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United Mitochondrial Disease Foundation

MITOCHONDRIAL NEWS

Volume 10 • Issue 1 • Winter 2005

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Worms with Mitochondrial Diseases

*Bernard Lemire, Ph.D.
Department of Biochemistry
University of Alberta
Edmonton, Alberta, Canada*

UMDF Grant Recipient 2003

My research lab studies mitochondrial diseases and dysfunction in worms. Rather obscure and not terribly useful, you think? How can research on worms help us better understand and treat mitochondrial diseases in humans? Energy generation by mitochondria is such a fundamental process to life that it is highly similar in all animals. The mitochondrial respiratory chain (MRC) consists of a series of complex proteins (called complexes I to V) that convert high-energy electrons into ATP, the energy currency of most cells (See Fig. 1 on Page 10). Most of these high-energy electrons, derived from foods

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Mark your Calendars NOW! Mitochondrial Medicine 2005 Gateway to a Cure

*Scientific Sessions:
June 15-17, 2005*

*Family Sessions:
June 17-18, 2005*

*Clinician Sessions:
June 18, 2005*

*Hyatt Regency Union Station
St. Louis, Missouri*

*Scientific Program Chair
Bruce H. Cohen, MD*

Call for Abstracts

www.umdf.org/conferences

See Pages 8 & 9



**Alabama 5K Raises
more than \$34,000**
*McLeod and Peek Families
Pictured Above*
**More Fundraisers on
Pages 11-12**



By Popular Demand Energy Bands are HERE!

These silicone bracelets are UMDf-green and encircled with

★ **Energy for Life** ★ www.UMDF.org

The bracelets are a great way to raise awareness and support those affected by mitochondrial disease.

You can order online at www.umdf.org or contact the office at 412-793-8077 or email info@umdf.org for an order form.

Cost is \$4 each (postage and handling included)
OR

Package of 10 bracelets for \$10 (plus \$5 in postage and handling)
Get your friends together and split the cost!

Ask the Mito Doc

Living with mitochondrial disease presents many twists and turns - a maze of questions. UMDF is pleased to offer answers to some of those questions. All questions and responses are taken from www.umdff.org -- Ask the Mito Doc. 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.

Responders for this issue: Gerard T. Berry, MD, Jefferson Medical School, Philadelphia, PA and Amy Goldstein, MD, Children's Hospital of Pittsburgh.

The Question is:

Our daughter who is two and a half is suspected of having a metabolic disorder. The geneticist is leaning toward the mitochondrial area. Our daughter is hypotonic, has severe reflux, global development delays, heat intolerance, abnormally high pain tolerance, major regression after an illness and has balance problems. She cannot sit alone or stand alone. She has shown low carnitine levels and had elevated methomylonic acid levels during an illness. It has been suggested that we have a fundoplication. We would like to have more information from doctors who deal with these types of issues and how they will affect this procedure. What are the positive and negative issues? Our daughter can have bouts of vomiting sometimes up to forty times a day on a bad day. We have had a scope done of the esophagus and there was no damage. She does have a hiatal hernia. Any information you could share would be very valuable to our family.

Response From: Gerard T. Berry, MD

There are at least 2 issues. The first one is the need to establish in your daughter the correct diagnosis. And the

second is the need to provide the optimal treatment for gastroesophageal reflux (GER). The latter is most important as it is possible that a specific diagnosis cannot be made, but she needs the proper symptomatic treatment.

All of her clinical problems are compatible with a primary defect in mitochondrial oxidative (Ox-Phos)metabolism. The intermittent elevation in methylmalonic (MMA) acid levels may also be seen in mitochondrial Ox-Phos disorders. However, the MMA phenomenon may increase the likelihood that a specific diagnosis will not be made. As an aside, it is important that a primary defect in vitamin B12 metabolism be ruled out as well since they can be associated with intermittent elevation of urine MMA. Finding a high level of MMA and the amino acid, homocysteine, in plasma would indicate a defect in vitamin B12 as the cause of her problems. The main reason for finding the underlying metabolic cause, be it Ox-Phos or Vitamin B12, is that a specific therapy might help the vomiting and GER get better or even disappear.

Metabolic problems of many different types are associated with recurrent vomiting. And hypotonia from any cause may predispose an infant or child to GER and hiatal hernia. It is imperative that you work closely with an experienced pediatric gastroenterologist in making the decision whether a fundoplication is performed. It would be the logical procedure to do for GER alone or associated with minimal to moderate regurgitation. But if the vomiting is truly relentless and violent, it may, at the least cause the fundoplication to break down and, at the worst, cause tears or rupture of the stomach, if a natural outlet has been artificially obstructed and is necessary to expel the stomach contents during the course of uncontrolled vomiting. You all must use good judgment.

The Question is:

I am aware that there are different medications that people with mito disorders should avoid; however, I am not familiar with all of them. In my concern to avoid potential problems, is there a "list" of medications to avoid?

Response From: Amy Goldstein, MD

There are certain medications to take cautions with when you have a mitochondrial disorder. This is not an exhaustive list and does not pertain to every patient with a mitochondrial disorder. Review your individual disorder and medications with your personal physician.

Prior to any surgical procedure, review your medical history with the anesthesiologist. Certain anesthetics used in surgical procedures should be used with caution, and these should be reviewed with the anesthesiologist. The decision about whether to use specific drugs must be based on your disorder, your age, and the surgical procedure being performed. A review is provided in "Think Mitochondria" by Drs. Bruce Cohen, John Shoffner, and Glenn DeBoer, reprinted from the Spring 1998 UMDF Newsletter, and is available by calling the UMDF office. Patients with mitochondrial disorders could be at risk for a condition called malignant hyperthermia, and there is a protocol for the anesthesiologist to follow for this condition.

Valproic acid (Depakote) has been used as an anti-seizure medication in some patients safely; however, it has led to serious and fatal consequences in other patients. It should be avoided in the very young patient, especially when the diagnosis is uncertain. However, if a patient has been on Depakote without problems, with careful monitoring, it is generally safe to continue on this medication. Depakote can deplete the carnitine stores, so Carnitine should be supplemented while on Depakote.

If IV fluids are necessary, Lactated Ringers solution should be avoided as it contains lactic acid.

Antiretroviral drugs (anti-HIV drugs) are toxic to mitochondria and should be avoided if possible.

Doxorubicin, a chemotherapy medication, causes cardiomyopathy as a side effect, most likely through mitochondrial damage, and should be avoided.

Aminoglycoside antibiotics, such as gentamicin, streptomycin and tobramycin, can induce hearing loss by damaging mitochondria. This accounts for 5-10% of drug-induced deafness and 0.6% - 2% of the deafness population. These antibiotics should be avoided if the cause of the mitochondrial disorder is unknown. There are specific point mutations in the mtDNA that make one more susceptible to this ototoxic damage.

Certain antipsychotic medications can increase the risk of diabetes and should be used with caution and frequent monitoring.

Medications can be essential to your health and well-being. Please review any concerns you have with your physician. More information can be obtained from the UMDF website and through literature available from the UMDF office.

Chairman's Report

WORMS, MICE, YEAST

Money, time and effort for the study of worms, mice and yeast! Is it really necessary to spend hard earned money studying worms, mice and yeast? How long will we be funding research on worms, mice and yeast before we see clinical applications?

It wasn't until I read the lead article in this issue of *Mitochondrial News*, written by UMDF grant recipient Bernard Lemire, Ph.D., that I realized the importance and reason for studying worms, mice and yeast.

Dr. Lemire writes, "Energy generation by mitochondria is such a fundamental process to life that it is highly similar in all animals." So similar in fact that this simplest of all animals, the worm, actually generates energy (ATP) via the respiratory chain in much the same way as we do.

Worms, mice and yeast are readily accessible, affordable, easy to grow, small enough to carry around on a dish and, as of this writing, are not protected by labor unions or advocacy groups. They are the "guinea pig" of choice.

