siblings Brian Gardner and Erica Schulman in honor of their mother Susan Gardner.

Teams of “dystonia detectives” combed downtown Chicago for clues in the Hunt for a Cure for Dystonia, a scavenger hunt to promote greater awareness and support the DMRF organized in July by Beth Farber and Steve Laser. Special thanks to Joel Farber and Harriett Farber. The Farber family also organized the Chicago Basket Bash in October to raise funds in support of the DMRF. The family advocates for dystonia in honor and memory of Shari Farber Tritt who developed severe dystonia as a child.

The Indy Hunt for a Cure for Dystonia took place October 1 along the Indianapolis Canal Walk. The organizing committee included Chelsi Christman, Sally Ernstberger, Sarah Ernstberger, and Sunshine Fox.

Sheila Killham, leader of the Cedar Rapids Dystonia Support Group, organized the Marion, Iowa Dogs for Dystonia Walk on October 7.


Many thanks to Kohl’s Care Associates in Action and Target for providing Zoo Walk volunteers.

The DMRF thanks National Sponsors Allergan and Merz for their generous event support.
Inside this Issue

8 Finding a Cure is a Family Affair
Myoclonus-Dystonia Research Program

12 Act Now to Give Later
Learn about Brain Donation & Legacy Society

14 Discovery through DNA
Update on Dystonia Genetics

20 Controlled Explosions
Tiago Valente Unleashes Dystonia into Sculpture

22 Family Profile
Meet the Shaughnessys

On the Cover:
The human brain is a spectacularly complex system, and research to better understand a neurological disorder like dystonia must be strategic and multifaceted. One of the qualities that makes the DMRF unique is the close rapport between families and researchers. The DMRF was conceived on the idea that the relationship between the Board of Directors and the Medical & Scientific Advisory Council should be collaborative. Every member of the DMRF Board of Directors is personally affected by dystonia and passionate about knowing what research is being done, how we can support it, and where to find the expertise required for continued progress toward a cure.

Read about the exciting discoveries clinical and basic researchers are making in dystonia genetics on page 14. We’re also proud to highlight the Myoclonus-Dystonia Research Program on page 8.

Partial support of the Dystonia Dialogue is provided by educational grants from Allergan Foundation and Merz.

The Dystonia Dialogue is the magazine of the Dystonia Medical Research Foundation (DMRF). It is published three times a year to provide information to individuals affected by dystonia, family members, and supporters of the DMRF.

The Dystonia Medical Research Foundation (DMRF) is a non-profit, 501c(3) organization founded in 1976. The mission is to advance research for more effective treatments and a cure, to promote awareness and education, and to support the well being of affected individuals and families.

Dystonia Medical Research Foundation
One East Wacker Drive • Suite 1730
Chicago, Illinois 60601-1980
Phone: 312 755 0198 • 800 377 3978
Email: dystonia@dystonia-foundation.org
Web: www.dystonia-foundation.org

The Dystonia Dialogue reports on developments in dystonia research and treatments but does not endorse or recommend any of the therapies discussed. Individuals are urged to consult a physician with questions and concerns about their symptoms and care.

Staff
Janet L. Hieshetter
Executive Director
Veronica Diaz
Information Coordinator
Shannon Dick
Manager of Community Engagement
Debbie Durrer
Director of Development
Jessica Feeley
Editor and Special Projects
Jennifer McNabola
Director of Finance
Martha Murphy
Brain Bank Liaison
Emma Pinto
Development Manager
Jody Roosevelt
Science and Technology Manager
Jan Teller, MA, PhD
Chief Scientific Officer

Printed in the USA.
© Dystonia Medical Research Foundation
Dear Friends,

The DMRF is more than an organization dedicated to curing dystonia; it’s a place to belong when dystonia turns your life upside down. The DMRF is committed to providing a safety net of information and support for affected individuals and families while doing everything possible to advance research toward a cure.

We hear often from our members how contact with the DMRF was first time they felt understood, the first time they found answers: how to locate a qualified physician, a clear explanation of their dystonia diagnosis, an understanding of treatment options. In keeping with the DMRF’s commitment to providing the community with timely, accurate information, we have offered numerous meetings throughout the year including two dystonia symposia and 11 patient education forums. Videos from expert presentations are available for viewing on our YouTube channel. We are pleased to offer a number of new and updated brochures through our website and local support groups. The Dystonia Dialogue has a circulation of 49,000 copies an issue.

One of the DMRF’s highest priorities is providing connection to individuals and families who feel alone. DMRF online groups are often the first place our members communicate with others who know dystonia firsthand, and these groups become a lifeline for those who are geographically or socially isolated. At nearly every awareness, advocacy, or fundraising event, we meet at least one person who had never met someone else with dystonia face-to-face until that day. We often hear from attendees of DMRF educational meetings and support groups how validating it is to meet other people who share the diagnosis. DMRF’s dedicated support group leaders are on track to have organized 120 meetings across the country this year, welcoming individuals with all types of dystonia.

Thank you for supporting the DMRF. We appreciate the time you make to join us at events, attend support group meetings, and request information or assistance. The strength of the Foundation is the individuals and families who share our vision to cure dystonia and reach out to join us.

We cannot do it without you.

