UMDF connect

UNITED MITOCHONDRIAL DISEASE FOUNDATION®

HOPE. ENERGY. LIFE.

Quarterly publication
Volume 22, Issue 2, Spring 2018

The UMDF Staff was honored to join Karen Loftus (left) as she finished walking/hiking 10,000 miles for mitochondrial disease awareness! Karen, from Milwaukee, has been "Trailblazing for Mitochondrial Disease Awareness" since 2016 and drove to Pittsburgh, PA to finish her journey with the UMDF Staff!

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From the Chairman

by Brent Fields, UMDF Chairman

This is an incredibly busy time of year for the UMDF staff and Board of Trustees. As you read this, we are putting the finishing touches on Mitochondrial Medicine 2018: Nashville. I hope it is your plan to join us June 28-30, 2018, for Patient and Family sessions. We cover a lot of ground in the world of mitochondrial medicine over these three days. Everyone, from LHON patients to the undiagnosed come away with a wealth of information and questions answered about mitochondrial disease. It truly is an impactful opportunity that every parent, patient and caregiver should experience – I hope you will.

Mitochondrial Medicine 2018: Nashville is also serving as a critical 'on ramp' to the discovery of potential treatments and cures as part of our "Roadmap to a Cure." At symposium, we will start to lay the groundwork for our very first Patient Focused Drug Development (PFDD) meeting for the Food and Drug Administration (FDA). During our symposium this year, UMDF will conduct a mini PFDD meeting. Topics will include the parent perspective on the burdens of the disease; the parent perspective on management of care; adult patient perspective on the burdens of the disease; and adult patient perspective on management of care. Information gathered in these sessions will help us in our preparation for the larger meeting, which we believe will occur in the spring of 2019 in the Washington, DC area. We hope to reach out to the patient community further as we move forward with our efforts to bring therapies and potential cures to market.

The PFDD meeting is a collaborative effort between UMDF, other patient advocacy groups, patients, and caregivers. We also hope to provide you more details on a secondary collaborative effort that is part of the 'Roadmap' and that is the patient centered Mitochondrial Disease Care Network, or MCN. Our Chief Science and Alliance Officer, Phil Yeske, Ph.D., is working with various stakeholders in gathering proposals to create a pilot for this network. Our vision is to create a 'one stop shop' for the care and treatment of mitochondrial disease patients. More than 20 proposals from various medical facilities are now under consideration for this pilot.

One of the toughest tasks the UMDF Board of Trustees is currently working on is locating the right candidate to fill some very large shoes at the national office. As you know, Chuck Mohan is retiring from his position as CEO/Executive Director. Finding the person who can continue to grow and serve the patients and families of the UMDF is of paramount importance to the search committee. We have been diligently working on this process and we hope to have some news for you in the weeks and months ahead.

As I said, it's been very busy. You are always at the center of our work. I hope to see you in Nashville in June.

Energy to All!

Brent Fields

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Preclinical Testing in 3 Model Systems Suggests Some Antioxidants May Be Effective Mitochondrial Disease Treatments

A systematic study of seven antioxidants commonly taken by or suggested to benefit children and adults affected with mitochondrial disease provides intriguing clues that at least two compounds should be further evaluated in clinical trials.

"We are pursuing a precision medicine approach that investigates therapeutic candidates in preclinical models—simple laboratory animals and human cells—to discover the best potential leads to bring to patients in clinical trials," said study leader Marni J. Falk, MD, executive director of the Mitochondrial Medicine Frontier Program at Children's Hospital of Philadelphia (CHOP).

Mitochondrial disease results from malfunctions in mitochondria, the energy-generating "batteries" powering our cells. The disease is highly variable and may affect potentially any organ and body system. Given the lack of validated treatments, many patients take vitamins and supplements on an "empiric" basis, relying on the assumption that this somehow benefits their altered cellular metabolism. Unfortunately, most of these compounds are currently unregulated, unstandardized and untested, and have not been compared with one another to determine which may be the most safe, potent and effective in any given type of mitochondrial disease.

In the new study, published in Molecular Genetics and Metabolism, Falk and colleagues evaluated seven antioxidant compounds in two microscopic animal models of mitochondrial disease—zebrafish (D. rerio) and the worm species C. elegans. The study team also used a third model—cultures of fibroblasts (skin cells) obtained from human patients. The patient cells and the experimental animals all had genetically based malfunctions of the mitochondrial respiratory chain (RC): a crucial site within mitochondria in which cells process nutrients and oxygen to generate chemical energy.

One major factor common in RC disease is oxidative stress, when the body generates excessive oxygen-containing free radicals that damage cells, proteins and genes, contributing to the severity of disease. Antioxidants found in many foods, vitamins and supplements are generally thought to help "counteract" oxidative stress. However, some antioxidants can have undesired side effects, be ineffective, or be used at harmful doses.

In the current study, two compounds, the drug N-acetylcysteine (NAC) and vitamin E, showed compelling results in mitochondrial disease model animals. The compounds prolonged lifespan in mitochondrial complex I disease worms and protected complex I disease zebrafish from brain damage. NAC also improved survival in the cells obtained from a patient with mitochondrial complex I disease.

"In addition to showing clear benefits in animal survival and cellular viability in these animal models of genetic-based mitochondrial disease, we learned that these compounds effectively relieved oxidative stress that was present throughout the entire cell, not only within the mitochondria," said Falk. "Both NAC and vitamin E are the lead antioxidant candidates from this work to be evaluated in clinical trials, to determine whether they effectively benefit the survival, function and feeling of mitochondrial disease patients. They may have particular promise to improve the resiliency of the nervous system in patients with malfunctioning mitochondria."

Two other antioxidant compounds in the study, coenzyme Q10 and a type of coenzyme Q10 specifically targeted at mitochondria, improved some indicators of animal health in the mitochondrial disease worms, but only partially rescued their short lifespan. The other three compounds tested in the study were vitamin C, lipoate and orotate, which had more variable effects than those seen with the other compounds.

Overall, said Falk, the current study offers an efficient and relatively inexpensive paradigm for performing cost-effective preclinical testing to objectively prioritize drug candidates that are safe, potent and show preliminary evidence of comparative efficacy, to support their further clinical development in mitochondrial medicine. She added that such preclinical testing could also be used to evaluate multidrug combinations, such as the vitamin and supplement "cocktails" that are now frequently used on an empirical basis, without effective means to judge their utility, in patients with mitochondrial disease.

Intravenous Arginine Benefits Children after Acute Metabolic Strokes

Children with mitochondrial diseases who suffered acute metabolic strokes benefited from rapid intravenous treatment with the amino acid arginine, experiencing no side effects from the treatment. The diseases were caused by a range of different genetic disorders. In half of the stroke episodes, patients showed clinical improvements in symptoms such as seizures and partial paralysis.

Mitochondrial disease results from malfunctions in mitochondria, the energy-generating "batteries" dwelling within our cells. Caused by mutations in roughly 300 different genes, there are a broad variety of mitochondrial disorders, most of which currently have no effective treatment.

Two mitochondrial medicine experts from Children's Hospital of Philadelphia (CHOP) reported on eight years of clinical experience in providing intravenous (IV) arginine when new-onset neurologic problems concerning for acute stroke-like episode developed in nine pediatric mitochondrial disease patients. Their retrospective study appeared online Feb. 2 in Molecular Genetics and Metabolism.

Marni J. Falk, MD

"In half of our patients we saw at least partial reversal of their metabolic stroke symptoms," said study leader Marni J. Falk, MD, executive director of CHOP's Mitochondrial Medicine Frontier Program. "This is a single-center retrospective study of clinical practice outcomes, but one with promising results. While we need more research, conducted prospectively in larger groups of patients, this analysis expands the evidence base of potentially promising treatments for a wide range of otherwise very severe and progressive mitochondrial diseases." Falk's co-author was Rebecca D. Ganetzky, MD, a clinical geneticist and attending physician who specializes in metabolic diseases.

Metabolic strokes occur in a broad range of mitochondrial disorders. Arginine is already used to acutely treat these complex strokes in adult patients who have a well-known mitochondrial disease syndrome called MELAS (mitochondrial encephalopathy with lactic acidosis and stroke-like episodes). Unlike classic strokes caused by blood clots blocking major arteries in the brain, metabolic strokes result from energy deficiency at the cellular level in brain regions with a particularly high energy demand. Recent clinical practice guidelines from the Mitochondrial Medicine Society recommended using IV arginine in patients having stroke-like episodes from MELAS, and considering its use at the time of stroke-like episodes in other mitochondrial diseases. However, no previous systematic studies were performed to objectively evaluate benefits and risks of IV arginine in other mitochondrial diseases beyond MELAS.

The current study reported on nine unrelated patients treated at CHOP between 2009 and 2016 once or more for acute stroke-like events in which they developed new neurological problems. The team evaluated outcomes from a total of 17 different stroke-like episodes. Patients ranged in age from under 19 months to 23 years, with a median age of 8 years at the time of their metabolic stroke. All had non-MELAS mitochondrial disorders, resulting from diverse genetic causes.

Like many patients with mitochondrial disease, nearly all patients in this cohort were already taking oral "mitochondrial cocktails" of vitamins and cofactor supplements, commonly

including oral arginine, at the time of their stroke-like episode. Despite their frequent use, nearly all such nutritional supplements are unstandardized and untested. Ganetzky pointed out that intravenous arginine is much more potent than oral arginine, adding "This study was an opportunity to more systematically analyze a therapy that is clinically used on an empiric basis in the course of acute clinical care." Arginine is not used to treat classic, non-metabolic vascular strokes.