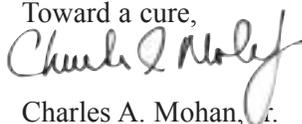
Researchers like Dr. Lemire, working with worms, mice and yeast, will have an impact that will someday provide clinical applications for easier diagnosis, better treatments and ultimately a cure for mitochondrial disease.

It's amazing that something as small as mitochondria, sub-cellular organelles 1/30,000th of an inch long, can have such an impact on our quality of life. Consider that it takes about 3,000,000,000,000,000,000 (3 Quintillion) molecules of ATP each second just to keep a human alive and that there are 10,000,000,000 (10 Billion) cells in the body containing an average of 600 mitochondria per cell. Therefore each cell must make about 5,000,000 (5 million) molecules of ATP each second and each mitochondria in that cell must

produce, on average, 8,333 molecules of ATP each second just to keep us alive. No wonder these small mechanisms are called the power house of the cell, and no wonder why a "glitch" in this process can have such varied results adversely affecting the quality of life in patients.

Hmm, if worms, mice and yeast are all that "simple" and yet that similar to us, perhaps we're not as complex as we think! Worms, mice and yeast – lions, tigers, and bears!

Toward a cure,



Charles A. Mohan, Jr.



In Memory of ...

This issue of *Mitochondrial News* is being dedicated to Chana Scholl, 10-15-57 to 2-3-05. Chana was the founder of the COX Foundation which was the nucleus for the formation of UMDF.

The UMDF Board

On page 12, you will find a brief description of the UMDF Board of Trustees and their roles in the foundation. If you would like to pose a question for our trustees, please send them to kara@umdf.org or mail them to UMDF, Attn: Kara, 8085 Saltsburg Road, Suite 201, Pittsburgh, PA 15239. More information about the Board is available at www.umdf.org (About UMDF).

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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.

Newsletter Editor

Kara Strittmatter
kara@umdf.org

Chapter Activities

NEW ENGLAND CHAPTER

Boston, MA
President: Bridget Willis
Phone: 413-593-5920 (Beverly Ingram)
Email: NEngChapter@umdf.org



Pictured Above: Emily & Jackie Tyler, Heidi Bailey, Darlene & Natalie Tongue, and Betel & Billy Arnold

The Longmeadow, MA, Mito-What? 5K Run/Walk was held on October 3, 2004 and raised more than \$37,800! Great work, New England!

Youth Fundraiser

In memory of Matthew Bailey, Mrs. Petrucci's Third Grade Class in Greenport, New York donated \$68 in the spirit of the holiday season.

ATLANTA AREA CHAPTER

Atlanta, GA
President: Holly Capp
Phone: 770-506-7441
Email: AtlChapter@umdf.org

Upcoming Events

- April 30, 2005 - Race for Riley, Whatever it Takes 5K Walk/Run and Tot Trot, Georgia Baptist Children's Home in Palmetto, GA. For more info, call Waynette & Rodney Peek at 770-463-0714 or email wayrod1@bellsouth.net.
- May 2005 - Benefit Dinner

Special Thanks

- Barbara Howard of Mansfield, MA, went door-to-door and collected money for UMDF in honor of Ryan Shea, son of Deb and Bill Shea.
- Mary Ryan hosted an Evening of Jewelry in honor of her son, William Ryan, and raised \$300.



In lieu of wedding favors, Aimee and Kevin Beam donated \$500 to UMDF in honor of their flower girl, Kayla Biagiotti. Thanks Aimee and Kevin - enjoy your new life together!!!



Volunteers braved the rain in September during the New England Air Show at Westover Air Reserve Base in Chicopee, MA. \$900 was donated to UMDF in honor of the Ingram Family.

★ Special Welcome to ★ UMDF's Newest Chapter

The Atlanta Area Chapter officially joined the ranks this past Fall and their officers are:

Holly Capp, *President*
Ashley DiLorenzo, *Vice President*
Katie Lyons, *Treasurer*
Mary Swinn, *Secretary*

1st Annual Fore-a-Cure Golf Tournament was a HUGE Success - raising more than \$40,000 in November. Well done!

NEW YORK METRO CHAPTER

Manhattan, NY
President: Mary Pisani
Phone: 203-287-0655
Email: NYMetroChapter@umdf.org

Annual UMDF Benefit Dinner raises more than \$15,000 in October. Special thanks to David, Angela, Nicholas and Brendan Nunno for all their HARD work!

Upcoming Events:

- February - Snow Tubing Event (partial proceeds to UMDF)
- May 7, 2005: Matthew Dudgeon Memorial Walk (partial proceeds)
- May 21: Walk in Chatham, NJ and 5K Run/Walk in North Haven, CT

Youth Fundraisers

- Floral Park Memorial High School, NY, raised \$130.67 in a Coins for a Cure campaign in honor of Nicole Kelli Nieves.
- In Honor of Brittany Berry, kids at Cordello Avenue School in Central Islip, NY, raised \$345 by having a UMDF Day. Each child wore green and was given a chance to win an ice cream party.

Special Thanks to all the children and youth who participated in these events. Your donations can and will Make a Difference!



The Atlanta Chapter celebrated the holidays together and enjoyed a visit from Santa



DELAWARE VALLEY CHAPTER

Philadelphia, PA
President: Maripat Shelly
Phone: 215-256-0273
Email: DelValChapter@umdf.org

Upcoming Events:

- 6th Annual Energy for Life Run/Walk (formerly Shelly's Heroes) -- Tentatively scheduled for May 7, 2005 (Check www.umdf.org).
- June 11, 2005 - Brew at the Zoo, Elmwood Park Zoo.
- Dodge for a Cure - Dodgeball Tournament for participants 18 years and over. Date and location TBA.
- COOKBOOKS - contact the chapter to order your cookbook today. \$15.00 mailed anywhere!

Successful Events

- DJs, 9 to 5, raised \$100 during a fundraiser in September.
- You Go Girl raised close to \$4,400 to benefit UMDF. Special thanks to Joe & Happy Halligan and Kevin Lawn.
- The chapter Fashion Show was also a success - raising close to \$5,775 in November. Special thanks to the Polsky Family!



Holiday Party Always FUN!

The chapter's annual holiday party at Merion Tribute House was filled with happy families doing crafts, enjoying magic and an impromptu talent show. Pictured above, the DiPietro boys show off their singing talents.

Crystal Beaded Bracelets

Beautiful crystal beaded bracelets are now available through the chapter. You can choose between three sterling silver messages (Hope, Miracles, Cure) or a single message (Hope). All bracelets have the awareness ribbon near the clasp. Pictures and order forms are available on the Delaware Valley Chapter web page at www.umdf.org.

Special thanks to Beth Hartman for starting this wonderful fundraiser to benefit UMDF.

INDIANA CHAPTER

Indianapolis, IN
President: Sue Ann Bube
Phone: 317-894-9099
Email: INChapter@umdf.org

Upcoming Event Pack The House

The Chapter is once again working together with a local hockey team, the Indiana Ice, for a victory against mitochondrial disease! Any person or company that purchases at least 30 tickets will have the chance to win two courtside Pacers tickets. The event will be held at Conseco Fieldhouse on February 12th at 7:00 p.m.

Coins for a Cure

Blue River Valley Schools, of Mount Summit, IN, raised \$1,100 in honor of Seth Boling.

"After coming back from the Pittsburgh UMDF conference, we decided to do a *Coins for a Cure* in our children's school. Our hopes and prayers are that many other schools will do this and together we will find a cure." - *The Boling Family*

KANSAS CITY CHAPTER

Kansas City, MO
President: Pam Johnson
Phone: 913-631-3070
Email: KCChapter@umdf.org

Save the DATE

Kansas City Chapter's **Second Annual "Mito What?" 5K Run and 1 mile walk** is set for Saturday, May 14, 2005. The event will be held in Corporate Woods Founders Park. Please contact Deidra Atchley at 816-537-6293 for more information and find out how you can help make this event a success once again!!