Sincerely,

Art Kessler
President

Janet L. Hieshetter
Executive Director

Your Gift is TWICE as NICE
Donate today and every dollar you give will be matched by a generous anonymous donor. Find details at dystonia-foundation.org/2017match or see the enclosed donation envelope.
DMRF-Funded Investigators Evaluate AZD1446 as Possible Dystonia Drug

DMRF and Cure Dystonia Now jointly supported a research investigation to explore whether a drug called AZD1446 could potentially provide relief for dystonia patients with fewer side effects than existing medications. Although AZD1446 did not demonstrate therapeutic effects in animal and cell models of DYT1 dystonia, the investigation produced important findings.

Experiments verified that dystonia is associated with abnormal neuron signaling in the striatum, part of the basal ganglia deep in the brain. This abnormal activity causes an imbalance of two neurotransmitters critical for muscle control: dopamine and acetylcholine.

AZD1446 belongs to a class of drugs called nicotinic agonists. These drugs mimic the action of acetylcholine in the brain. While the data indicate that AZD1446 is not a particularly promising candidate for development as a treatment for DYT1 dystonia, nicotinic agents do appear to have potential. The study suggests that nicotinic agents should continue to be studied to help better understand dystonia and identify new therapies.

DYT1 dystonia typically begins around age 10 years with the twisting of a foot or arm. Symptoms tend to progress to involve additional limbs and the torso. The symptoms tend to be less severe the later in life they start and if they start in a hand or arm. About 30% of individuals who have the DYT1 genetic mutation will develop dystonia. If a person does not manifest symptoms before the age of 28 years, they will usually remain symptom free for life—even if they have the DYT1 mutation.

The investigation was led by Antonio Pisani, MD, PhD, University of Rome Tor Vergata (Italy) and David Standaert, MD, PhD, University of Alabama Birmingham.


DYT6 Dystonia Protein Regulates Process Critical for Neuron Maturation

A team of investigators led by William Dauer, MD of University of Michigan has made new discoveries about DYT6 dystonia, which affects children. DYT6 dystonia occurs when the body cannot properly produce a protein called THAPI, whose role and function in cells is unknown. Using a mouse model, Dr. Dauer and colleagues discovered that THAPI is essential for myelination, a process during brain development that forms a protective coating around neurons. Myelination enables neurons to transmit signals more efficiently and is vitally important to healthy brain functioning. A number of diseases, including multiple sclerosis, are caused by damage to the protective myelin coating.

This study establishes a role for THAPI at the start of the myelination process and implicates abnormal timing of myelination in the pathogenesis of DYT6 dystonia. The findings point to a direct link between myelination and childhood-onset dystonia providing new insights into how and why certain types of dystonia might develop at specific stages of brain development.

Onset of DYT6 dystonia is usually in the late teens. Symptoms of DYT6 may occur as generalized dystonia or remain focal to a specific part of the body. Symptoms typically affect muscles groups above the neck: tongue, vocal cords, and face. About 40% of individuals who have a DYT6 mutation will develop dystonia.

The DMRF is proud to have supported this work. For an extended interview with Dr. Dauer about his groundbreaking research and longtime relationship with the DMRF, visit dystonia-foundation.org/dauer_interview

Dystonia Investigators Awarded DOD Funding

Did you know the Department of Defense (DOD) funds dystonia research? It does, but only because dystonia advocates fight every year to make sure dystonia is included in the DOD Congressionally-Directed Peer Review Medical Research Program. In Fiscal Year 2017, $2,600,000 was awarded to four dystonia investigators:

- David Peterson, MD, University of California at San Diego
- Mark LeDoux, MD, PhD, University of Tennessee Medical Center
- Cynthia Comella, MD, Rush University Medical Center
- Un Kang, MD, Columbia University Medical Center

This was possible because of the dedicated efforts of dystonia advocates who pushed Members of Congress for federal research funding. If you would like to help make sure the DOD continues to support dystonia investigators, join the Dystonia Advocacy Network. Learn more at dystonia-advocacy.org

Gimme 5

$5DollarCure4Dystonia has Raised $11K for Research

Scientific breakthroughs are unpredictable. What if your $5 donation made the difference to find a cure for dystonia? This is the premise behind $5DollarCure4Dystonia launched in February by dystonia awareness all-stars Mike Delise and Jason Dunn of Warren, Michigan. Nearly $11,000 has been collected via the website to date! Funds raised through $5DollarCure4Dystonia support dystonia research.

“The only way I know we are going to find a cure is by having a miracle happen or by research. I’m not waiting around for a miracle, and research costs money,” explains Mike. “The more we work together the faster we will find a cure. I feel that this website belongs to the whole dystonia community, and if we work together we could really raise some money and awareness. I want to thank everyone who has donated and shared the website.”

“It may seem like only $5, but you can’t really put a price tag on the love and support from family and friends,” adds Jason “I know for a fact that people who never heard of dystonia have donated, because a couple of them have messaged me.”

Deena Centofanti of Fox2 Detroit and several news outlets have covered the campaign and helped promote greater dystonia awareness throughout the metro area. Mike worked with the Governor’s Office to secure a proclamation acknowledging Dystonia Awareness Month in Michigan. The City of Warren lit up city hall in blue to recognize Dystonia Awareness Month.

Mike became passionate about dystonia advocacy after meeting Jason, a high school friend of his two daughters. Jason has lived with severe dystonia since childhood. Now in his 30s, he has undergone six brain surgeries and countless medications, injections, and medical consultations. While dystonia has taken his ability to speak and walk freely, he lives independently, travels, and is an active dystonia advocate, appearing on nationally broadcast television programs and in numerous media stories. Mike and Jason were presented with DMRF Star Awards for their tireless awareness efforts.