In eight (47%) of the 17 stroke-like episodes, positive clinical responses occurred, including stopped seizures, normalized strength, and resolved atonia (low muscle tone). Greater improvements occurred in children with acute hemiplegic stroke (weakness or paralysis on one side of the body). Magnetic resonance imaging (MRI) performed in some patients showed that brain changes caused by the stroke returned to normal after patients received IV arginine. Two patients who did not respond to IV arginine treatment for stroke-like episodes that developed during acute infections died of progressive, multi-system problems. No adverse effects were seen from the IV arginine treatment.

Overall, the best results from IV arginine occurred when patients received treatment immediately upon clinical recognition of a new neurologic problem that was concerning for an acute metabolic stroke. Previous research has suggested that arginine acts by improving the flow of nitric oxide, which relaxes blood vessels to improve circulation.

"Given these observed clinical benefits with low overall risks, our retrospective study data support the current use of IV arginine at the onset of acute metabolic strokes in children with many forms of mitochondrial disease," said Falk, who added that prospective, larger studies should be performed. "As we move forward in mitochondrial medicine, we strongly encourage the objective evaluation of all current practices and potential therapies as rigorously as possible, both in preclinical models and in robust clinical trials."are safe, potent and show preliminary evidence of comparative efficacy, to support their further clinical development in mitochondrial medicine. She added that such preclinical testing could also be used to evaluate multidrug combinations, such as the vitamin and supplement "cocktails" that are now frequently used on an empirical basis, without effective means to judge their utility, in patients with mitochondrial disease.

GenSight has demonstrated that its gene therapy for a rare disease causing blindness can significantly improve the vision of patients.

But so does the placebo.

GenSight Biologics has released the results of a Phase III clinical trial testing its gene therapy GS010 in patients suffering from Leber hereditary optic neuropathy (LHON). In the trial, 37 patients were injected with the gene therapy in one eye and with a sham injection in the other. The results show a significant improvement in the eye treated with the gene therapy, with patients being able to see in average 11 letters more in a traditional ETDRS test after almost a year. But, unexpectedly, the untreated eye also showed an equally big improvement of 11 ETDRS letters.

Spontaneous recovery of vision is possible in patients with LHON, but it is only reported in up to 22% of patients. GenSight has stated that they will further study the data to better understand what has happened, and CEO Bernard Gilly has hinted at the possibility that the gene therapy might be benefitting both eyes despite being used only in one of them.

The data seems to be quite different from the results of a previous Phase I/II, which showed a much bigger improvement in the eye treated with GenSight's gene therapy that was maintained after 2.5 years. However, that trial tested it in only five patients, which might have resulted in a bias.

The patients of this trial will continue to be monitored for another four years, and another two Phase III trials are underway. One is testing the therapy in patients that have been affected by LHON for less than six months (instead of between 6 and 12 months), and the other is studying the effect of injecting the gene therapy in both eyes.

GenSight BIOLOGICS

Study says road to diagnosis is difficult

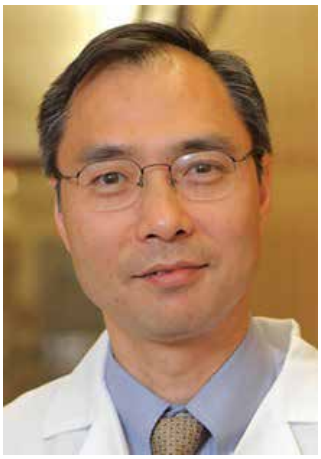
Many mitochondrial disease patients know that they face a difficult path to diagnosis.

A new study led by researchers at Columbia University Irving Medical Center and published in the journal *Neurology Genetics*, confirms this prolonged and difficult path. The study is titled "The Mitochondrial Disease Patient's Diagnostic Odyssey: Results of A Survey."

Researchers surveyed 210 patients who were diagnosed by a physician with a mitochondrial disease. According to the researchers, patients saw eight different physicians prior to getting a diagnosis. More than half reported they were misdiagnosed, and, of these, nearly one-third were misdiagnosed more than once. The most common misdiagnosis was a physchiatric disorder, followed by fibromyalgia, chronic fatigue syndrome and multiple sclerosis. Along their diagnostic journey, most patients underwent several diagnostics tests, including blood tests, brain MRIs, muscle biopsies, and genetic tests.

This study demonstrates that the road to a mitochondrial disease diagnosis is typically long and hard, involving visits to numerous clinical specialists, conflicting diagnoses, and repeated and sometimes painful and invasive testing," says Michio Hirano, MD, the paper's senior clinical author and chief of the Neuromuscular Division at Columbia University Irving Medical Center.

"As much as we wanted to ask them every question we had, we had to design a streamlined survey to get a good response," said Johnston Grier, the lead author, who collaborated with the United Mitochondrial Disease Foundation where he became familiar with the patient perspective and wove into the survey design.



Michio Hirano, MD

Johnston Grier

In all, survey participants reported more than 800 symptoms. The most common of these that motivated patients to see a doctor was weakness, followed by fatigue, difficulty walking, droopy eyelids, and impaired coordination. The most frequent mitochondrial disease diagnosis was myopathy followed by CPEO, impaired eye movements, and MELAS. Nearly one-third of participants reported "other" mitochondrial diseases.

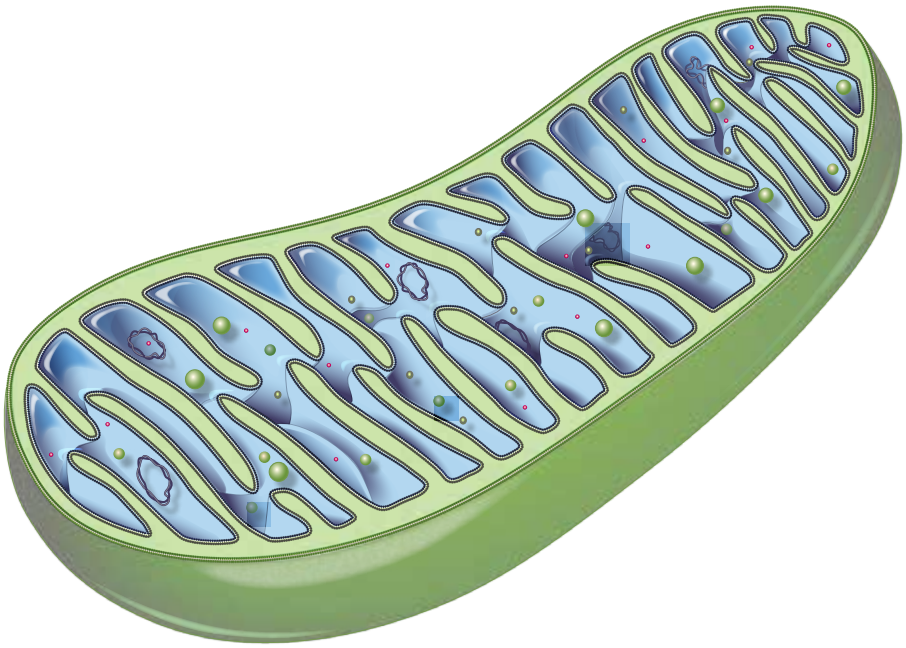
"The heterogeneity of symptoms plays a role in prolonging diagnosis," says Hirano. "Patients often start by seeing their primary care physician, most of whom, understandably, aren't familiar with mitochondrial disease, which can mimic other disorders.

"These findings signal a need for improved diagnostics, particularly in the areas of genetic testing, standardized diagnostic criteria, as well as improved clinical training," he adds. "We will continue to monitor the diagnostic process over the coming years."

Additional co-authors of the study, were Amel Karaa, MD, of Harvard University and Emma Shepard, a student at the Mailman School. The study was conducted under the auspices of the North American Mitochondrial Disease Consortium (NAMDC).

Stealth BioTherapeutics

is committed to the development of therapies for mitochondrial disease and proudly supports the advocacy efforts of the UMDF



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St. Bernadette's Catholic School students visit the University of Plttsburgh

One a penny, two a penny, three a penny, four!

The UMDF's coins for a cure campaign is pretty simple. Schools, churches, businesses and even in our home laundry rooms, boxes are used to collect coins for a cure. St. Bernadette's Catholic School in Monroeville, PA, has been collecting coins for the UMDF for 17 years!

St. Bernadette's holds a special place in the hearts of our fearless CEO, Chuck Mohan and his wife, Adrienne. Their daughter, Gina, started 3 year old preschool in those very classrooms.

Principal, Sister Carol Arch, recalls when Gina and little brother, Chuckie, were students at St. Bernadette's.

"Everyone knew Gina and Chuckie, and when Gina got sick, no one knew about mitochondrial disease," she said. "We continue to support this cause, because we feel it's a good learning experience for our students to learn to be helpful to others and look out for other people, like another current student who also has a mitochondrial disease. It's great to see our students give up their snacks at lunch so they can put that money in the 'Gina Jugs'."

Over those 17 years, students collected coins (and sometimes bills!), and the winning classrooms were treated with a popcorn party with a movie of their choice. In 2015, Chuck decided that popcorn and movies were great – but what if the challenge and reward were bigger? Chuck purchased a trophy (a VERY LARGE trophy) for the top winning classroom. In addition, the kids in grades 4-8 who collected the most were treated to a special field trip to the research labs at the University of Pittsburgh that perform mitochondrial disease research! Grades K-3 continued with the popcorn/movie party reward.

Thank you, St. Bernadette's Catholic School for collecting over $27,000 to support our mission. Your staff, students and families make such a big impact on our families!

Karen (left) completes her 10,000 mile journey in Pittsburgh with the UMDF staff

A 10,000 Mile Journey for Mito

Karen Loftus of, Wisconsin, began struggling to walk in 2014. In the spring of 2015, Loftus began working with another family whose daughter, Brianna, passed away from mitochondrial disease. Loftus was so inspired.