ARIZONA CHAPTER

Phoenix, AZ
President: Suzanne Perryman
Phone: 480-419-0167
Email: AZChapter@umdf.org

Suzanne Perryman, *President*
Courtney Whynott, *Vice President*
Marge Calabrese, *Treasurer*
Janet Churchward, *Secretary*
Thom Montgomery, *New Member*
Committee Chair

Special Thanks to:

- Anytime Women's Workout raised \$100 in honor of Anne and Alexandra Churchward. Thanks, Karen Fisch Hidalgo!



The new officers have been busy planning meetings and events for 2005 and beyond. A *Family & Friends Educational Day* is one event in the works for this revitalized chapter!

Chapter Activities

Upcoming Events

- March 5 - 2nd Annual "Bet on Baylee" Casino Night at Roseville Community Center (near Zanesville, OH)
- May 29 - Shadow Woodstock 2005 - an outdoor jamboree, and family fun event at 9911 Shadow Wood Circle, Chagrin Falls, Ohio 44023 at 4:00pm. For more information, please contact John Kobunski at 440-479-2371.
- June 4 - Fourth Annual KFC/UMDF 5K Run/Walk, Forest Hills Park in Cleveland Heights, Ohio. Please visit www.umdfohio.org for more information!

Special Thanks

- The Big Bear Farms (BBF) neighborhood raised \$850 in honor of Ellie Kovalcik during their annual hayride and bonfire.
- Park Road Bar & Grill raised \$124 in honor of Emily Plesko during a coins campaign.

OHIO CHAPTER

Cleveland, OH

President: Jennifer Lyman

Phone: 330-929-4430

Email: OHChapter@umdf.org

- Frank and Paul Melison, of New Image Haircutters in Willowick, OH, held several hair cut-a-thons this summer during the Lake County Captains baseball games. These wonderful cutters raised \$745.67 in honor of Jonathan Kucaric.

Energy for Life Campaigns

- Mary Ann Donut Shoppe, Inc. raised \$470 in honor of Amanda Welden.
- In honor of Dori Anne Szelesta, Thomas Wiedt sent in \$150.

Second Annual Family Spaghetti Dinner in Mentor, OH

Hosted by the Arnold and Keeney Families on January 8, the dinner raised more than \$6,200 in honor of Maiya Keeney and the many other individuals affected by mitochondrial disease. Keep up the great work!

Take me Out to the Ballgame and Get a Haircut to Benefit UMDF

New Image Haircutters, of Willowick, Ohio, will once again hold a cut-a-thon during the following Lake County Captains games:

Friday, May 20, 2005

Friday, June 17, 2005

Friday, July 29, 2005

Friday, August 12, 2005

Friday, September 2, 2005

If you would like to volunteer to help hand out information about UMDF and Mitochondrial Disease, please contact the chapter.



Hope Bracelets

The Ohio Chapter is selling bracelets with custom-made, sterling silver beads, large cube, and round Swarovski crystals. It is completed with a large silver heart charm with HOPE engraved on both sides near clasp.

For ordering information, contact Melissa Nadja at La'Jules 440-937-9947. Picture of the bracelet is available online on the chapter webpage at www.umdf.org.

SOUTHERN CALIFORNIA CHAPTER

Lakewood, CA

President: Linda Cooper

Phone: 714-921-2324

Email: S-CalChapter@umdf.org

New Leadership Positions!

The Chapter has reorganized for 2005, and new officers have been assigned. **The new officers are:**

Linda Cooper, President

Alison DeVriendt, Treasurer

Laura Maese, Fundraising Chair

Tia Acosta, Membership Chair

Debi Connelley, Meetings Chair

Thank you all for your ongoing commitment and for accepting your new positions.

Thankful Hearts

Looking back to 2004, the Chapter would like to thank all the family, friends, neighbors, coworkers, and communities for all of their support and help with the UMDF mission and our fundraising efforts. A great big THANK YOU to Alison DeVriendt and Laura Maese for making the 2004 Wine Tasting event so successful in May. Bob and Linda Cooper's family, friends, and co-workers at Smith-Cooper International raised \$3,500.00 for the UMDF as an end of the year holiday gift for them. What a great way to end 2004, with kindness and thanksgiving.

Upcoming Events

Visit www.umdf.org for dates and locations for the Chapter Wine Tasting Event and the Chapter Golf Outing.

UMDF Development Corner

Action Required

A Donor is Waiting . . . And It's Up to You

Bulletin!!

Several major companies are ready to provide funds that can be donated to UMDF - and you can have the deduction.

Money is waiting, and only you can make it happen. In fact, securing these funds for UMDF's work could actually save you money.

Is there any reason that you can say "No" to someone else providing you with money to give to UMDF and the fight against mitochondrial disease? Is there any reason you would say "No" if it meant more money in your pocket, or a larger balance in your retirement account?

The "Catch"?

You'd have to allow world-class money management firms and portfolio managers to work with your retirement assets.

100% of your money goes to work from Day 1, with no up-front sales charges, in your choice of investment vehicles from America's leading fund families and managers. And you can actually get more dollars into your individual retirement account...even if you're already making the maximum contribution...more dollars to grow and to compound tax-free until you access them!

You could be eligible for one of these programs, if you fit into any of the following scenarios:

- If you have retirement money in an IRA, mutual funds, a retirement annuity, a 403 (b) plan or a qualified plan that allows in-service distributions;
- If you have recently retired or left the employ of a company with a vested balance in their plan;
- If you are a business owner, or have a professional practice

There are a great many choices, advantages, caveats, restrictions and requirements that you should be aware of. UMDF has experts on hand to explain how it works in your particular case.

Here's an example:

John is a 54-year-old professional in the 35% tax bracket, and plans to retire at age 65. He has \$90,000 in his IRA, and makes the maximum contribution each year; he also has \$100,000 in mutual funds and will invest an additional \$10,000 this year.

If John follows this plan and makes a \$3,500 IRA contribution for 2004, he would have a \$93,500 balance in his IRA and \$110,000 in mutual funds, for a total of \$203,500 between the two, plus or minus market performance.

But John actively supports the UMDF. He makes his contribution and then elects to roll over his IRA to one of the companies offering the program. John receives a bonus of 4%, or \$3,740, bringing his IRA balance to \$97,240.

John then takes \$3,740 from the \$10,000 earmarked for investment, the amount of his bonus IRA credit, and donates it to UMDF. This charitable contribution, in the 35% tax bracket, yields a tax savings of \$1,309. He invests the \$6,260 remainder and the \$1,309 tax savings in his mutual funds.

John now has \$97,240 plus \$107,569 for a total of \$204,809 (vs. \$203,500) - after sending \$3,740 to UMDF. And more of his money is in the tax advantaged IRA!

Could you help?

Money is waiting, money you can contribute, if only you'll agree to learn more about it. Call the UMDF office today, and we'll get you all the information, with no strings attached. It is within your power to provide help...meaningful help...now. Don't let this opportunity slip away.

Newsletter Correction New England Chapter

The Walk to Create Awareness in North Haven, CT was organized in honor of Mary and Matthew Pisani's son, **Nicholas** Pisani - not Matthew.

Carry American Express?

You can donate to UMDF through the American Express Donation Site (www.americanexpress.com/give) which is powered by JustGive.org. To date, UMDF has received \$48.88!

Mitochondrial Disease Benefit Concert

Saturday April 2, 2005
Hamilton Place Studio Theatre,
Ontario, Canada
For more information,
Call Andy McDonald at 905-524-1951
or email csaoandy@yahoo.ca
Proceeds benefit mitochondrial disease efforts in Canada.