For more information about $5DollarCure4Dystonia and to donate, visit 5dollarcure.com
Finding a Cure is a Family Affair
Myoclonus-Dystonia Research Program Fuels Discoveries Beyond Rare Disorder

The Myoclonus-Dystonia Research Program is a partnership between the DMRF and the Brown Family Foundation (BFF) focused on advancing knowledge of this little-known movement disorder. Although myoclonus-dystonia (M-D) is considered a rare disease, research on M-D is making progress in areas relevant to other dystonias: molecular biology, genetic risk and inheritance patterns, non-motor symptoms, and quality of life.

Connie and Jim Brown established the BFF to make a difference in health and education, and invited their six children to serve with them on the Board of Directors. “When our daughter Ginny received a firm diagnosis of myoclonus-dystonia in her early 20s, we had many questions that we needed to answer,” says Judith Bryan, Connie and Jim’s daughter. “The BFF went right to work to find the best partner to fund medical research. DMRF was the answer, and over the last decade we have forged a fruitful and warm relationship.”

The Myoclonus-Dystonia Research Program funds innovative research projects and workshops that bring experts together to review what is known about M-D and assess next steps for the field. Judith explains the BFF’s goals were clear from the beginning: “First, because Ginny had received several diagnoses over the years, we wanted to expand the understanding of the disease across the medical horizon in order to help other patients receive an early and accurate diagnosis for treatment and support. Second, we were all too well aware of the psychosocial difficulties associated with M-D and the emotional demand it places on patients and families. We wanted patients and families to have access to accurate, current, and helpful information as they navigate diagnosis and appropriate treatment. Third, and most significantly, we wanted Ginny and others to receive the very best treatment available—and we wanted to keep pressing for even better interventions.”

Since 2009, the Myoclonus-Dystonia Research Program has held three M-D-focused scientific meetings and funded 11 research projects.

“The BFF is inspired by the commitment of clinicians and researchers to make the disease better known through publications and international conferences,” says Judith. “We are heartened by the studies that focus on both basic defects and clinical interventions. You can imagine how grateful Ginny, my husband Rick, and I are for the generosity of the BFF—especially my parents Connie and Jim Brown—and the energetic and competent commitment of the DMRF. There is much work to do, but we have confidence that the DMRF will stay the course with us.”

Recent Discoveries
Research on M-D is conducted at centers around the world and focused on developing a more thorough understanding of the disorder while seeking breakthroughs in genetics and
What is Myoclonus-Dystonia?
M-D is characterized by a combination of rapid, brief muscle contractions (myoclonus) and sustained twisting and repetitive movements that result in abnormal postures (dystonia). Non-movement features may include obsessive compulsive disorder, depression, anxiety, personality disorders, alcohol abuse, and panic attacks. Symptoms typically begin in childhood or adolescence, and rarely in adulthood. M-D may affect multiple members in a family or occur without a family history. Little is known about how prevalent M-D is within the United States or elsewhere. M-D affects males and females equally across different ethnicities and nationalities.

About 30-40% of individuals with M-D have alterations in the DYT11/SGCE gene. Children who inherit an SGCE mutation from their father are very likely to develop symptoms, while only 5% of children who inherit the mutation from their mother will develop symptoms. It is possible to be a carrier of the mutation without having M-D symptoms. Carriers can also pass along the mutation to their biological children.

therapeutics. Below are just a few recent advancements, many of which were supported by the Brown Family Foundation.

• New gene mutations. The first gene associated with M-D was DYT11/SGCE. Close to 80 different pathogenic gene variants or deletions in the gene have been reported.

• Other genes have been associated with M-D: DYT1/TOR1A, DYT15, DYT26/KCTD17, RELN, and possibly CACNAIB.

• Dysfunction of the cerebellum contributes to the pathophysiology of M-D as well as other types of dystonia including focal and DYT1/TOR1A dystonias.

• The combination of myoclonus and dystonic symptoms seem to reflect specific dysfunctions in the M-D brain that set it apart from isolated (primary) dystonias.

• A recent clinical trial demonstrated that zonisamide improves myoclonus in individuals with M-D.

• Deep brain stimulation (DBS) is being applied with success in increasing numbers of M-D patients.

Continued on page 10
Myoclonus-Dystonia Research Projects 2017

The following research projects were initiated this year thanks to support from the Brown Family Foundation. Each of these projects represents a step toward a better understanding and improved treatment options for M-D and other dystonias.

An International Study to Investigate the Non-Motor and Psychological Impact of Myoclonus-Dystonia
Kathryn Peall, MD, Cardiff University (United Kingdom)
The objective of this project is to survey a large, international group of individuals with M-D. The study will assess a broad spectrum of non-motor symptoms and quality of life with use of a standardized questionnaire.

Myoclonus-Dystonia, a Study of Motor and Non-Motor Symptoms: Is there a Role for Serotonin?
Marina A.J. de Koning-Tijssen, MD, PhD, University of Groningen (The Netherlands)
This study will compare the present symptoms of M-D patients to the symptoms they had 10 years ago to assess how the symptoms evolve over time. Since M-D patients frequently experience non-motor symptoms including psychological difficulties, sleep disturbances, and fatigue, it is believed these symptoms are part of the disease, not secondary consequences, and may result from an altered metabolism of a brain neurotransmitter called serotonin. This study will analyze serotonin levels in the blood of M-D patients, healthy controls, and cervical dystonia patients. A genetic study of serotonin-related genes will also be performed.