As soon as she was able to walk -- first with assistance of Cam Walkers, and now cane's, boots, family, friends and sheer will, -- she turned her daily walks into something larger, using Brianna as her Trail Angel.

The Appalachian Trail hike is something Loftus has wanted do since she was a teenager. Mitochondrial disease has kept her from that dream until now. That hike turned into a round trip that encompassed the entire Eastern Continental Trail - 10,000 miles for Mitochondrial Disease Awareness.

Although the physical activity is challenging, many days Loftus feels that walking has helped to improve some of her symptoms of her disease.

"In doing this challenge, it forces me to get up every day and get moving," she said. Karen serves as a UMDF Ambassador and was also recognized with the UMDF Energy Award in 2016.

Do It Yourself Fundraising - The Mito Way!

DIY

Become a fundraiser and start the process of raising funds to support the Roadmap to a Cure.

The steps are easy:

1. **Come up with a fundraising idea**
2. **Create a fundraising page**
3. **Share with your family & friends**
4. **Watch your page as you reach your fundraising goals!**

Let's Fundraise!

You want to fundraise - we have the place!

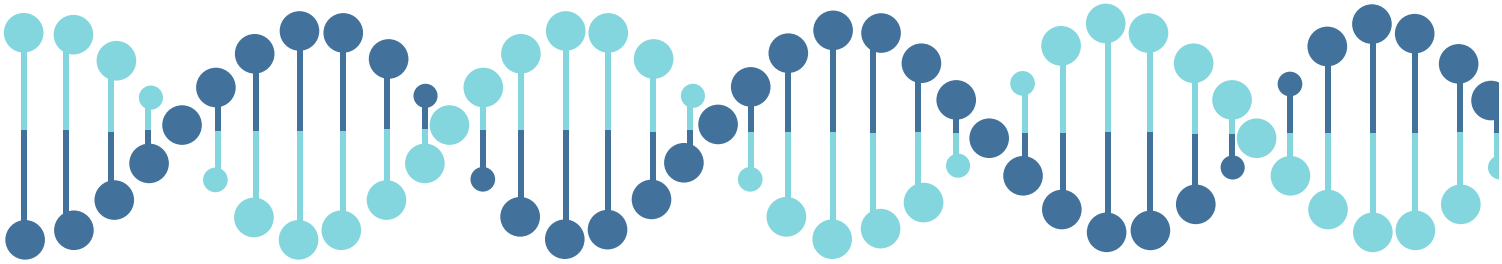
www.umdf.org/diyfundraising

In Memoriam

The UMDF is saddened to learn the following have lost their battle with mitochondrial disease. Below are the names of those who, according to our records, became Mito Angels between January 22, 2018 and May 1, 2018.

Kenley Montes
Lilly Waeghe
Velma McAllister
Derek Swanson
Miranda Williams
Haley Royko
Jordan "Jojo" Kalua Cline
Thomas Evans

UMDF has created a brick in memory of each on UMDF's Path to a Cure. To visit each path, go to *www.umdfpathtoacure.org*



Update On 2018 UMDF Research Grant Program

For more than 20 years, the United Mitochondrial Disease Foundation has been privileged to be the largest non-governmental funder of research towards the treatment and cure of mitochondrial disease. In that time, through the hard work and dedication of our patients, their families, and donors, UMDF has provided close to $12 million in scientific research that was demonstrated to move us closer to a cure.

As part of our commitment to bring patients and families to treatments and cures, UMDF is refocusing our research grant program. In 2018, our grant program will focus on Leigh's Disease research. Our scientists and clinicians believe that in exploring this type of mitochondrial disease, they can have a broad impact on the diagnosis and treatment of other mitochondrial diseases.

You will be hearing more about this as we move through the spring and summer. UMDF looks forward to announcing requests for proposals to the scientific community shortly with research grant awards to be made before the end of 2018.

Investments for Treatments and Cures *or* How Do You Make an Apple Pie?

by Chuck Mohan, UMDF CEO

A recipe is a formula, a method or procedure for combining ingredients in a manner that will hopefully produce a desired result.

Ingredients are elements, constituents and components necessary to achieve a desired result.

Research is the ingredient of investigation, study and exploration that is always made with an anticipated return greater than when it was started and within an expected time period.

Investment is an ingredient consisting of speculation, an outlay or a venture that is always made with an anticipated return greater than when it was started and within an expected time period.

UMDF has worked hard over the years to develop a recipe that identifies the necessary ingredients to justify your investment in research that will produce tasteful and fulfilling results. In the beginning we were in need of ingredients that did not exist. We had to re-think how best to combine what we had and what we knew. We had to spend time and resources adjusting the recipe.

Albert Einstein said, "If we knew what we were doing, it wouldn't be called research." We needed to know what we were doing so we could develop a recipe that would produce beneficial results while still gathering necessary ingredients. To help in that process we established the UMDF Scientific and Medical Advisory Board along with a rigorous grant review process that enabled us to continue to make adjustments and further fine-tune our recipe.

UMDF has invested over $11 million on projects that we felt would produce a return greater than the investment you trusted us to make. The $11 million that you trusted UMDF to invest has resulted in over $100 million of additional research at the NIH and the Department of Defense focused on mitochondrial disease. Every $1.00 you donated to UMDF, trusting us to invest, has resulted in a return of over $10.00. Your $11 million investment in UMDF has returned nearly $120 million dollars of mitochondrial research!

The results of increased research has enabled us to gather additional ingredients resulting in UMDF being able to write our own proposals for specific projects to fund that we know will produce beneficial results across many mitochondrial diseases.

The UMDF recipe for treatments and cures IS the UMDF Roadmap. This roadmap has many ingredients that are all centered on three main elements, or pillars, of Diagnostics, Patient Care and Therapeutic Development.

Our advocacy ingredient impacts all three pillars. We are gathering the needed ingredients that continues to educate the House and Senate on the value of mitochondrial research. Our Congressional approach and UMDF Mitochondrial Disease Caucus has produced a level of awareness that has increased the allocation of funds to over $100 million at the NIH and DOD in support of mitochondrial disease research.

Our Mitochondrial Disease Community Registry (MDCR) ingredient will gather patient information helping UMDF identify eligible patients for future clinical trials.

Our investment in the North American Mitochondrial Disease Consortium (NAMDC) ingredient has brought together 16 academic sites from across the US. In partnership with UMDF, NAMDC has obtained more than $8 million in NIH funding and has established the NAMDC Clinical Registry which has more than 1,200 patients enrolled. We have established the NAMDC Biorepository, which has collected blood and tissue samples from over 200 patients; samples that have been shared with researchers in the US and abroad. We have trained five outstanding clinician investigators who will lead the next generation of mitochondrial disease research.

Our investment in the Mitochondrial Disease Sequence Data Resource (MSeqDR) ingredient is a centralized and comprehensive genomic resource built by the mitochondrial community to facilitate clinical diagnosis and research investigations of patient phenotypes, genomes, genes and variants. MSeqDR will enable researchers from around the world to use web-based tools to analyze data, DNA, and exome and genome sequencing as a method towards treatments, therapies and potential cures.

Our involvement with the Mitochondrial Medicine Society (MMS) developing and supporting the Mitochondrial Care Network is a most important ingredient. The first of its kind, MCN's will formally unify clinicians who provide medical care to individuals with mitochondrial disease. They will define, design and implement best practices in mitochondrial medicine and optimize management and care for patients with mitochondrial disease.

The UMDF Roadmap, supported by investments in the three pillars: Diagnostics, Patient Care and Therapeutic Development, and combining the necessary ingredients, will result in a recipe, when properly baked, will produce treatments and ultimately cures.

In the meantime, this is a great recipe with available ingredients that will produce tasteful and fulfilling results:

Apple Pie

ingredients:

Dough

(Enough for top and bottom of 9" Pie)

- 2 1/2 cups all-purpose flour, plus extra for rolling
- 1 cup (2 sticks or 8 ounces) unsalted butter, very-cold, cut into 1/2 inch cubes
- 1 teaspoon salt
- 1 teaspoon sugar
- 6 to 8 Tbsp ice water

Filling

- 6 cups thinly sliced, peeled apples (6 medium)
- ¾ cup sugar
- 2 tablespoons all-purpose flour
- ¾ teaspoon ground cinnamon
- ¼ teaspoon salt
- 1/8 teaspoon ground nutmeg
- 1 tablespoon lemon juice

directions:

1. Put flour, sugar, and salt into the bowl of a food processor and pulse a couple times to mix. Add about half of the butter to the food processor and pulse several times. Then add the rest of the butter and pulse 6 to 8 times until the largest pieces of butter are about the size of large peas. Sprinkle the mixture with about 1/4 cup of ice water (make sure there are no ice cubes in the water!) and pulse again. Then add more ice water, a tablespoon at a time, pulsing once or twice after each addition until the dough just barely begins to hold together.
2. You know that the mixture is ready if when you pinch some of the crumbly dough together with your fingers, it holds together. Be cautious with the amount of water you add, too much and the crust will be tough.
3. Carefully empty the crumbly dough mixture from the food processor on to a clean, dry, flat surface. Gather the mixture in a mound. At this point, if you want, you can do what the French call fraisage: push down with the palm of your hand on the dough crumbles a few times. This will help flatten the pieces of butter into layers which will help your crust be flaky.
4. Divide the dough mixture into two even-sized mounds. Use your hands to form each one into a disk. Do not over-knead! Kneading develops gluten which will toughen the dough, not something you want in a pastry crust.
5. If you started with cold butter you should be able to see small chunks of butter speckling the dough. This is a good thing. These small bits of butter will spread out into layers as the crust cooks so you have a flaky crust!
6. Sprinkle each disk with a little flour, wrap each one in plastic wrap, and refrigerate for one hour or up to 2 days.
7. Remove one crust disk from the refrigerator. Let sit at room temperature for 5-10 minutes in order to soften just enough to make rolling out a bit easier. Roll out with a rolling pin on a lightly floured surface to a 12-inch circle; about 1/8 of an inch thick. As you roll out the dough, check if the dough is sticking to the surface below. If necessary, add a few sprinkles of flour under the dough to keep the dough from sticking. Carefully place onto a 9-inch pie plate. Gently press the pie dough down so that it lines the bottom and sides of the pie plate. Use a pair of kitchen scissors to trim the dough to within 1/2 inch of the edge of the pie dish.
8. Add filling to the pie.
9. Roll out second disk of dough, as before. Gently place onto the top of the filling in the pie. Pinch top and bottom of dough rounds firmly together. Trim excess dough with kitchen shears, leaving a 3/4 inch overhang. Fold the edge of the top piece of dough over and under the edge of the bottom piece of dough, pressing together. Flute edges using thumb and forefinger or press with a fork. Score the top of the pie with four 2-inch long cuts, so that steam from the cooking pie can escape.
10. Use leftover dough to cut into letters "UMDF" and place on top of crust
11. Brush top crust with egg whites and sprinkle lightly with sugar.
12. Heat oven to 425°F. Place 1 pie crust in ungreased 9-inch glass pie plate. Press firmly against side and bottom.
13. In large bowl, gently mix filling ingredients; spoon into crust-lined pie plate. Top with second crust. Wrap excess top crust under bottom crust edge, pressing edges together to seal; flute. Cut slits or shapes in several places in top crust.
14. Bake 40 to 45 minutes or until apples are tender and crust is golden brown. Cover edge of crust with 2- to 3-inch wide strips of foil after first 15 to 20 minutes of baking to prevent excessive browning. Cool on cooling rack at least 2 hours before serving.

The MOTOR Study

A study of omaveloxolone (RTA 408) in mitochondrial myopathies

MOTOR is a double blind, placebo-controlled, multi-center Phase 2 study of the safety and efficacy of omaveloxolone (RTA 408) in mitochondrial myopathies

About the Study

- Treatment: Omaveloxolone or placebo capsules taken by mouth once daily
- Approximately 8 visits to the study site over 16 weeks
- Primary endpoint: Change in peak workload, measured on a recumbent bicycle
- Cost of travel may be reimbursed

Criteria for Participation

- Between ages 18 and 75
- Exercise intolerance with genetically confirmed mitochondrial disease (testing may be provided)
- Willing to discontinue some medications
- Not pregnant, planning a pregnancy, or breastfeeding

Recruiting Study Center Locations

- Los Angeles, California: UCLA
  Perry Shieh, MD
- Dallas, Texas: Institute for Exercise Medicine
  Ronald Haller, MD
- Houston, Texas: University of Texas Houston
  Mary Kay Koenig, MD
- Houston, Texas: Baylor College of Medicine
  Fernando Scaglia, MD
- Akron, Ohio: Akron Children's Hospital
  Bruce Cohen, MD
- Pittsburgh, Pennsylvania: University of Pittsburgh
  Gerard Vockley, MD
- Philadelphia, Pennsylvania: CHOP
  Marni Falk, MD
- Boston, Massachussetts: Mass General
  Amel Karaa, MD
- Copenhagen, Denmark: University of Copenhagen
  Karen Madsen, MD

MOTOR

Contact information for participating study centers can be found on the clinicaltrials.gov listing

REATA PHARMACEUTICALS

Go to www.clinicaltrials.gov/ct2/show/NCT02255422 for more information

Version 1; September 2016

Research Fund Spotlight: Robert Graham Collins

Robert Graham Collins was born on November 17, 2015. Graham was born prematurely at 24 weeks and four days. He weighed less than 2 lbs. Graham could not breathe on his own, eat on his own, and his tiny, yet perfect, body simply needed more time to grow. Graham spent 105 days in the NICU. He overcame breathing challenges, heart complications, and feeding issues. With the help of many doctors, nurses, specialists and our Heavenly Father, Graham was thriving for a 24-weeker!! Every doctor who met him after the NICU was amazed that he was a micro-preemie because he was doing so well. His demeanor and abilities were on par with his adjusted age and it was clear he was progressing perfectly for a former 24-weeker.

On November 22, 2016 – 5 days after he turned 1 – Graham experienced a prolonged seizure that forced him to be hospitalized at Children's Healthcare of Atlanta. The seizure did not respond to any medications, so the doctors put him in a medical coma to give his brain a break. After waiting 4 days, they started to wake him up. As the medicine wore off, Graham started to seize again. The doctors were forced to sedate him again as they worked to determine a cause for the seizures. Countless doctors and specialists tried to understand his condition. Many assumed his premature birth contributed to the seizure, but later discovered it was unrelated. They performed numerous tests to determine a cause or diagnosis. Understanding his conditions was difficult, and without a diagnosis, it was impossible to treat. Finally, on January 16, 2017, Graham was diagnosed with Alpers' disease. This mitochondrial disease is characterized by developmental regression, seizures, and liver disease – and Graham had all of these symptoms. It is a very rare disease only affecting less than one in every 200,000 people. There is no cure for Alpers' disease and no way to slow its progression.

Graham's symptoms indicated he had a more severe case. Treatment for this disease is symptomatic and supportive, and the prognosis for individuals with Alpers' disease is very poor. The life expectancy is anywhere from a few months to 10 years. Graham passed away on January 24, 2017, 10 weeks after his first seizure.

We spent weeks searching for answers, medications, anything to help ease Graham's suffering and provide us with understanding. Because mitochondrial disorders like Alpers' disease are difficult to diagnose, Graham was diagnosed with several different disorders, endured many pointless tests, and even received medication that accelerated his condition. We know the doctors were doing everything in Graham's best interests, but we wish he was diagnosed earlier on and we were spared some of this pain. We wish it was easier to diagnose genetic diseases like mitochondrial disorders. We hope with further research, doctors can identify diseases like this and understand how to treat disorders like Alpers' disease better. We have formed this research fund so families like ours can be spared the suffering and loss we experienced.

In 2017, we teamed up with UMDF to organize an event to raise awareness and funding for mitochondrial diseases – Mimosas for Mito. The event included brunch and mimosas, but also access to an impressive silent auction with items ranging from football tickets, golf certificates, jewelry, and more! Between ticket sales and the silent auction, we collected $10,000 to give to the organization! This event is important to us since it helps with research and education for the diagnosis, treatment, and cure for mitochondrial disorders like the one which impacted our family's life, and it also encourages people to talk about mitochondrial disease! With greater awareness, there will be more funding for research, and ultimately there will be a cure.

Donate to the
Graham Collins Family Research Fund at:
www.umdf.org/grahamcollins

Please contact us if you are interested in partnering with UMDF in the establishment of a Family Research Fund.

Listen to those who tell you that you CAN!

The Power of Recurring Giving

Anthony and Regina Nicolas met while they were both working at AT&T. When Regina moved to Atlanta for work, Anthony followed her. Soon enough, they married and had their first baby, Evan. With Evan, Regina knew something wasn't quite right when he started missing his milestones. Searching for answers, Regina and Anthony learned that Evan had mitochondrial disease. Regina immediately started researching and seeking connection with and information from other families. When they had their second son, Aidan, two years later, he also was impacted by the disease.

Soon after Aidan's birth, they moved to San Antonio to be near family for support. At that time, doctors in San Antonio "didn't get it." Regina found herself constantly saying, "Go to UMDF.org if you want to know more." Like so many of our UMDF families, Regina and Anthony have done all they could to advocate for their sons—for medical care, therapies, and educational opportunities. Early on, doctors and therapists told them that the boys would never walk, be verbal, or engage with others. Today, as captivating teenagers, Evan (16) and Aidan (14) walk everywhere around the house; are able to communicate via word approximations, signs, and pictures; and attend school every day. They are heading to high school next year. To Regina, the boys are a testament to the power of advocacy. As she says, "Don't listen to people who tell you that you can't—listen to those who tell you that you can."

AT&T has been great to their family. Since 2012 when they saw that UMDF was a charitable option through AT&T's employee giving program, Anthony and Regina have both been enrolled in recurring gifts for UMDF. Both have been champions of charitable giving at the company. Anthony recently requested a giving impact sheet from UMDF to share with his co-workers who give (call the UMDF office to request this info!). When Regina's co-workers mention that they don't know where to give, she shares her story and tells them about UMDF. As she noted, even giving two dollars through employee giving—that's skipping one coffee. In the end, those dollars add up to incredible impact for UMDF.

In their six years of recurring gifts, Anthony and Regina have given over $6,500! Regina and Anthony give in hopes of clinical trials and future treatments for their sons, to help other families find the information and answers they need, and to continue spreading awareness and education. Evan and Aidan's doctors, today, know all about mitochondrial disease, but there are so many people who don't. To the Nicolas family, knowledge has given them power; their heart for making a difference through UMDF powers hope and support for so many others.

Many companies, like AT&T, have employee giving programs. Many companies also MATCH their employees' charitable donations. Discuss employee giving opportunities with your company's HR department. If you would like to find out about corporate matches for UMDF, follow these simple instructions:

1. Head to *www.doublethedonation.com/umdf*, and enter your company's name in the search bar.
2. If your company participates in a match program, click the blue bar that says: "Your company offers a matching gifts program. Please click here to start the process."
3. You will also see how much your company will match and if they offer volunteer grants! WOW! *If your company isn't listed, check with your HR department as there are companies outside of Double the Donation that do offer match programs.

Double Your Donation: It's Easy Like Sunday Morning....

Did you know that you can DOUBLE your donation with a corporate matching gift? And, just like Lionel Richie said, it's 'Easy like Sunday Morning'!

So, what exactly is a corporate matching gift?