United Mitochondrial Disease Foundation Mitochondrial Medicine 2005 Gateway to a Cure



THE CLEVELAND CLINIC

The Scientific Topics and Speakers

Day 1: Wednesday, June 15, 2005

Platform Session 1: Regulation of Mitochondrial Function

- Regulation of Mitochondrial Function by Post-translational Modification, *Roderick Capaldi, PhD*
- Ethylmalonic Aciduria: a Marker of Mitochondrial Stress? *Niels Gregersen, PhD*

Platform Session 2: Epidemiology of Mitochondrial Disease

- Epidemiology of Primary Mitochondrial Disorders, *Patrick F. Chinnery, PhD, MRCP*
- Epidemiology of Environmental and Acquired Mitochondrial Disorders, *William C. Copeland, PhD*
- Acquired Mitochondrial Disease and HIV Drugs, *Grace McComsey, MD*

Day 2: Thursday, June 16, 2005

Platform Session 3: Mitochondrial and Nuclear Communications

- PGC-1a: A Versatile Integrator of the Mitochondrial Biogenic Program, *Daniel P. Kelly, MD*
- The Retrograde Response: How and Why Mitochondria Talk to the Nucleus, *Ron A. Butow, PhD*
- Fatty Acids, Nuclear Factors, and Biogenesis, *Deborah G. Murdock, PhD*

Platform Session 4: Mitochondrial Disease and Anesthesia

- Mitochondrial Disease: Anesthetic Considerations in the Preoperative Period and Intraoperative Concerns, *Joseph Farlo, MD*
- C. Elegans Mitochondrial Function--Can Worms be a Model for Humans? *Margaret Sedensky, MD*
- Anesthetics and Mitochondrial Patients, *Phil Morgan, MD*

Day 3: Friday, June 17, 2005

Platform Session 5: Diabetes and Mitochondrial Dysfunction

- Mitochondrial Defects in Type 2 Diabetes, *Gerald I. Shulman, MD, PhD*
- Mitochondrial Dysfunction in the Diabetic Heart, *Daniel P. Kelly, MD*

Platform Session 6: Gene Targeted Therapies and Mitochondrial Disorders

- Clinical Aspects & Gene Therapy of Leber Hereditary Optic Neuropathy, *John R. Guy, MD and Alfred S. Lewin, PhD*
- Development of Mitochondrial Gene Replacement Therapies, *James P. Bennett, Jr., PhD*
- Approaches to Mitochondrial Gene Therapy, *Volkmar Weissig, PhD*
- Banquet Keynote: *Douglas C. Wallace, PhD*

Day 4: Clinical Program Saturday, June 18, 2005

Clinical Session (For Physicians and Families) - Morning

- Introduction to Mitochondrial Disease, *Douglas C. Wallace, PhD*
- Ophthalmology and Mitochondrial Disease, *John R. Guy, MD*
- Why do Viral Infections Cause Setbacks in Mitochondrial Disease? *Robert K. Naviaux, MD*
- Cardiac PET Imaging: Application in Mitochondrial Disease, *Robert J. Gropler, MD*

Clinical Session (For Physicians and Families) - Afternoon

- Symptom Management in Mitochondrial Disorders, *Bruce H. Cohen, MD*
- Mitochondrial Patients Having Anesthesia, What to Expect? *Phil Morgan, MD*
- Coenzyme Q10 and Mitochondrial Disease, *Richard H. Haas, MB, BChir*



Meet us in St. Louis!
**Mitochondrial
Medicine 2005**
Gateway to a Cure
June 15-18, 2005

**Hyatt Regency St. Louis at
Union Station**

G Family Meetings Gateway to a Cure

Friday, June 17, 2005

Morning Sessions

- Working with Volunteers
- UMDF Present and Future - Ask the Trustee
- Funding the Cure
- Insurance Issues
- Living with Mitochondrial Disease

Afternoon Sessions

- Mito Basics for the Newly Diagnosed
John Shoffner, MD
- Diabetes and the Mitochondrial Adult Patient
Douglas C. Wallace, PhD
- Therapeutics and Nutrition
Richard H. Haas, MB, BChir

Saturday, June 18, 2005

- Ask the Mito Doc Panel: *John Shoffner, MD; Richard Haas, MB, BChir; Russell Saneto, DO; and David Whiteman, MD*
- UMDF Funded Research - Hear Progress Reports from the Bench
- Genetics and Mitochondrial Disease, *Susan Winter, MD*
- What to Expect as we Age with Mitochondrial Disease, *Douglas Wallace, PhD*
- Management Strategy for Acute Illness in Patients with Mitochondrial Disease, *Russell Saneto, DO*
- **Networking room** gives families a designated spot to meet and share experiences.
- The **"Doctor is In"** booth is a favorite among past attendees and will be back for 2005. Attendees speak one-on-one with top specialists.
- **UMDF presents grant money to mitochondrial researchers** and families hear progress reports from past projects funded by UMDF. \$1 million will be awarded in 2005!

Registration Brochures will be mailed to UMDF members and physicians in February. If you do not receive a brochure, please email info@umdf.org to get on our mailing list. The brochures will also be available online at www.umdf.org.

Special Thanks to

Morgan's FOODS, INC.

Beginning in 2003, Morgan's Foods Inc., based out of Beachwood, Ohio, graciously placed coin collection banks in Kentucky Fried Chicken (KFC) restaurants across Western Pennsylvania.

These wonderful KFC franchises have raised more than \$20,000 to benefit UMDF.

On behalf of all our UMDF families and friends, thank you Morgan's Foods for helping us Redefine HOPE for those battling mitochondrial disease and giving them the Energy for LIFE!



Premier Restaurant Management Company

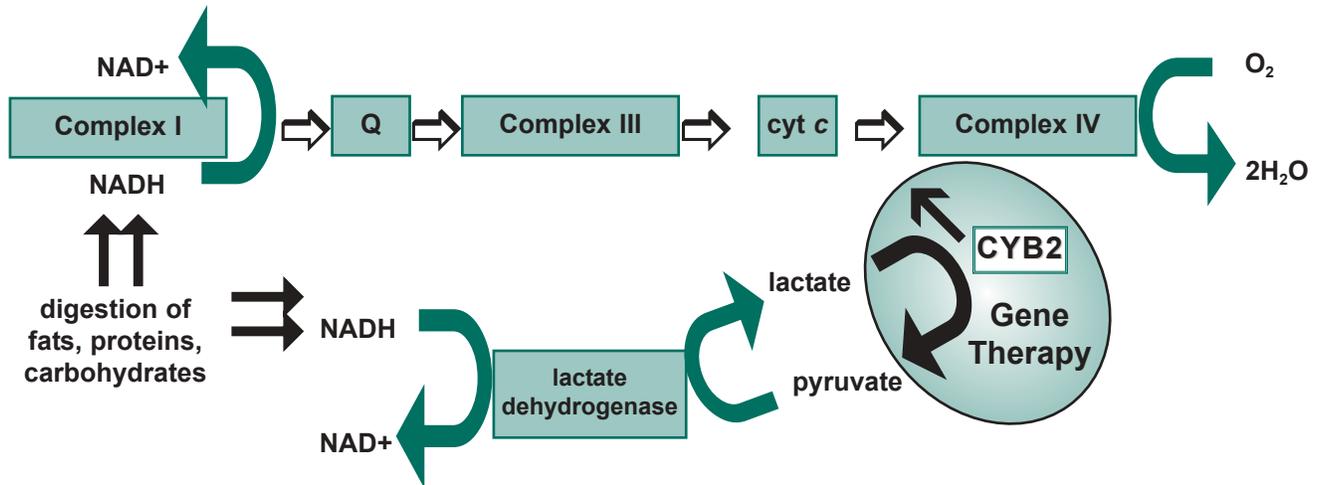
Thanks to Tom Arnold, grandfather to Bobby Arnold, Premier Restaurant Management Company's Kentucky Fried Chicken franchises have also been busy collecting coins to benefit UMDF. More than \$5,400 has been donated to UMDF since May of 2003. The coin collectors ask patrons to "Donate your change and help UMDF find a CURE for Mitochondrial Disease!" Tom also introduced UMDF to Morgan's Foods and Premier Restaurant/KFC is the title sponsor for the Ohio Run/Walk - donating \$10K annually to help UMDF move *One Step Closer to a Cure!*

Your Continued Support is Priceless!!!