Identification of Neuronal Mechanisms of Agency in Myoclonus-Dystonia
Yulia Worbe, MD, PhD, Salpetriere Hospital (France)
The sense of agency, which refers to the experience of initiating and controlling one’s actions, is an integral part of cognitive movement control. In this study, investigators aim to show that an altered sense of agency is a common mechanism across the different types of dystonia by investigating M-D patients. Investigators will use a battery of computerized tests, the results from which will be integrated with brain imaging to identify brain pathways implicated in the sense of agency. The goal is to provide a new perspective on the fundamental mechanism of M-D and direct involvement of cognitive processes in dystonia.

A Comparative Study of Myoclonus-Dystonia Deep Brain Stimulation Efficacy in the US and Europe
Marie Vidailhet, MD, Salpetriere Hospital (France)
This retrospective study will compare the efficacy and impact of deep brain stimulation (DBS) in M-D patients in Europe and the United States. The project will systematically assess the impact of DBS on patients’ lives and should provide novel insight into DBS targets, programming, and protocols.

Myoclonus-Dystonia Patient Registry
Kathryn Peall, MD, Cardiff University (United Kingdom)
Patient registries centralize clinical information that may be helpful to investigators for future studies. Dr. Peall is establishing a registry to support ongoing and future M-D research.

Banking of Myoclonus-Dystonia Biological Materials
Ebba Lohmann, MD, University of Tubingen (Germany)
A complementary project to the M-D patient registry described above will collect, catalog, and store relevant biological M-D materials obtained from patients. Biorepositories store and distribute biological samples (for example, blood, DNA, and cells) to support future scientific investigation.
DYSTONIA

FREQUENTLY ASKED QUESTIONS

The DMRF is available by phone, email, web, and social media to those looking for information and support. Support groups and online groups are also valuable resources for individuals seeking assistance. These are among the most common questions received.

What is Dystonia?
Dystonia is a neurological disorder that causes involuntary muscle contractions. These muscle contractions result in abnormal movements and postures, making it difficult for individuals to control their body movements.

Dystonia can affect any region of the body including the eyelids, face, jaw, neck, vocal cords, torso, limbs, hands, and feet. Depending on the region of the body affected, dystonia may look quite different from person to person. The movements and postures may be painful.

In addition to abnormal movements, depression and anxiety are common non-motor symptoms of dystonia.

Who is Affected by Dystonia?
Dystonia affects men, women, and children of all ages and backgrounds. Dystonia is the third most common movement disorder. Conservative estimates suggest dystonia affects no fewer than 250,000 people in the United States and potentially millions worldwide.

What Causes Dystonia?
There are many causes for dystonia. Dystonia may occur due to an inherited or new genetic mutation. Dystonia may also result from changes in brain activity caused by another health condition such as Parkinson’s disease or traumatic brain injury. Certain drugs are known to cause dystonia. However, for many people who develop dystonia, there is no identifiable cause.

Are There Different Types of Dystonia?
Yes. Dystonia can take many forms. Dystonia may affect a single body area or multiple areas throughout the body. The movement symptoms of dystonia may be chronic or occur periodically. Dystonia may be the only movement symptom a person has, or it can occur with other abnormal movements (for example, tremor). Dystonia may occur by itself or as a symptom of other diseases.

The age at which symptoms begin may influence prognosis and treatment. Dystonia that begins in childhood is more likely to involve multiple body parts and more likely to be associated with additional movement and neurological symptoms. Dystonia that develops during adulthood is more likely to remain focal to a specific body area.

What Type of Doctor Treats Dystonia?
Seeking treatment from an appropriately trained medical team, including a movement disorder specialist, is critical to living well with dystonia. A movement disorder specialist is a neurologist with training in the diagnosis and treatment of movement disorders such as dystonia. Physiatrists, otolaryngologists, speech-language pathologists, and neuro-ophtalmologists may treat specific dystonias that fall under their specialties.

Is Dystonia Fatal?
No, dystonia is almost never fatal. Dystonia does not affect vital organs such as the heart.

In extreme cases, the development of increasingly frequent or continuous episodes of severe dystonia may cause a medical emergency called status dystonicus. If untreated, this rare condition can cause life-threatening complications. Status dystonicus is a treatable condition and, with prompt medical attention, symptoms typically can be brought under control.

What Research is Happening?
Investigators are working every day to improve dystonia treatment options and find a cure. For detailed information about the DMRF’s research efforts, including how you can make a difference by participating in research, visit dystonia-foundation.org/research

Interviews with dystonia researchers are available for viewing at youtube.com/FacesOfDystonia

Find DMRF brochures for mail order or free download at dystonia-foundation.org/brochures
While the DMRF cannot operate without the generous cash donations received every day, there are some gifts for which we are happy to patiently wait. You can make a commitment of support to the DMRF today that is fulfilled in the future.

**JOIN THE LEGACY SOCIETY**

The DMRF established the Legacy Society to acknowledge those who have made a lasting commitment to supporting dystonia research by naming DMRF in their estate plans. By including the DMRF in your estate plans, you help to ensure that dystonia research will be supported until we achieve our mission to find a cure. Your legacy can be a future free from dystonia.

**Types of Gifts**
- Bequest in a will
- Charitable gift annuity
- IRA or retirement plan
- Revocable trust
- Life insurance policy
- Charitable remainder trust
- Retirement fund
- Charitable lead trust

**Advantages of Planned Giving**

- **FLEXIBILITY.** You can select the planned gift that is best for you.
- **TAX BENEFITS.** You may be eligible for tax savings.
- **GENEROSITY.** You may be able to contribute more in the future that you can today.