Corporate matching gift programs are charitable giving programs set up by corporations in which the company matches donations made by employees to eligible nonprofit organizations, like us! Pretty cool, right?

Here is how it works:

1. Make a donation to the UMDF via ANY of our fundraising vehicles; Our Energy for Life Walks, General Donation, Research Funds or any special event.

2. Head to www.doublethedonation.com/umdf and enter your companies name in the search bar.

3. If your company participates in a match program – just click the blue bar that says: 'Your company offers a matching gifts program. Please click here to start the process.'

4. You will also see how much your company will match, and if they also do a volunteer grant! WOW! *If your company isn't listed, check with your HR department, as there are additional companies that do offer employee giving programs.

5. Then – just complete the form to your company and VIOLA! Your gift was matched!

We told you it was easy!

Double the Donation
matching gifts made easy

Thousands of companies offer matching gift programs.
Here are just a few!

General Electric

Soros Fund Management

BP

Gap Corporation

State Street Corporation

ExxonMobil

CarMax

Johnson & Johnson

Boeing

Microsoft

Pfizer

Capital Group

Bristol-Myers Squibb

Coca-Cola

IBM

AACT - ADULT CORNER PAGE

KAILEY AND DEVIN'S FAMILY STORY
AACT COUNCIL MEMBER AND CANADIAN AMBASSADOR

My husband, Devin, and I met in University through a mutual friend. We dated for three years and then got married. I actually met him after my first muscle biopsy. After graduation, we moved to Toronto and continued with further education. I completed my post grad certificate in Career Counseling, and he completed a post grad in HR. We got our first jobs together and then purchased a condo in Toronto.

I started seeing Dr. Mark Tarnopolsky of McMaster University for further testing and another biopsy in my 20's and after almost 10 years was given a specific diagnosis CPEO+ (a form of Kearns–Sayre Syndrome). I wanted to start a career after University and College and was hired by a non profit as an Employment Consultant and later an Employment Counselor.

In my late 20's, I met with Dr Tarnopolsky for further testing and worked with a Genetic Counselor at McMaster. My condition is sporadic so Devin and I decided that we would love to start a family. I had the support of my family doctor, neurologist, and a fertility specialist.

Once I was pregnant I was referred to SunnyBrook Hospital in Toronto as high risk Obstetrical Case. Because of my muscle weakness and chronic fatigue, it was decided that I would have a planned cesarian section. I was able to work until around 7 months and then decided to take my vacation time to rest.

We delivered a very healthy and happy little guy in June 2015 by c-section with no complications. Sometimes, I have to do things differently or be creative with Jude when I am having hard days. But, we live close to family so they are supportive. Since I can't drive, my parents have a car seat for Jude. I plan many activities and play dates for Jude each week and I am fortunate to have such great friends and neighbors. We often host at my house as it's easier!

Devin is a wonderful partner and dad. He is very involved and does a lot of the more physical activities with Jude like swim lessons, walks, and playing at the park - we make a great team!

To save energy, I have a house cleaner come in once a month and food prep every second week. We attend programs at the Library and at the Early Years Center. Jude is a very social but chill guy. If I am having a hard day, he loves to read books, listen to music, draw, etc. I am currently 20 weeks pregnant with our second child so I am considering a part time nanny or mother's helper for support. We are very excited to welcome our new arrival soon!

UNITED MITOCHONDRIAL DISEASE FOUNDATION

AACT Purpose

To represent and serve the unique needs of the affected adult community and to ensure that those needs are adequately represented to UMDF resulting in enhanced services to the affected adult population. AACT is a liaison to the UMDF Board of Trustees who will assess and evaluate, provide advice and guidance, and make recommendations to UMDF on all adult related issues and/ or needs.

www.umdf.org/AACT
connect@umdf.org

In conjunction with UMDF, we are excited and pleased to preview the Adult and Young Adult Program that will be presented at Mitochondrial Medicine 2018: Nashville:

Thursday, June 28, 2018
12th Annual Adult Gathering
6:00 pm to 8:00 pm.

Friday, June 29, 2018
Ask the Mito Doc Panel - UMDF Staff Panel Speakers: Zarazuela Zolkipli Cunningham, MD; Mary Kay Koenig, MD; Andrea Gropman, MD;

Navigating Social Security Disability Panel
Moderator: Donald E. Garrison, JD
Panel Speakers: Carol Rabideau, LCSW; John P. Garner, JD, Social Security Disability Attorney; Tim Takacs, JD, Certified Elder Law Attorney; and Joy and Bryan Krumdiack.

Saturday, June 30, 2018
Genetics 101 Talk - Speaker: Tyler Reimschisel, MD.

Other sessions of special interest....
Practical Strategies to Enhance Independence Workshop I
Mitochondrial Disease of Non-Genetic Origin
Cardiology Issues in the Mitochondrial Disease Patient

To read the entire program and to register, click here. http://www.umdf.org/wp-content/uploads/2018/03/2018-Family-Program_WEB.pdf

We look forward to seeing you in Nashville!

DIET TIP

Dr. Bruce Cohen- MD, FAAN

"Always discuss your diet with your physician or provider. Diets are different for people with gastrointestinal disorders and low muscle mass. For those that are overweight, the use of a modified low-carbohydrate diet is reasonable. These would include the "Eat-Fat, Get-Thin Diet" by Mark Hyman, MD, but there are others. Portion control diets (Nutrasystem, Weight Watchers) do work.

*I talk to my patients about the **No-White, Rainbow Diet**: Stay away from food that comes in cardboard boxes; fresh fruits and veggies are best. If the base of the food is white (rice, grain, wheat, potato, sugar, corn syrup) then avoid. If the base of the food is full of color (dark green, orange, yellow, red, purple) then consider it a friend. High quality meats and fish are fine. Some people do better with small frequent meals. Calories do count. But calorie restriction without a plan for the long term is usually not successful in the long run.*

https://www.healthline.com/health-news/hacking-cells-to-reduce-diseases-of-aging#1

UMDF

events

The energy providing education,support and research.

Past Fundraisers Benefitting the UMDF

April 6, 2018 *A Kendra Scott Gives Back event was held in Sugar Land, Texas to benefit the Houston EFL walk/run. The event raised $457.*

January, 2018 Our Indianapolis EFL team, River Strong, launched their annual bracelet and t-shirt fundraisers. This year they are not only fundraising for the Indianapolis EFL set for September 8th, but also to support mom Jeannie's run on UMDF Team Hope Energy Life in the Bank of America Chicago Marathon on October 7th. Thank you River Strong!

January 17, 2018 Runners participated in the Tri-City Medical Center Carlsbad Marathon and Half Marathon in support of the LHON Project Fund with the UMDF! Thank you to all of those who were out activating their mitochondria on behalf of those who can't – you are awesome!

February 5, 2018 Homie's Hope held two fundraisers in 2017 to support the UMDF and the Energy for Life: Indianapolis Walkathon. Cornhole for Hope and Golden Tee for Hope were highly successfully and raised $4,780 for the UMDF mission! Thank you Homie's Hope!

February 12 and March 2, 2018 Love the LL's Smith Family of the Chicago EFL organized two fundraising nights at Chicago Bulls games. The attendees had amazing seats to see some great basketball and raised $80 to support the Chicago EFL.

February 20, 2018 The England Family hosted a Kendra Scott Gives Back Night in Las Vegas, NV *(right)*. The adorable London was the hostess of the event and was able to raise over $1,118. London said "it was the best day ever!" We agree London – great job!!

February 25, 2018 Team Kaden of the Houston EFL walk/run held a Premier Jewelry fundraiser raising almost $200! Thank you to Laura O'Hara for organizing this event each year!

February 25, 2018 Brady's Thirty-One Fundraiser was organized by Tiffany Grove of Olney, Illinois to support the Brady Sterchi Research Fund. This has been an annual event for the research fund and has raised over $8,700 in its history – WOW! It's ongoing through April, so this support will grow again for this year as well!

March 24, 2018 A Help Fund a Cure night was held in remembrance of Kenley Montes.

January 2018 St. Bernadette Catholic School in Monroeville, PA, participated in their 17th Annual Coins for a Cure Campaign in memory of Gina Mohan, who attended St. Bernadette's school. Grades K-8 raised $1,688 for the UMDF! Thank you for your many years of support!

London England

The Junior Class Executive Committee from Altoona High School with UMDF CEO Chuck Mohan

March 10, 2018 The 'Maddie-Thon' was held at A-C Valley High, Foxburg, PA, in honor of Maddie Stewart. The Student Council organized the event that included carnival games, sliming the Principal and duct taping a teacher! Over $4,000 was raised for Team Maddie for the Energy for Life Walk in Pittsburgh. Thank you students, teachers and staff!

March 11, 2018 The 2nd Annual Quarter Auction for Team Miles for Myles for the Energy for Life Pittsburgh was another great success! Organizer, Miranda Corcoran rallied her troops to raise over $2,500! Thank you so much for all your support!

March 24, 2018 Help Fund a Cure – In Remembrance of Kenley Montes.

March 24, 2018 The 9th Annual Jackson Culley Mito-What? 5k was held in Millington, TN. With over 300 runners, the 9th annual event was a huge success! Thank you, Angie, Cindy and the Culley Family for all your support!

March 29, 2018 The Chi Omega Chapter at University of Nebraska Lincoln held their annual Cup of Joe with Chi O to benefit the UMDF. They honor their sorority sister Tricia Melland and support her EFL Kansas City walk team. Thank you Chi O!

March 31, 2018 Fitness 1440 in Seymour, Indiana held the Fools 5K to benefit the United Mitochondrial Disease Foundation. The group honored River Dicken's and her family with donations from the event. Thank you!