Worms with Mitochondrial Diseases

Continued from page 1

Figure 1: Cytochrome b2-Mediated NADH Oxidation



Q: ubiquinone
cyt c: cytochrome c

we eat, are stored on a molecule called NADH. MRC proteins and the chemical reactions they perform are highly conserved among simple and complex animals. When conserved proteins are found in many organisms, investigators will often choose to use a non-human or even a non-animal model system that simplifies or accelerates experiments and the acquisition of knowledge.

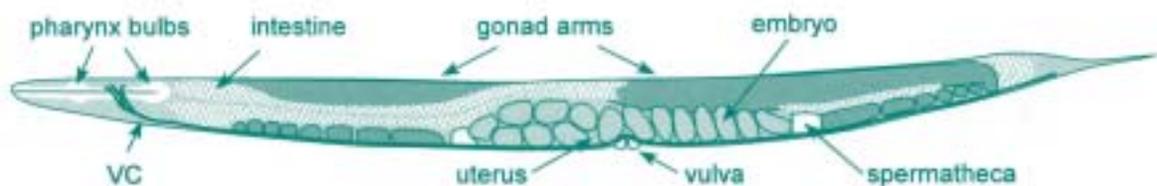
A Worm Model System

Caenorhabditis elegans, a free-living worm or nematode, is one of the simplest known animals (Fig. 2). Using this worm as a model system offers several key experimental advantages: the worm is simple in its anatomy and genome, it is transparent, it is easy to grow in the lab, it has a short life cycle, and it is well suited to genetic analysis. The worm's native habitat is in soil, especially decomposing vegetation, where it feeds on microbes. *C. elegans* is of no direct economic importance to man and yet it is one of the most studied animals in science. Adult worms are about 1 millimeter (1/25th of an inch) in length. *C. elegans* worms usually reproduce as hermaphrodites;

they produce both eggs and sperm and a new generation of 250-300 progeny are born every 3-4 days. Through genetic manipulation, it is possible to establish specific *C. elegans* lines or strains in which the progeny are all genetically identical, having inherited both the maternal and paternal genes from the hermaphrodite. Thus, millions of genetically identical animals can be cultured for biochemical or other analyses in a very short time.

C. elegans is physically a very simple animal; when an egg hatches, the first stage larva has exactly 558 cells. The number of cells increases as each worm develops through 4 larval stages into the adult hermaphrodite, to a final total of 959 non-reproductive cells. For comparison, a tadpole has about 1 million cells. Each adult hermaphrodite contains 302 nerve cells (some of which serve as a primitive brain), 95 body muscle cells, 20 pharyngeal muscle cells (the pharynx is a mouth-like organ involved in grinding and pumping food before sending it into the intestine), and other cells that form defined tissue types. Worms have specific behaviors such as being attracted to or repelled by

Figure 2



Continued on page 13

Fundraisers

Mustache for Kids - Raises More than \$1,400

This unique event began on November 17 in Columbus, Ohio, by Carson Roger's uncle, Darren Meyer. Carson lives in Greer, SC. For four weeks, Darren's co-workers participated in a mustache growing competition and donations were collected.

Weekly updates were emailed to the UMDF national office to show the progress of the growing



'staches. A variety of awards were given to competitors: *Rockin'est Mustache*, *The Chef Boyardee*, and *Best in Show/Sweetest 'Stache of 2004* were just a few.

The sister of one of the competitors mentioned the campaign to her class and the students joined the fun by holding their own competition. With the help of markers and a little make-up, these middle schoolers raised almost \$400.



Thank you to all employees at MSI Design and to Watkins Middle School in Pataskala, Ohio! What a Blast!!!



The **4th Annual Mito-What? Margaritaville Cruise** raised \$3,000 on August 27 in honor of Morgan Kozuch. Pictured above - Morgan with Michigan firefighter Karey Prieur, who won the \$500 cash prize and graciously donated it back to the Foundation. What a guy! Next year's Cruise is set for August 17, 2005!

Thanks Kozuch Family!!!



The **First Annual 5K Walk in Alabama** raised more than \$34,193.75 on October 9, 2004. Ann Washburn, of Birmingham, organized the event with the help of family and friends to honor the memory of her son, Brock. Pictured above are Ann's identical twin nieces who were enjoying the day!

In Memory of Noah Moore, Aker Kvaerner of Pittsburgh chose UMDF as the recipient of their 2nd Annual Chinese Auction for Charity.

Employees raised more than \$7,900 in memory of Noah. Thank YOU Aker Kvaerner employees!

THANKS

★ More UMDF ★ Fundraising Stars

- *Coins for a Cure* - In honor of Asher Gould - \$277.55. Thanks Carol's Kitchen of Boca Raton, FL.
- *2004 2nd Annual Crop for Carson (Rogers)* in Greer, SC - \$1,418.75.
- *2004 Energy for Life* in honor of Riley Peek - \$319.50. Thank you RBC Centura Bank of Palmetto, GA.
- *2004 Entertainment/Enjoy Books* raises \$2,502. Way to go Ron & Donna Miklos!!!
- *2004 Season for Giving* - shopping event raises \$228 at Monroeville Mall, PA.
- *Angelica & UMDF Golfing For a Cure Outing and Angelica/UMDF Family Fun Day* raised a total of \$3,886.74 in Cypress, TX. Thanks Cynthia!
- The Crespi Mothers Golf Club donated \$100 in memory of Cody Bracken.
- In lieu of gifts for her 10th Birthday, McKinsi Thompson donated \$300 to benefit UMDF!
- Misty Brown, mother to Abigail and Mikaela, is a Mary Kay consultant and has pledged to donate 10% of every sale she makes to UMDF. So far, she has donated \$100 - BEAUTIFUL!!!
- James Lomeo, Mayor of Monroeville, PA, performs wedding ceremonies and various other mayoral duties. In lieu of his fee, he has asked individuals to donate to UMDF. Thanks Jim!!!

Meet The UMDF Board

Bruce H. Cohen, MD Cleveland, Ohio

Dr. Cohen joined the UMDF Board in 1998. He has chaired the Chapter Committee, serves on the Executive Committee and presently chairs the Symposium Committee.

Gerald A. Cook, Esq. Pittsburgh, PA

Mr. Cook joined the UMDF Board in 2004 and serves on the Program/Policy Committee. He has also served as legal counsel in the past.

Stan Davis, Treasurer Pepper Pike, Ohio

Mr. Davis joined the UMDF Board in 2001, and currently chairs the Finance Committee, which analyzes UMDF's investment strategies.

John A. DiCecco, Vice Chairman Apollo, Pennsylvania

Mr. DiCecco served as Board Treasurer from 1998 to 2003, guiding UMDF in developing its financial policies and systems. He currently chairs the Governance Committee.

Charles L. Hoppel, MD Cleveland, Ohio

Dr. Hoppel joined the UMDF Board in 2002, bringing the perspective of medical researcher to the Board. Presently, Dr. Hoppel chairs the Research and SAB Restructuring Subcommittees.

Richard W. Kubach, Jr. Newtown Square, Pennsylvania

Mr. Kubach was appointed to the UMDF Board in November 2003 and chairs the Planning/Marketing Committee.

Charles A. Mohan, Jr., Chairman Monroeville, Pennsylvania

Mr. Mohan helped found UMDF in 1996, and has served as Board Chairman since its inception. He chairs the Executive Committee and appoints committee chairs.

Fundraisers



- Candy machines continue to raise money and awareness in Mohan's Restaurant, RibKens, Pennzoil and LaCava's Italian Market - \$444.06. Thanks Chuck!
- D Morgans Restaurant raised \$307 during a Fine Arts Festival in honor of Sherry Mathis in Cartersville, GA.
- Rib-Kens Restaurant in Monroeville, PA collects coins and donated \$111.11 its first quarter.
- *Cans for Ashley* raised \$387.50 in 2004. Thanks Randy, Sandi and Ashley!
- UMDF Staff paid \$5 each to "dress down" in memory of Gina Marie Mohan on January 20 and raised \$40.
- *Heartbeats for Mito* event in the University Mall, Tuscaloosa, Alabama raises \$713 in October. Great job Ann Eide!