It is not necessary to disclose the value of a planned gift, though we do appreciate being informed that you are considering the DMRF in your estate planning.

**How do I learn more about joining the Legacy Society?**
Contact us at legacysociety@dystonia-foundation.org or call 800-377-3978.

“It shows how committed he was to the DMRF. Jim knew the DMRF is a dedicated and professional organization that is going to use the money wisely.”

—Caroline Davidson’s late husband Jim Kilik left a generous bequest to the DMRF to support research. The DMRF created the James C. Kilik Memorial Research Awards in his honor.
...the amount of data available on the pathological features of dystonia is surprisingly limited. Even in genetically defined forms of the disorder there are at most a few cases which have been closely studied, and there is much still to be learned about the structural features of dystonias.”

From “Update on Pathology of Dystonia,” by David G. Standaert, MD, PhD, Neurobiology of Disease

### FAQ

- **Who can register?** Individuals with dystonia and biological relatives who reside in the 48 contiguous USA.
- **What might prevent someone from becoming a brain donor?** Unfortunately, certain health conditions such as HIV or hepatitis preclude individuals from donating.
- **Can I register if I have had deep brain stimulation (DBS)?** Yes.

### How Do I Get Started?

1. Let us know you are interested in learning more about registering as a brain donor by visiting dystonia-foundation.org/brain or calling 800-377-3978.
2. Inform your next-of-kin or legal representative that you are registering to donate your brain to dystonia research.

The DMRF works in partnership with the Harvard Brain Tissue Resource Center (HBTRC) at McLean Hospital in Belmont, Massachusetts.
Novel sophisticated research tools are providing investigators new ways to explore the genetics of dystonia. Researchers have the ability to quickly sequence individual genes, analyze whole genomes, and analyze gene expression patterns. Individuals and families who volunteer for genetic studies contribute invaluably to research progress.

Discoveries are happening at a rapid rate, and the genetic landscape of dystonia is growing increasingly complex. This complexity is revealing fascinating new data about the origins of dystonia and opening up opportunities for further research. The ultimate goal of better understanding dystonia genetics is the development of treatment and prevention methods.
How Many Dystonia Genes?
More than 200 genes have been linked to dystonia. Detrimental changes in some of these genes cause specific types of dystonia such as DYT1/TOR1A, DYT6/THAP1, and DYT11/SGCE. Many of the 200 genes are linked to neurodegenerative and metabolic diseases for which dystonia is often a symptom.

Genes cause dystonia when they contain specific mutations (gene variants) that alter the gene. A wide variety of genes and mutations contribute to the complexity of hereditary dystonias. In the case of DYT1/TOR1A, nearly all patients have the same mutation in the gene. By contrast, about 100 different mutations have been reported in patients with DYT6/THAP1 dystonia.

Christine Klein, MD heads the University of Luebeck’s Institute of Neurogenetics and is the Principal Investigator of the Institute’s Translational Neurogenetics section. She is a past member of the DMRF Medical & Scientific Advisory Council and much of her research focuses on inherited dystonias. Dr. Klein explains: “First of all, it can often be difficult to clearly distinguish between a truly disease-causing mutation and a benign variant that is simply very rare. We all carry a large number of variants in our genes which account for the differences between people and very few, if any, cause disease. Second, many of the recently identified genes were found in small families and represent the ‘most likely candidate’ among several genes that harbor variants and possible mutations. This has led to a situation where some dystonia genes could not be confirmed and it can thus be challenging for neurologists and geneticists to interpret genetic testing results which may be less clear-cut than one would have hoped for.”

Recent Advancements
Discoveries in dystonia genetics are providing answers and inspiring new questions. Here are just a few examples:

One Gene, Three Disorders - Rapid-onset dystonia parkinsonism (RDP) is characterized by abrupt onset of dystonic and parkinsonian symptoms with possible psychiatric features. RDP is caused by mutations in DYT12/ATP1A3. Different mutations in this same gene cause two other neurological disorders: alternating hemiplegia of childhood and CAPOS syndrome. Researchers are trying to determine how mutations in the same gene can produce such neurologically distinct disorders. These discoveries demonstrate how complex medical genetics can be.

New Cause for Pediatric Dystonia - A newly discovered dystonia gene, DYT28/KMT2B, may be among the most common causes of childhood onset generalized dystonia. The expression of this gene seems to range from mild dystonia to a complex dystonia syndrome including microcephaly, intellectual disability, developmental delay, seizures, spasticity, and other symptoms. Researchers have just begun to learn more about the gene and clinical signs.

Continued on page 16
Discovery through DNA  Continued from page 15

New Cause for Episodic Dystonia -
Mutations in ECHS1 are associated with Leigh’s disease, a severe neurological disorder characterized by progressive decline in mental and movement abilities and respiratory failure. However, mutations in ECHS1 have recently been associated with a less severe diagnosis that includes paroxysmal exertion-induced dystonia and appears more responsive to treatment. Genetic testing may help clarify treatment strategy for patients presenting with Leigh syndrome-like symptoms and unexplained paroxysmal exertion-induced dystonia.

Protective Gene - A single mutation in the DYT1/TOR1A gene is responsible for up to 60% of generalized dystonia in non-Jewish populations and 90% in Ashkenazi Jewish communities. However, most people who inherit the mutated gene never develop symptoms. Researchers discovered a gene modifier that may protect from the negative effects of the mutation. Only a fraction of people who have this gene variant develop dystonia, but it is very rare in the general population. This demonstrates that understanding the genetics of dystonia has the potential to identify not only dystonia-causing mutations but also perhaps protective gene modifiers that may help in developing treatment or prevention strategies.