April 7, 2018 Bet on Baylee held its final show in Roseville, Ohio. Over 150 people attended the final event with a silent and live auction, food, music and fun! A big goal was met on the 14th year - raising over $100,000! Thank you for all your support, Thompson Family!

April 8, 2018 A Kendra Scott Gives Back event was held in Dallas, Texas. The event supported the Dallas-Fort Worth EFL walk/run which will be held on April 28th in Arlington, Texas.

April 8, 2018 Dawgs for a Cure at Butler University in Indianapolis, Indiana held an Egg Hunt with candy, fun games and the Easter Bunny. The event supported the Jack Edwards Research Fund. Thank you Dawgs!

April 8, 2018 Danica's Pride of the Dallas-Fort Worth EFL held their annual T-Shirt Fundraiser *(left)*. The event is organized each year by Janet Howell and other members of Danica's Pride. Their goal is to raise $1,000 this year and exceed the $750 they raised last year. Thank you Danica's Pride!

April 18, 2018 The Junior Class Executive Committee of students at Altoona High School in Pennsylvania dropped by the UMDF office in Pittsburgh to present a check on behalf of Brielle Harmon for EFL Pittsburgh *(top)*.

Bet on Baylee

Saturday, April 7, 2018 was the final Bet on Baylee and her mom, Jody Thompson, had a big goal: $100,000. Coming into the night, Jody knew she needed to raise $9,600 and with over 150 in attendance, emotions were high.

The night started with over 60 live auction items, with Sheriff Matt Lutz at the microphone. Items donated ranged from a signed Pete Rose Poster from 1971, the Ohio State University 3D Stadium pictures, season passes for Midway Speedway to handmade furniture. There were also a lot of silent auction items that gave attendees a chance to bid and win great gift certificates and merchandise from local restaurants and services.

With so much love and support for Baylee, Jody, her family and UMDF, that it was no wonder that Jody was able to hit her goal before the half time mark of the live auction. Closing the night, was a final live auction item, a handmade quilt of t-shirts from previous Bet on Baylee events. Bets came in so quickly that Matt nearly lost his breath!

Raising $1,400, many folks came together to buy the quilt to donate back to Jody for her to treasure for life.

It was an honor for UMDF Staffers, Chuck Mohan, Kara Strittmatter, Tania Hanscom and Nicole McCaslin to attend. Jody, thank you so much for your love, support and dedication for a cure.

Even though Bet on Baylee may be over, we know your fight never will be. The Thompson Family will forever remain in our hearts and minds!

Special Event Highlight: Jackson Culley Mito-What?

The phrase “it takes a village” is probably pretty common with our families. So, when Jackson Culley’s grandparents asked their church, Grace Community in Millington, Tennessee, for help with the Mito-What? 5k, they didn’t blink an eye.

Nine years later, the Annual Jackson Culley Mito-What? 5K, is still going strong. The event has had 400-500 registered participants, with an average of 300 racers annually.

Millington may be a small town but if you ask, most people will know the answer to ‘Mito-What?’ Angie Nunn and Cindy Kraft are the organizers of the event.

“We started this 9 years ago to show our support for Jackson’s Family,” Angie said. “In turn it spread awareness about Mitochondrial Disease. Little did we know it would become an annual event.”

Along the way, local businesses have reached out and sponsored every year: banks, landscaping, sign companies, dentist, builders, and churches. Those businesses never blink an eye to support them each and every year. One of the top supporters of the event is Grace Community Church. From day one, they have used the church to pack goodie bags, sort shirts and more.

“We are so grateful not only to Grace but to our little community here in Millington and all the friends, family, and businesses that come out every single year to support our cause,” Angie said. “We hope that by Year 10 we can reach a total of $200,000 raised. I have no doubts we will get there thanks to all the love shown over the last nine years.’

Thank you, Angie, Cindy, Grace Community Church, Millington Community and everyone else involved in making the Annual Jackson Culley Mito-What? 5k so very successful!

Ric Walters and Ben Jr.

Volunteer Spotlight: Houston EFL Committee

The 2018 Energy for Life Walkathon and 5K season is in full swing. The events are critical to funding needed research, providing education opportunities and supporting families. The Energy for Life Planning Committee is made up of local volunteer leaders who provide input, plan and execute the events. The committee is critical to the success of the event.

Many EFL committees are made of volunteers who are the primary care-givers. In Houston, Texas, the Planning Committee is made up of 3 mighty members who are all extended-relations to mitochondrial disease.

Ric Walters calls himself the "angry grandfather". His family lost Ben Jr. to mitochondrial disease in 2012. Ric decided to chair the 2018 Houston event and harness that angry energy. "I hope that our work will bring us to a point where no child suffers the pain and misery my beautiful grandson did and that no family will ever have to grieve the death of their child from any disease like my precious daughter Ruth and her husband Ben Sr. did."

Bobby and Kris Neelon joined the committee after being asked by Kris's aunt, UMDF Director of Development Beth Whitehouse. Although Bobby and Kris do not personally know someone affected by mitochondrial disease, they were familiar with the UMDF through Beth. "We didn't hesitate to volunteer for the committee. We love the mission and are happy to be a part of it for the benefit of current and future families."

The committee and all volunteers brought an ENERGY to Houston that was truly apparent on event day April 7th. Kris said, "We have enjoyed the spirit and the passion of working with the Houston committee. Although it is a small group, it has been a great joy."

Grandparents, friends, cousins, neighbors. You could be a part of something great in your community!

To find a walk/run near you, please visit www.energyforlifewalk.org. If you'd like to learn more about committee or volunteer opportunities, please reach out to us!

Team Heidi Marie

EFL Team Spotlight: Team Heidi Marie

April marks a milestone for the Energy for Life Walkathon in the San Francisco Bay Area. The month marks the 7th time this walk has occurred and it will be the 7th year in a row that Team Heidi Marie will be walking with their bright PINK team shirts. Not only will they be walking – but they will be out there volunteering in full force! Team Captain and Heidi's Mom, Norma Gibson, has been one of the event co-Chairs since the beginning!

Norma, along with her family and many friends, travels down from Ukiah, CA, each year for their love of Heidi and the UMDF. Since starting this walk, members of Team Heidi Marie have raised over $50,000! Prior to helping to organize the walk, Norma hosted numerous annual BBQ fundraisers at the family home– it was the highlight of the year for Heidi!

Heidi was first diagnosed in 1987 with MELAS. Her symptoms started with a failed eye exam at age 8, then optic nerve atrophy, left side muscle atrophy and finally diagnosed at age 12. Her disease progressed to hearing impaired, speech impaired, further vision impairment and finally into a wheelchair. Through it all, Heidi maintained a great sense of humor, loved people, and was a joy to everyone. Heidi was a bright and spunky young lady until mitochondrial disease took over her life. She fought valiantly through the years until she passed away in 2001. She loved UMDF and all of the staff – especially Chuck Mohan.

"She would be so proud to know that you are supporting her cause by being a part of the Energy for Life Walk toward a cure for mitochondrial disease," said Norma.

Team Heidi Marie has been working hard towards funding research towards treatments and cures.

They have stepped up their efforts through the EFL Walkathon. They are able to collect generous donations, corporate donation matches, wrap around fundraisers and birthday donations all in support of their team! In fact both Norma and her granddaughter, Farrah, have asked for donations to the walk team in lieu of birthday gifts!

Norma has been a faithful UMDF Volunteer since 1997 and continues to fight for all of our families. She not only chairs the walkathon, she is a huge help in carrying out all of the preparations. She can be seen on walk day setting up tables, blowing up balloons, marking the walk route, climbing in and out of her truck and, most importantly – talking to the families who are coming out to the walk! Not only does she cheer on Team Heidi Marie – she cheers on every single team who walks with us! We know that Heidi would be over the moon proud of what her mom is doing for her!

EFL: Central Texas

Upcoming Events

May 2018 Tyler Byrd of Clovis, CA is organizing a Coins for a Cure campaign and other fundraising at his high school. Tyler is helping to spread awareness of mitochondrial disease and raising funds at the same time! GO TYLER!

May 6, 2018 If you are running in the Pittsburgh Marathon – please be sure to join our Fundraising Team! UMDF is a Contributing Charity for the 2018 Marathon. For more information, please visit *www.crowdrise.com/umdfpitt2018*.

June 2, 2018 Ride for Mitochondrial Disease will take place in Ford City, PA. This annual motorcycle event benefits Team Connor for the Energy for Life Walkathon in Pittsburgh.

June 8, 2018 Go Pro for Mito Golf Tournament in Columbus, GA. This annual event happens at the Maple Ridge Golf Club.

June 15, 2018 The 6th Annual Thomas Golf Tournament will take place in Bridgewater, MA. The event will be held at Olde Scotland Links Golf Course. Golfers have the opportunity to win a new Nissan Altima with a hole in one.

May 3-6, 2018 Join Wolf Pack vs. Mito at a Muffins for Mito event they will hold during the 100 Mile Garage Sale in Red Wing, Minnesota. The event will support the Minnesota EFL that will be held on Saturday, August 18th.

May 4, 2018 A Kendra Scott Gives Back event will be held in Chicago at the Michigan Avenue store from 5:00-7:00pm. 20% of proceeds will be donated to support the Energy for Life Walkathon in Chicago that will be held on Sunday, September 16th

May 8, 2018 Kendra Scott has opened in Wisconsin! The Southern Wisconsin Energy for Life walk will hold a fundraiser at the store in Brookfield from 6:00-8:00pm. 20% of proceeds will be donated to support the EFL walk that will be held on Saturday, September 29th.

May 10, 2018 A Panera Fundraiser will be held at the Chesterfield, Missouri location from 4:00-8:00pm. Join Olivia and Liam's Crew as they raise funds and awareness for the St. Louis EFL.