Mary Pisani North Haven, Connecticut

Mrs. Pisani was appointed to the UMDF Board in 2004 as the new Chapter Liaison and also serves as the President of the New York Metro Chapter of UMDF. She currently chairs the Chapter Committee.

Joseph Rice Saint James, New York

Mr. Rice was appointed to the UMDF Board in November 2003 and helped found the UMDF New York Metro Chapter and chairs the Human Resources Committee.

Nick Rillo, Secretary Chicago, Illinois

Mr. Rillo has served on the UMDF Board since 1996. He has

Thank YOU to more of our
★ Fundraising Stars ★

- Emily Kusuhara (pictured left with Riki), of Japan, loves her brother so much that she donated most of her savings to UMDF in honor of Riki's 6th Birthday. Emily & her friends donated \$200 - what a gift!

• Connelle Salon of Boca Raton, FL held a raffle in honor of Asher Gould raising \$3,879.50.



HELP! We Need your Jewish Holiday Recipes

13-year-old Hannah Roberts, from Canton, Ohio, is working on a Jewish Holiday Cookbook for her Bat Mitzvah. The money will go to UMDF to help us move One Step Closer to a Cure. Please send Jewish Holiday Recipes to 1253 Linwood Avenue SW, North Canton, OH 44720. Deadline to submit recipes is May 31, 2005.

chairs the IT Committee and provides valuable insight on technical concerns.

Sharon Shaw Cave Creek, Arizona

Ms. Shaw was appointed to the UMDF Board in November 2003 and also served as President of the Southern California Chapter of UMDF for three years, stepping down in 2003. Ms. Shaw also serves on the Symposium Committee.

W. Dan Wright Vernon, TX

Mr. Wright joined the UMDF Board in 2004 to complete Rand Wortman's term. He currently chairs the Search Subcommittee for the new Executive Director.

certain chemicals and are capable of rudimentary learning. *C. elegans* is transparent, allowing for the microscopic examination of anatomy and behavior in live animals. The average lifespan of a worm is 2 to 3 weeks; after reproducing, the worm ages, loses vigor, and finally dies.

The *C. elegans* genome consists of 100 million base pairs of nuclear DNA (nDNA), about 30-fold fewer base pairs than in the human genome. The mitochondrial DNA (mtDNA), at 13,794 base pairs, is very similar in size and gene content to human mtDNA (16,569 base pairs). Human mtDNA encodes thirteen proteins of the MRC, and twelve of these same proteins are produced from worm mtDNA.

Although *C. elegans* does not have complex organs such as a heart or a liver, its simplicity as an animal and its sophistication as an experimental model allow us to probe the fundamental biological mechanisms that operate in healthy and in disease states. Even more, certain mutations related to disease would be lethal in more complex organisms. These mutations are tolerated by worms and can thus be studied in detail.

Worms With Mitochondrial Disease

Unfortunately, most mitochondrial disorders are so rare that the relationships between mitochondrial mutations and disease mechanisms remain poorly understood. The MRC provides the majority of a cell's energy requirements, and at first glance, it might be expected that mitochondrial diseases are manifestations of energy shortages. The diversity of symptoms and complexity of multisystemic mitochondrial diseases argues against a simple energy shortage model. Our worm model system is proving useful in identifying additional, non-energy related mechanisms by which mitochondrial dysfunction impairs normal cell function. We have identified at least three pathological mechanisms that contribute to disease: lactic acidosis (a metabolic imbalance related to excess NADH), impaired assembly or function of MRC protein complexes not directly affected by a mutation, and the production of reactive oxygen species.

We are focussing our work on mitochondrial disease caused by defects in complex I. Complex I is the first and largest of the MRC proteins and is responsible for the capture of energy from the high-energy electrons stored on NADH molecules. The *C. elegans* gene called *nuo-1* is the source of one component of complex I, the protein subunit that recognizes and binds NADH. The NUO-1 protein is the worm equivalent of the human 51-kilodalton protein (produced from the human NDUFV1 gene). The worm NUO-1 protein and the human 51-kilodalton protein share about 75% identical

amino acids, a strong indication that their functions are very similar in both organisms. When both copies of the worm *nuo-1* gene harbor a severe mutation, mutant animals begin early development normally but arrest in the third larval stage and remain at this juvenile stage for the remainder of their lives. This arrested development highlights the importance of normal complex I and MRC function for development, maturation, and reproduction in *C. elegans*.

Mutations affecting a single MRC protein are responsible for some mitochondrial diseases in humans (see Table 1). We can use our worm model system to study the effects of such mutations on the analogous MRC proteins in worms. To better understand how human complex I mutations can produce disease, we introduced three reported mutations in the human NDUFV1 gene into the *C. elegans* *nuo-1* gene. Each of these mutations modifies only one amino acid of the protein and is believed to reduce complex I activity but not to completely inactivate it. All three mutations affect amino acids conserved between the worm and human proteins; conserved amino acids are more often important for protein function.

Each mutated *nuo-1* gene was introduced into *C. elegans* hermaphrodites and offspring carrying these genes were isolated. The three mutated NUO-1 proteins were produced in the corresponding offspring and incorporated into complex I of the offspring. Compared to the worms with a normal NUO-1 protein, the mutated proteins led to significantly lower complex I activities. Although the mutated proteins allow sufficient energy production for development and reproduction to proceed, the worms display reduced fitness. We measure fitness by determining brood sizes (total number of offspring per hermaphrodite) and lifespans. Worms carrying the mutated proteins also show reduced levels of respiration (oxygen consumption) and signs of premature aging, such as muscle degeneration.

In the worm models for human disease-causing mutations of complex I, we have identified at least three molecular mechanisms that are contributing to the disease phenotype or symptoms:

- Worms carrying the T434M, A352V, and A443F mutations (Table 1) all had significantly elevated levels of lactate. Lactic acidosis can occur when MRC function is impaired. NADH accumulates and is diverted towards the formation of lactic acid (lactate, Fig. 1). In humans, excess lactate can produce malaise, muscle weakness, exercise intolerance, and vomiting. It may also contribute to

Continued on page 14

Table 1

Human Mutations	Human Disease	C. elegans Mutations	C. elegans Disease
T423M/R59X compound heterozygotes	<ul style="list-style-type: none"> • vomiting • progressive muscular hypotonia • myoclonic epilepsy • psychomotor regression • lactic acidosis • death at 14 and 17 months 	T434M	<ul style="list-style-type: none"> • moderate reduction in brood size • moderate decrease in lifespan • modest signs of premature aging • moderate drop in respiration • moderate lactic acidosis • hypersensitive to oxidative stress • responsive to riboflavin
A341V	<ul style="list-style-type: none"> • myoclonic epilepsy • muscular hypotonia • psychomotor regression • macrocephaly • elevated CSF lactate • patient, age 10, is blind and severely spastic 	A352V	<ul style="list-style-type: none"> • severe reduction in brood size • severe decrease in lifespan • severe premature aging • severe drop in respiration • moderate lactic acidosis • complex IV deficiency • hypersensitive to oxidative stress • responsive to riboflavin, sodium dichloroacetate, ascorbate, thiamine
A432P/2base pair deletion compound heterozygote	<ul style="list-style-type: none"> • vomiting • hypotonia • lethargy • apnea • lactic acidosis • death at 18 months of metabolic acidosis 	A443F	<ul style="list-style-type: none"> • severe reduction in brood size • severe decrease in lifespan • severe premature aging • severe drop in respiration • severe lactic acidosis • complex IV deficiency • hypersensitive to oxidative stress • responsive to riboflavin, sodium dichloroacetate, ascorbate.

Continued on page 13

long-term mitochondrial disease progression by affecting the production of other proteins related to energy metabolism.