No Gene is an Island: Common Pathways
Now that researchers have identified all these dystonia genes—and undoubtedly there will be more—Dr. LeDoux and others are exploring what the genes have in common. “Each gene and its encoded protein are a piece of the jigsaw puzzle,” he explains. Investigators are working to determine what these proteins do, and to identify biochemical processes in which these proteins may act and cooperate. “Genes causally associated with particular medical disorders tend to function in similar cellular pathways. In this regard, several dystonia genes contribute to cell-cycle control, chromatin structure, and DNA repair pathways in the nucleus of neurons.”

Cell Cycle – Cells have a life cycle with distinct phases. Several dystonia proteins are linked to the early phases in which a cell grows and duplicates its DNA. These proteins may also be involved in packaging DNA in the cell nucleus (in complexes called chromatin) and repairing broken DNA.

Transport & Trafficking – Several dystonia proteins congregate to cell structures involved with moving molecules through cell membranes. These functions link the proteins to molecules that can ultimately cause nervous system malfunction, for example neurotransmitters.

Neuron Signaling – Dystonia occurs due to an imbalance in neurotransmitters and neuron signaling, which upsets the brain pathways responsible for movement. There is ample evidence that dystonia results from an imbalance of dopamine, and several dystonia proteins can be linked to problems in dopamine production.

Next Steps
Geneticists seek to understand how changes in DNA ultimately lead to signs and symptoms of dystonia. This is a critical mechanism to understand because it may uncover opportunities to intervene on the disease process with innovative treatment approaches. Genetics may also explain why certain types of dystonia are more common in specific populations and help identify ways to protect and/or treat populations who may be at risk.

“The more patients contribute their histories and blood samples, the more we can learn,” says Dr. Klein. “We are grateful for the enormous commitment from our patients who generously donate time and biosamples. We hope and work hard to translate our findings into improved or novel therapies, which is the urgently needed next step.”

This article is the second of a two-part series. “Test Taking Tips: Genetic Counselors Inform Patients & Families about Testing for Dystonia” appeared in the Summer 2017 Dystonia Dialogue and is available online at dystonia-foundation.org/archive
The treatment of choice for adults and children with DRD is oral levodopa-carbidopa medication. Clinicians in Germany even reported a remarkable case treating a child with a rare and severe form of DRD during pregnancy. Prenatal levodopa therapy appeared to reduce motor and mental impairments, and continued therapy after the baby was born further controlled the disease.
People on the Move

The DMRF is extremely grateful for grassroots volunteers working in their communities to improve dystonia awareness and raise funds for medical research. Every volunteer makes a difference!

Former DMRF Clinical Fellow Dr. Harini Sarva partnered with the DMRF to host a half-day educational meeting on dystonia in New York City featuring colleagues from Weil Cornell Medicine.

This summer, movement disorder specialist Dr. Patrick Hogan and wife Joan hosted a dystonia support group meeting and provided DMRF awareness t-shirts to anyone who did not already possess one, encouraging them to make donation to the Foundation if able. The meeting was coordinated with DMRF support leaders Jen Dolan and Judy Yoon. Guest speaker Ron Pero spoke about transcendental meditation for stress and pain control.

In honor of Olivia and Madison Phelps, who are affected by generalized dystonia due to tyrosine hydroxylase deficiency, their best buddies Kylie and Zera Edwards (with help from mom Kristen Edwards) set up a lemonade stand with proceeds donated to the DMRF. Olivia and Madison’s mom Melissa Phelps is a member of the DMRF’s Community Leadership Council and organizes the Annual Cincinnati Dystonia Zoo Walk which celebrated its 5th anniversary this year.

Among the most dedicated Chicago Basket Bash supporters are siblings Sam and Dani Fingard, who work-year round to solicit prizes while promoting dystonia awareness. Raising donations for dystonia research was Sam’s Bar Mitzvah community service project. Dani is co-founder of Stone Slimes, which creates and sells play slime and proceeds support the DMRF. Follow stone_slimes_ on Instagram to learn more.

Michigan State University and DMRF collaborated on a Mid-Michigan Dystonia Symposium in September led by Gina Rosendall-Saucedo, who leads the Mid-Michigan Dystonia Support Group based in Lansing. The program included presentations by movement disorder experts from multiple medical institutions. Area support group leaders Deb Davis and Rosemary Young participated.

Hartford HealthCare collaborated with the Connecticut Dystonia Support Group led by Larry Stahl to offer a Dystonia Awareness Symposium on September 17. Speakers included Drs. Duarte G. Machado, J. Antonelle de Marcaida, Patrick Senatus, and DMRF Leadership Chair Paula Schneider.

DC Hathaway organized a benefit to raise awareness of dystonia and support the DMRF on September 10 at Halligan’s in Auburn, Massachusetts. Performers included Neon Alley, Acoustic Radio, Kala Farnham, Mariah Delage, and more.

The Chicago White Sox and Boston Red Sox simultaneously hosted “Dystonia Day” on September 27 in partnership with the DMRF. Local dystonia patients, their families, and members of the medical community were in attendance at Guaranteed Rate Field and Fenway Park.

Kathaleen Thouvenin worked with the Mayors of Canton and Massillon, Ohio to obtain proclamations acknowledging Dystonia Awareness Month.
Martha Murphy and members of the Dystonia Support & Advocacy Group of San Diego County were presented with a Dystonia Awareness Month proclamation from the San Diego City Council, represented by City Council member Georgette Gomez.