June 23, 2018 The 6th Annual Nicholas J. Torpey Butterfly Golf Classic will be held Sycamore Hills Golf Club in Macomb, MI. Proceeds will benefit the Nicholas J. Torpey Research Fund through the UMDF.

October 8, 2018 Team Hope Energy Life will be represented at the Bank of America Chicago Marathon. The team currently has 25 members. If you would like to learn more about our runners or support their efforts visit *https://www.crowdrise.com/o/en/team/bank-of-america-chicago-marathon-2018*

For a full list of events, visit ***www.umdf.org/events!***


EFL: San Francisco Bay Area

Upcoming EFL Walkathons

The Energy for Life Walkathons are well underway and we are gearing up for another great walk season this fall. Our walks would not be possible without our amazing volunteer planning committees, our team captains, walkers, donors and corporate partners! We thank you!! We would love to see YOU at a walk near you….

THANK YOU TO:

Houston
www.energyforlifewalk.org/houston

Nashville
www.energyforlifewalk.org/nashville

San Francisco Bay Area
www.energyforlifewalk.org/sanfrancisco

Tampa Bay
www.energyforlifewalk.org/tampabay

Dallas/Fort Worth
www.energyforlifewalk.org/dallasfortworth

Atlanta
www.energyforlifewalk.org/atlanta

COMING SOON:

We are looking forward to our Spring Walks! Please help us reach those goals by supporting one of these amazing cities!

May 6, 2018 - New England
www.energyforlifewalk.org/newengland

May 20, 2018 - Columbus
www.energyforlifewalk.org/columbus

June 9, 2018 - St. Louis
www.energyforlifewalk.org/stlouis

June 9, 2018 - Pittsburgh
www.energyforlifewalk.org/pittsburgh

August 18, 2018 - Minnesota
www.energyforlifewalk.org/minnesota

September 8, 2018 - Indianapolis
www.energyforlifewalk.org/indianapolis

September 8, 2018 - Delaware Valley
www.energyforlifewalk.org/delval

September 15, 2018 - Western New York
www.energyforlifewalk.org/westernny

September 15, 2018 - Kansas City
www.energyforlifewalk.org/kansascity

September 15, 2018 - Detroit
www.energyforlifewalk.org/detroit

September 16, 2018 - Chicago
www.energyforlifewalk.org/chicago

September 29, 2018 - Southern Wisconsin
www.energyforlifewalk.org/westernny

September 30, 2018 - Seattle
www.energyforlifewalk.org

October 13, 2018 - Central Texas
www.energyforlifewalk.org/centraltexas

October 13, 2018 - Charlotte
www.energyforlifewalk.org/charlotte

P.S. It's not too late to make a donation or to double your donation with a matching gift! Ask your employer if they match gifts!

Ask the Mito Doc℠

Living with mitochondrial disease presents many twists and turns, and a maze of questions. UMDF is pleased to offer answers to some of those questions as taken from Ask the Mito Doc℠ at www.umdf.org. Please note that information contained in Ask the Mito Doc℠ is for informational and educational purposes only. Such information is not intended to replace and should not be interpreted or relied upon as professional advice, whether medical or otherwise.

Q: Can an MRI of a patient with mitochondrial disease look similar to an MRI of a patient with MS (brain/Spine). In other words, can similar patterns on demyelination occur in both diseases?

A: In the strictest sense - the MRI in an MS patient would not look like an MRI seen in mitochondrial disease. Some features may overlap - but the patient's clinical course, exam and MRI findings should be distinct enough to allow for an expert to distinguish between the two. If that is not enough - the lab work and spinal fluid analysis usually helps.
Sumit Parikh, MD

Q: I have mitochondrial dysfunction and just diagnosed with breast cancer. How likely is post operative radiation therapy going to cause more trouble, such as myopathy? Any way to limit damage?

A: This is a difficult question to answer without more medical details. Primary mitochondrial disease may worsen with cancer treatments - but some patients may remain stable. It is not clear if cancer therapies impact patient with other diseases causing secondary mitochondrial dysfunction.
Sumit Parikh, MD

Q: Can Mito Disease cause a 15 1/2 year old girl to not menstruate yet?

A: Endocrine changes in primary mitochondrial disease may cause delayed menstruation but we would not automatically attribute this symptom to mitochondrial disease. We would still recommend a comprehensive evaluation by endocrinology to look for any treatable or modifiable cause.
Sumit Parikh,MD

Q: Can mitochondrial disorder cause stomach pain upon exertion? My son (7 years old) is being evaluated (Genetic Specialist appt March 12) and besides the obvious symptoms, he complains of stomach pain after physical activity, to the point where he grabs his stomach and has to sit. He cannot tolerate physical activity for a long time on some days and other days he is ok. He is already on Prilosec.

A: It appears by the question that the etiology of this child's issues is not yet known and that he/she is undergoing evaluation. As such, it is far more important to determine the underlying cause of his or her problems then attempting to determine if abdominal pain is secondary to mitochondrial disease. If it is mitochondrial disease then it may be due to over exertion in unconditioned or diseased muscle. Or, it could actually be Neurovisceral pain. As stated, The overall cause of the child's problems needs to be determined before any particular symptoms can be attributed to the diagnosis or to another etiology.
Fran Kendall,MD

Q: What is the difference between Exome/Genome & Nuclear/mtDNA? Which test do you find gives a clearer picture?

A: There is no specific test that is better or worse for all patients as it depends on the clinical findings and features in a given individual patient and the concerns of the evaluating clinician. For example, I have had two separate patients present recently with a history of myoclonic epilepsy and lipomas concerning for MERRF. As such, I ordered a single mtDNA mutation analysis test and diagnosed them both with this disease.

In other patients who clearly have mitochondrial disease, for example patients with clinical, radiographic, and biochemical evidence of Leigh Disease, both mtDNA and nuclear mitochondrial gene sequencing may be indicated.

In regards to more advanced genomics, again, it depends on the patient and their clinical features. For example, some patients who present to my office for evaluation of mitochondrial disease clearly have other disorders. As such, depending on my concerns, I may elect to do more advanced genomics and not focus on mitochondrial genes at all.

Although whole genome sequencing is now available clinically, my understanding is that it is not generally covered by insurance and at least one large clinical testing laboratory has indicated that they currently have no overwhelming evidence that suggests it is far more efficacious than whole exome sequencing in regards to diagnostic rates and exome IS covered by most insurance companies. As such, for now, exome sequencing is likely the best bet when advance genomics are required.

The bottom line is that patients need to be evaluated by physicians who have a clear understanding of testing and what is appropriate for a specific individual. Nothing can take the place of an experienced clinician.
Fran Kendall,MD

Corporate Partnership Spotlight

Who are they?
Santhera Pharmaceuticals is focusing on the development of treatments for neuro-ophthalmological, neuromuscular and pulmonary diseases that currently lack treatment options, such as Leber's hereditary optic neuropathy (LHON), Duchenne muscular dystrophy (DMD), congenital muscular dystrophy (CMD) and cystic fibrosis (CF).

They have dedicated more than a decade to researching potential treatments in their ongoing mission to make effective medicines available for these often overlooked, life-altering diseases. They are passionate about improving patients' quality of life and are well on the way to becoming leaders in rare mitochondrial and neuromuscular disorders.

Santhera Pharmaceuticals (*www.santhera.com*) was founded in September 2004 through the merger of two start-up biotech companies, MyoContract AG (Switzerland) and Graffinity Pharmaceuticals AG (Germany). Santhera's headquarters are located in Pratteln, Switzerland (near Basel), with subsidiaries in Germany, the UK, Italy, the Netherlands, the US and Canada. Santhera's U.S. office is located in Burlington, outside Boston. Santhera's shares have been listed on the SIX Swiss Exchange under the ticker "SANN" since November 2006.

From the beginning, they have been committed to helping patients through the discovery, development and commercialization of medicines for rare diseases. Since 2004, they have developed their pipeline by conducting numerous clinical studies in Europe and North America.

In September 2015, Santhera received their first approval, the European Marketing Authorization, for Raxone® (idebenone) in the treatment of patients with LHON. This makes Raxone the first and only medicine to be approved for this condition. Indeed, it is the first approved for any mitochondrial disorder: a major milestone in addressing the unmet medical need represented by this group of rare diseases. As part of their European approval, Santhera is conducting additional efficacy research with their product for patients with LHON, which includes conducting an open-label trial. This trial named LEROSalso is open for enrolment in the U.S. for patients who have not taken idebenone previously and have had LHON symptoms for less than five years.

What do they do for UMDF?
Santhera Pharmaceuticals has been partnering with UMDF in the fight against mitochondrial disease since 2014. Santhera began their support of UMDF at our National Symposium focusing on the LHON educational program. Since that time, they have increased their generous partnership by sponsoring our symposium scholarship and registration fund. Jodi Wolff, Santhera's Head of Patient Advocacy for the U.S., is one of the founding members of our Industry Advisory Council and Registry Advisory Board. Santhera has worked closely with UMDF and the LHON community to raise awareness of LHON.

Santhera says…
Santhera is proud to support UMDF's mission of finding treatments for mitochondrial disease and educating and supporting families. UMDF has been a vital resource for Santhera as we aim to develop treatments for mitochondrial and other rare diseases. We applaud UMDF's leadership in the mitochondrial field, their deep commitment to uniting the mitochondrial community, and look forward to our continued work together.

UMDF Staff says…
We are so grateful to the entire Santhera team for their dedication to and focus on the development of treatments for mitochondrial disease. We value their generous partnership with us and look forward to continued collaboration to improve the lives of those living with this devastating disease.

Symposium Preview

Mark your calendars for June, as UMDF brings the national symposium to Nashville. Scientist and clinicians will gather June 27-30, 2018. The UMDF Patient/Family will be held June 29-30, 2018. LHON program runs June 28-29.