- Our worms with mutations in complex I proteins suffered from a deficiency in complex IV, the enzyme that transfers electrons from the MRC to oxygen to form water (Fig. 1). Complex IV protein levels as well as activity levels were significantly reduced in worms with complex I mutations, suggesting that complexes I and IV are in some way interdependent. Impaired complex IV activity likely exacerbates energy shortages and lactic acidosis.
- Finally, we noted that our nuo-1 mutant worms are hypersensitive to oxidative stress, which results in elevated levels of damaging reactive oxygen species. The hypersensitivity can be attenuated by sodium dichloroacetate or by riboflavin. Furthermore, both the A352V and the A443F mutants show improved fitness when supplemented with ascorbate, a reactive oxygen species scavenger. Rather than efficiently harnessing the energy in NADH for the synthesis of ATP, mutant forms of complex I leak high-energy electrons to oxygen, forming reactive oxygen species. These results suggest that mutated complex I produces damaging reactive oxygen species that

may contribute to the premature aging and diminished lifespans of the mutant worms.

Molecular Mechanisms and Therapies

Some forms of mitochondrial disease can be improved by pharmacological agents such as vitamins. We have tested the response of the mutant worms in our model system to some of these agents. The goal of this part of our research is to determine how such pharmacological agents influence the molecular mechanisms of mitochondrial disease.

- Riboflavin supplementation significantly increased brood sizes in all three types of mutant worms. Interestingly, the riboflavin reduced observed levels of lactate in the A443F mutant, but not in the other two mutants.
- Thiamine supplementation increased brood sizes in the A352V mutant.
- Sodium dichloroacetate (an activator of the pyruvate dehydrogenase complex) increased the brood sizes of the A352V and the A443F mutants. It also markedly reduced their lactate levels. Because the beneficial effects of riboflavin on the A352V mutant are not associated with reduced lactate levels, we suggest that the mechanisms of action for sodium

Worms with Mitochondrial Diseases

Continued from page 14

dichloroacetate and riboflavin are different.

Our results indicate that lactic acidosis is responsible for at least some of the pathogenic effects of complex I mutations, but clearly other mechanisms also play a role in these diseases.

Gene therapy involves the introduction of foreign genes to replace or compensate for missing or damaged genes. Gene therapy offers the possibility of a cure or of providing a long term treatment in many diseases. Gene therapy for complex I dysfunction is challenging because of the large number of genes needed to assemble complex I (~37 nuclear and 7 mitochondrial genes). Furthermore, the mtDNA is not currently accessible for such genetic manipulation.

We are investigating the use of gene therapy as a means of compensating for the loss of complex I activity by moderating the effects of lactic acidosis. One possible route to this goal is the introduction of a new enzyme into the equation. The yeast enzyme cytochrome b2 (CYB2) is a mitochondrial enzyme; CYB2-like enzymes are not found in mammals or in nematodes. CYB2 converts lactate to pyruvate and reduces cytochrome c (Fig. 1). The pyruvate is re-converted to lactate by an endogenous lactate dehydrogenase, using up NADH in the process. The net result of the CYB2 and lactate dehydrogenase reactions is the reduction of 2 molecules of cytochrome c and the conversion of 1 NADH to NAD⁺. The reduced cytochrome c molecules provide electrons to complex IV in the normal functioning of the MRC, and the complex IV reaction contributes to ATP synthesis in mitochondria. Thus, the added presence of CYB2 in mammals and worms should lower lactate and

NADH levels while contributing to ATP synthesis.

We have expressed the CYB2 gene in the more severe A352V and A443F complex I mutants. With CYB2 active in the worms, mutant brood sizes are increased 150-225%. Lifespans are lengthened by almost one third and respiration rates are stimulated from 40-50% of normal levels in the mutants to 85-90% of normal levels with CYB2 expression. To further document the effects of CYB2, we are measuring the levels of CYB2 protein and activity present in isolated worm mitochondria. We also predict that CYB2 expression will significantly decrease lactate levels and sensitivity to oxidative stress. We believe that the beneficial effects of CYB2 expression are directly due to reductions in lactate and NADH levels.

In conclusion, the significantly improved fitness of CYB2-expressing mitochondrial mutants suggests that lactic acidosis is responsible for much of the severity of complex I-associated disease. The development of therapies or treatments that address metabolic acidosis may prove most beneficial in moderating the pathological effects of MRC dysfunction. In the longer term, gene therapy approaches that directly target lactic acidosis in the worm may also be adapted to provide long term clinical benefits to those that suffer from mitochondrial dysfunction.

Matching Gifts . . .

Does your employer participate in a Corporate Matching Gift Program? If so, your gift could be doubled. The following companies have matched gifts to UMDF in the past. If you or a loved one works for one of these companies, check out the matching gift program and help us move one step closer to a cure!!

Aon Association Services
AT&T
AXA Foundation
Adams, Harkness & Hill, Inc.
Altria Group, Inc. (Phillip Morris Companies, Inc.)
American Refining Group, Inc.
BD Matching Gift Program
Bank of America
Babson Capital Management, LLC
Bell South
CNA Foundation
Capital Group Companies
Chubb Corporation
Crail-Johnson Foundation
EOG Resources, Inc.
FM Global Foundation
Fleet
Frito-Lay (Pepsi-Cola)
Gap Foundation
Grainger
Hewlett-Packard Company
HP Financial
Key Foundation
Kimberly-Clark Foundation
Kraft Foods
The JP Morgan Chase Foundation
Johnson & Johnson Family of Companies
Lehman Brothers
Loomis, Sayles & Company, LP
Massachusetts Mutual Life Insurance Company
McMasters-Carr Supply Company
Merrill Lynch & Company
Microsoft
Neiman Marcus Group
Newsweek (The Washington Post Company)
Nordson Corporation
Oppenheimer Funds, Inc.
Oracle Corporation
PepsiCo
Pfizer Inc.
Rockwell International Corporation
Saint-Gobain Corporation
Sallie Mae
State Street Corporation
TCF Financial Corporation
Tenet Healthcare Foundation
Trans Union, LLC
United Technologies Corporation
World Reach, Inc. DBA The Charity Giving Station
Yahoo, Inc.

Mito Adults Corner

Traveling with Mitochondrial Disease

by Julie Martin

The hassles of traveling include delayed departures, cramped quarters, and lost luggage. But for many with mitochondrial disease, concerns about travel go far beyond what happens when you land in Florida and your luggage lands in the Philippines. This month, adult mitochondrial patient and UMDF member Melissa Nixon shares her advice on how to lessen the turbulence when traveling with a disability.

If flying, one of the first things to do is contact the airline's disability issues desk after getting your reservation. "You can tell them your needs; they can tell you their rules," Nixon says. "Things are worked out way in advance so, hopefully, there are no surprises."

It's also a good idea, she says, to check about seating arrangements, such as bulkhead seating, which can provide more leg (or service dog) room. Seating can be pre-reserved.

If traveling by train, it's not a bad idea to touch base ahead of time either. There may be doorways that are too narrow for wheelchairs or limited special seating for the disabled. It's good to know in advance.

Make sure there are necessary accommodations for any equipment you need. BIPAP (Bilevel Positive Airway Pressure) and CPAP (Continuous Positive Airway Pressure) machines can be plugged into airplanes, but on trains, hook up isn't guaranteed. Because of this, Nixon was once left eating the cost of a nonrefundable ticket.

"It would have been a far worse disaster to get on the train, start the trek, and then discover I could not get power for the BIPAP and was in respiratory failure," she says.

Airlines are required to provide oxygen, given notice, but generally charge \$50 per leg of travel. Since you won't be traveling with your own oxygen, make arrangements with the supplier to have fresh tanks waiting at your destination. Decide what will work best for your needs, such as meeting the supplier at the airport or having the tanks set up in your hotel room before you arrive.

Another suggestion by Nixon is in regard to medications. It is better to keep medications in their original prescription bottles in carry-on luggage. Pills loaded into containers other than their original prescription containers may be confiscated, and one most definitely does not want to lose his/her meds.

Though Nixon has heard horror stories of traveling with Jazzy Chairs, including dissected batteries and dropped chairs. She says some folding wheelchairs can travel well by plane. However, there are no guarantees that your chair will be allowed in the passenger area on any given flight. With a cooperative crew, your folding chair may be stashed in the passenger closet.