Dystonia awareness all-star Pat Brogan is competing in a series of races to raise dystonia awareness and fundraise for the DMRF. Pat’s Help Find A Cure 4 dystonia Benefit has cumulatively raised more than $191,000 to support DMRF research and programs. In September he competed in the 10-miler Dewey Beach and Dewey Beach Triathlon. Next up are the TCS New York City Marathon (11/5), Berwick 9-miler (11/23), and Volunteer Rehoboth Beach Seashore Marathon (12/2). Look for a report from Team DMRF in the New York City Marathon in the next Dystonia Dialogue.

DMRF members were selected as Patient Ambassadors for a series of meetings about living well with cervical dystonia organized in partnership with Allergan. The DMRF appreciates each of the Patient Ambassadors for sharing their stories at these meetings: Guido Battaglini; MaryRae Nee, Co-Leader, Western Pennsylvania Dystonia Support Group; Gina R. Saucedo, Leader, Mid-Michigan Dystonia Group; and Tom Seaman, Co-Moderator, Cervical Dystonia Support Forum. Meetings took place in Pittsburgh, Philadelphia, Long Island, Cleveland, Seattle, Nashville, Columbus (Ohio), Grand Rapids, New York City, and Rochester (New York).
Controlled Explosions

Tiago Valente Unleashes Dystonia into Sculpture

Tiago Valente’s art stokes curiosity, enticing the viewer to step inside and explore. The artist peels back assumptions about the world to reveal a completely original place that feels otherworldly, universal, intimate, and vast.

His portfolio includes sculpture, installation, performance, public intervention, costume and set design; media range from traditional handcrafts to the latest digital technology. Among his recent projects is a collection of sculptural headpieces that render his experience of facial and oromandibular dystonia. With the precision of a master magician, he fuses ideas and objects to spark potent experiences for the audience.

“After all these years,” Tiago explains, “and looking back to the multiple adventures and different lives I had the fortune to live so far, I must say that perhaps what defines my creative practice is storytelling. I love to tell stories, I always have, and I’ll continue finding new and unexpected ways and formats to share these.”

Tiago’s background includes acting, journalism, anthropology, and fashion design. He has traveled the world. All of these influences are evident in his work. His art has been exhibited and critically acclaimed in the United States, China, Hong Kong, Argentina, Spain, United Kingdom, India, Papua New Guinea, Solomon Islands, Fiji, Tonga, and Vanuatu.

“I study human behaviors and their relationships with their surroundings and other individuals. In each of my projects there’s always an underlying tendency to redefine [the subjects’] physical or social landscapes and think about how they would adapt in order to survive in those fictitious realities. Once I understand their internal circumstances and what motivates their behaviors in these worlds, I proceed to give them their respective skin and physical appearance.”

His experience with dystonia may have begun well before he knew what it was. “I guess I always had ‘nervous tics’ on my face since I was a kid” he says. “I was never diagnosed at that time. It would randomly come and go, depending on different external factors: stress, lack of sleep.”

This changed in 2013, while living in Shanghai, China. “I went through a very stressful personal moment that struck me with an explosive episode of facial/oromandibular dystonia as I had never experienced before. I got so scared, I went to a neurologist. He diagnosed me with facial dystonia.”

Shocked by the diagnosis and alarmed by the potential side effects of the medication he was prescribed (and ultimately refused), Tiago proceeded immediately to his studio. “I sat in front of my table and I cried. Then I stood up and looked at myself in the mirror, slightly embarrassed from my own facial spasms and those sadly weird faces, trying to understand what the hell was going on in my brain and my nervous system.”

He decided to study and observe the symptoms using video and time-lapse photography. He describes what he saw as the manifestation of “explosions in my nervous system.” He noted patterns in intensity and frequency, eventually using mathematics to sketch out two-dimensional and then three-dimensional shapes. “I was finally able to ‘freeze’ those explosions and understand...”
better those cryptic messages from my brain. And so to build the headpieces of the project.”

Using wood and crystals, Tiago constructed wearable sculptures to express outwardly what he felt was happening inside his brain. The collection represents more than his visceral experience with dystonia, but a broader examination of medicine, healthcare, capitalism, and humanity.

“Today my facial dystonia is really mild, and sometimes you can’t even notice it. I also developed my own secret ways to hide those occasional little spasms.” He credits yoga as being among the most helpful methods to manage stress and symptoms.

Tiago’s current projects include partnering with a number of global brands as creative consultant and strategist. His latest personal project involves the use of virtual reality and augmented reality technologies in applications such as lifestyle, education, entertainment, and health “to humanize the use of these technologies, in order to engage and connect emotionally, at a deeper level, with different audiences. I am determined to keep proving how important creativity can be to enhance and improve our lives in many different areas, without forgetting our human nature, in this digital era we are facing.”

For more information about Tiago Valente, his work, and showings visit tiagovalente.name and patreon.com/tiagovalente
FAMILY PROFILE
Meet the Shaughnessys

“It was very clear through most of his life that my father had myoclonus and, more than likely, dystonia with it,” says Mark Shaughnessy. “He would shake so hard that he couldn’t drink or eat. But, officially, Connor was the first to be diagnosed, and then Sara, then me.”

Over the years, the Shaughnessy family learned that at least three generations have been affected by myoclonus-dystonia (M-D)—and very likely others before them. Mark and Becky Shaughnessy have two children, Connor (21) and Sara (16). Connor began having symptoms around age eight, but was not correctly diagnosed until well into his teens. “He would get dropped off to school in a wheelchair because he had no control over his legs,” Becky recalls. “He was falling, he was dragging his legs. Some nights he would army crawl through the house because it was the only way he could do it safely.”