For patients and families, the UMDF symposium is designed to enable you to network with many families and individuals who, like you, are seeking more information about mitochondrial disease. The UMDF symposium offers unique access to many of the top mitochondrial specialists through session presentations, Ask the Mito Doc panels, and on a one-to-one basis through the Doctor Is In forum. You will also be able to speak with our exhibitors about new products and diagnostic testing that is available.

Our Scientific and Clinical sessions are being led this year by Vamsi Mootha, MD, from the Harvard Medical School. The theme this year will be Mitochondrial Chemical Biology. Bruce Cohen, MD, from Akron Children's Hospital, is the CME Chair for the symposium.

SAVE THE DATE!

Mitochondrial Medicine 2018: Nashville
Sheraton Music City, Nashville, TN
Scientific/Clinical Sessions: June 27-30, 2018
LHON Sessions: June 28-29, 2018
Patient/Family Sessions: June 29-30, 2018

For more information, visit *www.umdf.org/symposium*

FAMILY PROGRAM REGISTRATION FORM
Mitochondrial Medicine 2018: Nashville
Sheraton Music City - Nashville, TN
June 28 - 30, 2018

REGISTER NOW TO GUARANTEE YOUR ATTENDANCE!

Three Ways to Register:

1. Complete the registration form below and mail it back to the UMDF.
2. Complete the registration form below and fax it to UMDF at 412-793-6477.
3. Register online at www.umdf.org/symposium/registration.

Scholarships
For those experiencing financial hardship, limited funding is available to offset part of the cost of attending the symposium. To inquire, contact the UMDF toll free at 1-888-317-UMDF or visit www.umdf.org/symposium for more information. The application deadline is April 15, 2018.

Accessibility
Handicapped-accessible rooms are available upon request, and there is wheelchair access in all public areas. If you have any special needs that require additional assistance, please contact the UMDF staff at 1-888-317-UMDF. Requests should be received at least two weeks prior to the conference.

Scooters
UMDF has arranged for scooters for those in need of this type of assistance. In order to ensure that we can meet your needs, please be sure to request a scooter on your registration form.

Cancellation Policy
All cancellations will be subject to a service charge based on registration fee amounts - a small percentage must be deducted to cover processing charges to the foundation. A written notification of cancellation must be made to UMDF in order to process any refunds. No refunds will be issued after Friday, June 30, 2018.

Permission to Use Image
By registering for this conference, you have given the UMDF permission to use images (photo and/or video) from this event for educational and promotional purposes for this and future conferences. If you do not want your image to be used, please submit a letter by July 1, 2018, to UMDF, Attn: Cliff Gorski, 8085 Saltsburg Road, Suite 201, Pittsburgh, PA 15239.

Marketing Opt-Out
As a 'thank you' to exhibitors for participating and financially supporting our efforts, the UMDF has agreed to provide them with the names and addresses of our attendees. If you do not want your name and address to be released, please submit a written letter prior to the conference to:

UMDF Development Department
8085 Saltsburg Road
Suite 201
Pittsburgh, PA 15239

REGISTRATION RATES

Early Bird	After May 31	Registration
☐ $115	☐ $225	Individual Registration
☐ $225	☐ $450	Family Registration *(2 adults/same household)*
☐ $42	☐ $85	LHON Program **Only**
☐ $65	☐ $65	Additional Friday Night Banquet tickets *(per ticket)*

Individual and Family Registration Rates include syllabus, daily continental breakfast, refreshment breaks, two lunches, LHON Program and Friday's banquet. **Daily Rates are available online.**

TEEN MEALS

Early Bird	After May 31	
☐ $35	☐ $45	Teen Meals *(includes lunches, breaks, dinner, and dance)*

Special Assistance ☐ Scooter ☐ Other _____

Special Dietary Requirements ☐ Vegetarian ☐ Gluten-Free Other _____

Are you visually impaired? ☐ Yes

Total Full Registration Fee: **$** _____

One form per registrant. Please copy this form for additional attendees and TEENS.

Online registration closes Wednesday, June 20, 2018

Please make all checks payable to: **United Mitochondrial Disease Foundation** or **UMDF**

Please charge this registration to the following: Visa MasterCard Discover American Express

Card Number _____ Expiration Date _____

Name as listed on card (please print) _____ CVV:_____

Signature _____ (invalid without signature)

PLEASE PRINT CLEARLY

Last Name _____ First Name _____ MI _____

Degree/Suffix _____ Specialty_____

Address_____

City_____ State/Province_____

Country _____ Zip/Postal _____

Email:_____

Phone:_____ Fax _____

Mail to UMDF, 8085 Saltsburg Road, Suite 201, Pittsburgh, PA 15239 or fax to 412-793-6477

UMDF advocacy

RARE DISEASE DAY ADVOCACY

The United Mitochondrial Disease Foundation joined rare advocates from across the nation for Rare Disease Week on Capitol Hill, February 25-March 1, 2018. The week-long advocacy conference began with more than 450 advocates for the Legislative Conference, with more than 125 participating remotely through the event livestream. Experts from Capitol Hill and patient advocacy organizations discussed what to expect from Congress following changes to the Orphan Drug Tax Credit, how to build effective relationships with Members of Congress and their staff, and key pieces of legislation for 2018.

On February 27, advocates began Lobby Day at breakfast with remarks by Joel White, Founder and President of Horizon Government Affairs. Mr. White was followed by Dr. William Gahl, Head of the Undiagnosed Diseases Program at the National Institutes of Health (NIH) and Debra Lewis, who serves as Acting Director of the Food and Drug Administration's Office of Orphan Product Development. Advocates left the breakfast energized by the speakers and ready to educate Members of Congress and their staff about issues affecting the rare disease community.

371 advocates representing 49 states participated for a total of 294 Lobby Day meetings, discussing the Rare Disease Congressional Caucus, precision medicine legislation, incentives for rare disease drug development and other key legislative topics.

VISIT THE UMDF ACTION CENTER

UMDF is committed to empowering our entire community through governmental advocacy. We will work with you on the federal and state level to help educate and impact decisions that address the needs of the entire mitochondrial disease patient community as part of the "Roadmap to a Cure". Please check in frequently at *http://www.umdf.org/advocate*

COMING THIS FALL

Since we are more than a year away from our next "Day on the Hill", we are planning an event around Awareness Week (September 16-22, 2018.) More details will be coming, but we are planning an advocacy event for you to complete in your home town, or from your home. More details soon!

Want to learn more and lend your voice? Visit the UMDF Advocacy Action Center and TAKE ACTION on the issues impacting our community.

UMDF national

News from the national office.

Are you looking for someone to connect with? Connect with a UMDF Ambassador, an affected individual/family member who would be happy to network with you. To get started, email info@umdf.org or call us toll-free at 1-888-317-8633.

WHAT UMDF REGION DO YOU LIVE IN?

East Region
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www.umdf.org/regions/east

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West Region
Tania Hanscom
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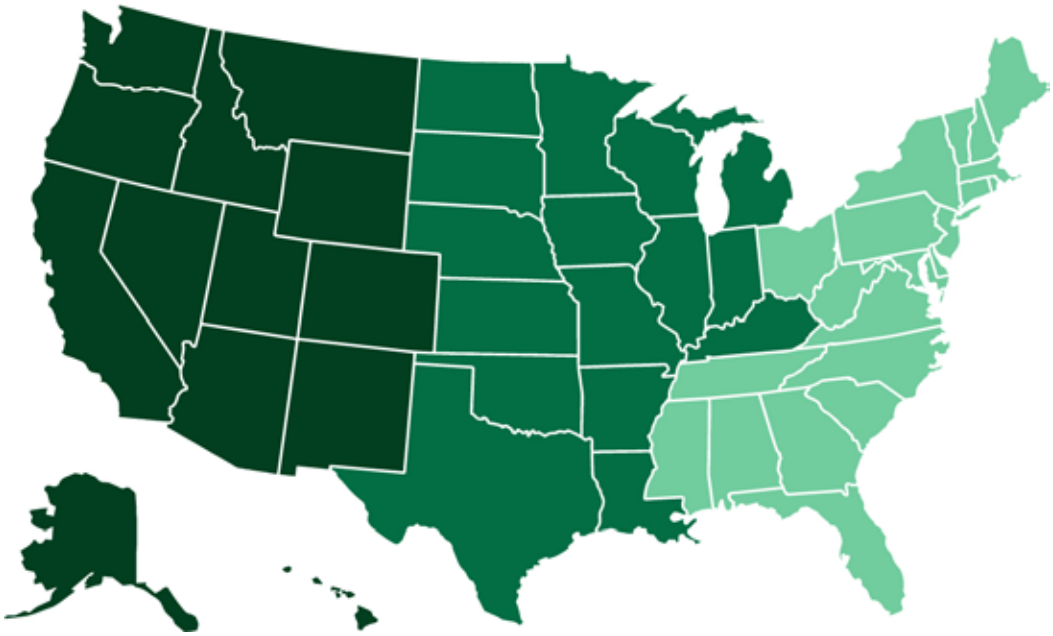

United Mitochondrial Disease Foundation Staff

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UMDF Mission

To promote research and education for the diagnosis, treatment and cure of mitochondrial disorders and to provide support to affected individuals and families.

The UMDF focuses on coordination, communication and collaboration.

We bring people and resources together to make an impact on diagnoses, treatments and a cure for mitochondrial disease.

ADVANCING MITOCHONDRIAL MEDICINE

We are a Swiss specialty pharmaceutical company committed to developing medicines to meet the needs of patients living with mitochondrial disorders and other rare diseases.

Our focus is on the development of treatments for neuromuscular and neuro-ophthalmological diseases that currently lack treatment options and our passion is on improving patients' quality of life.

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