After the Shaughnessys consulted numerous doctors, Connor was diagnosed with M-D at a major movement disorder center in Boston. Genetic testing helped piece together that the symptoms his dad and sister were experiencing were also M-D.

“For all of us, it started differently,” explained Sara. “For Connor, it was in his legs, mine was in my upper leg and my back, and my Dad’s was in his shoulders and neck. All the same gene.”

Sara continues: “I explain dystonia as two things pushing, pulling your muscles—that’s how I think it feels. With the myoclonus, you randomly twitch. If I am on my phone I have to have a good grip because I will twitch and it has happened where I just throw it.”

“A lot of people don’t realize that anxiety and depression are part of it,” explains Becky. “With the myoclonus-dystonia, a lot of times you also have anxiety, depression, OCD [obsessive-compulsive disorder]. That’s what we unfortunately call our package deal, because they all have it.”

“The depression is really bad,” agrees Connor. “I would say sometimes it’s worse than the physical symptoms.”

Mark was just diagnosed last June, but in retrospect recognizes that the symptoms date back many years: “Even as a teenager, I always had severe muscle pain in my neck and shoulders and upper back, and it got worse the older I got. Depression, anxiety—I had the same whole package just unfortunately undiagnosed for a very long time.”

Mark’s treatment involves oral medications and regular botulinum neurotoxin injections. Connor had deep brain stimulation (DBS) in April of 2014 as a senior in high school. The results of the surgery were so profound he walked across the stage at graduation in June. “The only treatment that actually worked for me is DBS,” he says. “Both the myoclonus and the dystonia are pretty much gone.”

By 2015, Sara’s M-D had progressed to the point that she was also a candidate for DBS. “I got the surgery, and it didn’t work,” she says. Sara developed a serious infection following surgery, the first in a series of devastating complications.
Myoclonus-dystonia (M-D) is characterized by a combination of rapid, brief muscle contractions (myoclonus) and/or twisting, repetitive movements and abnormal postures (dystonia). Non-movement features may include obsessive compulsive disorder, depression, anxiety, personality disorders, alcohol abuse, and panic attacks. About 30-40% of cases are caused by mutations in the DYT11/SGCE gene.

She was hospitalized multiple times, was in a coma for nine days, developed seizures, and suffered a stroke. Ultimately, the DBS devices were removed from her body. Remarkably, Sara is without regret and does not want her story to deter others who may be DBS candidates: “The stroke, there was literally like a 1% chance that could happen. Normally I don’t mention it to people who are contemplating DBS because it just scares them. I want people to know that everything that happened to me was the smallest chance.” Her treatment at the moment mostly consists of oral medications. “We’re really just playing with my meds, trying to avoid having to get a baclofen pump [intrathecal baclofen] because that’s our next, last hope. A lot of the meds that can help with dystonia give me a no energy, zombie-like feeling so it’s a choice between pain, or no pain but you’re asleep.”

“It’s very hard,” says Becky. “You want your kids and your husband to be in great health and have a great life. There are plenty of times that we cry over dystonia; it’s a horrible thing. But you have to stay positive, be happy for what you have. We are blessed that we have two beautiful children, they have hearts of gold, and we’re blessed for the young people they are growing up to be. We have a great support system within the four of us, and then we have family who support us; we have friends.”

The Shaughnessys are dedicated dystonia advocates, taking any opportunity to promote awareness. “Everybody that knows us knows dystonia,” Becky continues. “We get together with the support group in Rhode Island and we’ve attended three Zoo Walks. Sara has [pamphlets] in her backpack at school, and if someone’s giving her trouble she’ll say, here read up on this, this is what I deal with every day. We wear our dystonia t-shirts everywhere—I’m wearing one now.”

The Shaughnessys’ team at multiple Zoo Walks in New England has included extended family from out of state. They have raised hundreds of dollars in support of the DMRF. “The DMRF, you guys are awesome,” says Becky. “Even like this, you guys are reaching out to us to educate the world about myoclonus-dystonia, which a lot of people don’t know about.”

Mark adds, “I encourage people to look at the DMRF website—it’s one stop shopping for dystonia education. The DMRF also offers clinical training for doctors, which makes them aware of what’s going on, so they can benefit the patients.”

“It’s good to get the word out because maybe we can find something that’s as effective as brain surgery but less invasive to help people,” says Connor.

The Shaughnessys have built an extensive network of fellow individuals and families impacted by all forms of dystonia, communicating frequently online and arranging visits. “It’s amazing the bonds you have when you make these friendships with other people with dystonia because you can relate to how they are living,” says Becky.

“Some people [on Facebook] are like when is this going to get better—that breaks my heart,” says Sara. “All you can do is tell them there are things that can help. If any of my friends on Facebook are having a hard time I will message them and talk to them. The support of family and your friends—and your doctors—is so important.”

Mark Shaughnessy is retired from a career in federal law enforcement. Becky works in medical device manufacturing. Sara is a junior in high school and works part-time. Mark, Becky, and Sara reside in New Hampshire. Connor is a college student in New York studying criminal justice administration and works in security.

For more information about M-D and the DMRF’s Myoclonus-Dystonia Research Program, see page 8.
Donate today and every dollar you give will be matched by a generous anonymous donor.

Find details at dystonia-foundation.org/2017match or see the enclosed donation envelope.