"It's less likely to be roughly handled or dissected since it's always in your line of vision," Nixon said. "Storing a chair nearby can also make for easy disembarking."

Though airport security tightened in the wake of 9/11, Nixon says initially airport screeners "for the most part, bent over backwards not to offend the disabled." Now, the attitudes are changing. Wheelchair cushions are inspected; canes and walkers, x-rayed; walking sticks, forbidden. Even service dogs can be searched.

"I have no objection to this," Nixon says. "My dog is properly trained, and I want any lurking bad guys to understand that the dog's accoutrements are going to be inspected."



If traveling with a service dog, Nixon suggests that you arrive at least one hour earlier than you would if you weren't traveling with one. Anyone traveling to Europe with a service dog will need to check on the new dog passport system recently started there.

Sometimes, even the best laid travel plans can go awry. Even good can come from these situations . . . at least in a way. Nixon once had to take a city bus to a hospital. A bus driver wouldn't let her get on because the wheelchair lift would have to be lowered twice, once for Nixon and the wheelchair and another time for her oxygen tanks and suitcase.

"A wonderfully kind young man saw what happened," she says. "When the next bus came he made sure I got on that bus-suitcase, oxygen tanks, and all-and then he stayed with me through a couple of transfers all the way to the reception desk of the hospital."

"I was so sick I was put straight into cardiac ICU," she says, "but I will always remember my tall cool angel with the gorgeous basketball shoes."

Mito Adults Corner

Calling all Mito Adults: The Mitochondrial News Needs YOU!

UMDF could use more helpers. Please consider joining the committee, submitting an article for review or send us your experiences with a specific topic of interest. If you are willing to help, please email Kara Strittmatter at kara@umdf.org or call 412-793-8077, ext. 106. We look forward to hearing from you!



Vacation Toward a Cure

Courtesy of
American Airlines

Official Airline of the
United Mitochondrial Disease
Foundation

You Could Win ...

- Round trip air transportation for two to any **American Airlines** destination in the contiguous 48 states, courtesy of **American Airlines**.
- \$1,500 AAA gift voucher toward any cruise or vacation.

All proceeds to benefit the
United Mitochondrial
Disease Foundation.

Drawing Date: June 17, 2005.

Drawing will take place at the
**Mitochondrial Medicine 2005
Conference in St. Louis, MO.**

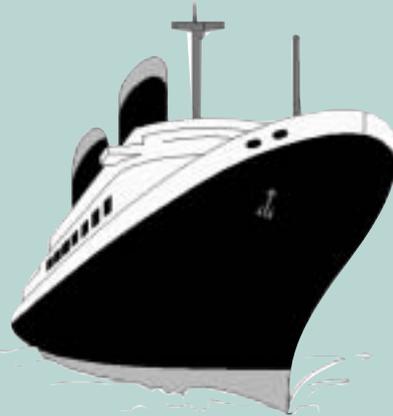
\$5 per ticket

\$25 for book of 6 tickets

For more information on buying
or selling the tickets, please
contact UMDF at 412-793-8077.
Contest rules are available on the
UMDF web site and/or noted on
the raffle tickets.

**Individuals who sell ten books
of tickets will win a UMDF
Throw (blanket)!**

Attention Groups and Chapters: Sell Vacation Toward a Cure Tickets and WIN!!!



Grand Prize
Group or Chapter selling the
most raffle tickets (at least
\$5,000 in ticket sales)
will **WIN** \$1,000 in
scholarship money for
support group/chapter
members to attend the
2006 UMDF Symposium in
Atlanta

\$\$\$Cash\$\$\$

For all groups and/or chapters selling at
least \$1,000 in raffle tickets.
Your group sells together and then celebrates together
with a little extra cash for your next meeting!

Tomato Face Foods



**YOU can help
Tomato Face Foods**

continue reaching thousands
across the U.S. Do you
know someone in your local supermarket, school
cafeteria, college food service, or grocery chain? If so,
please contact Barbara and Allen at 216-382-0232 or
sebrook1@aol.com.

Allen, Barbara and Dana are still working on their goal
to catch Oprah's attention as well as other national
television production companies. Keep up the great
work Tomato Face Foods!

Mitochondrial Disease Awareness Week in Pennsylvania

The House of Representatives plans to designate the week of **May 8-14, 2005** as "**Mitochondrial Disease Awareness Week**" and will urge all citizens of this Commonwealth to become better informed about the disease and its impact.

If you would like to spread the word through your local media in PA, please contact kara@umdf.org for a press kit.

Help UMDF Identify Everyday Heroes

UMDF LEAP Award

Living, Encouraging, Achieving & Persisting

Purpose: To recognize an individual living positively with mitochondrial disease, highlighting the person's accomplishments and volunteer service.

Eligibility: Age 14 years or older

Criteria: Individual with confirmed or suspected mitochondrial disease who overcomes daily challenges to achieve goals in career, family, and volunteer service. The individual demonstrates a positive attitude, hope for a brighter future, and an enthusiasm that inspires others.

UMDF Heartstrings Award

Recognizing a youth commitment that tugs on the heartstrings

Purpose: To recognize a child or teen who has donated or raised funds for UMDF, enabling UMDF to continue its mission.

Eligibility: The individual recognized must be under 18 years of age at the time of the donation or fundraising activity.

Criteria: The winner is chosen based on related criteria of age, time invested, talents demonstrated, effectiveness, and generosity. For nominees who implement fund raising projects, the judges will consider the uniqueness and creativity of the project, communication, the time invested, and the amount raised in comparison to the age of the individual. For nominees who donate funds, the judges will consider the generous spirit shown, communication, and amount donated in relation to the age of the individual.

Deadline for Nominations is April 1, 2005!!!!

Nomination forms and more instructions are available on the UMDF Web Site at www.umdff.org. Or request forms by calling Melinda at 412-793-8077 or emailing melinda@umdff.org.

★ Mark your Calendars ★

See pages 4-6 for more details on Chapter Events

- February 12, 2005 - Pack the House Ice Hockey fundraiser (Indiana Chapter)
- March 5, 2005 - 2nd Annual Bet on Baylee Casino Night (Ohio Chapter)
- March 5, 2005 - Writers at the Beach: Pure Sea Glass, a one-day writers' conference, in the Rehoboth/Dewey Beach area in Delaware. For more information, contact Mary Beth Fischer at mbfischer@att.net.
- April 16, 2005 - 2nd Annual "Mito-What?" 5K Run/Walk and Family Fun Day, Shrine of Our Lady of the Snows, Belleville, IL. For information, call Marsha Hohe at 618-233-6919.
- April 30, 2005 - *Race for Riley, Whatever it Takes* 5K Walk/Run and Tot Trot, Georgia Baptist Children's Home in Palmetto, GA. (Atlanta Chapter)
- May 7, 2005 - 6th Annual Energy for Life Run/Walk (formerly Shelly's Heroes) (DeVal Chapter)
- May 14, 2005 - 2nd Annual "Mito-What?" 5K Run and 1 Mile Walk, Corporate Woods Founders Park (KC Chapter)
- May 20, 2005 - Hair cut-a-thon, Lake County Captains baseball game (Ohio Chapter)
- May 21, 2005 - Two events on one special day: a Walk in Chatham, NJ and a 5K Run/Walk in North Haven, CT (NY Metro Chapter)
- May 29, 2005 - Shadow Woodstock 2005, Chagrin Falls, OH (Ohio Chapter)
- June 4, 2005 - 3rd Annual Pittsburgh UMDF 5K Run/Walk at North Park
- June 4, 2005 - 4th Annual KFC/UMDF 5K Run/Walk, Forest Hills Park in Cleveland (Ohio Chapter)
- June 8, 2005 - 2nd Annual Ally Brunk Memorial 5K Walk/Run, Pottersville, MI. For more information, email Daniel at brunkb@pps.k12.mi.us.
- June 11, 2005 - Brew at the Zoo (DeVal Chapter)
- June 15-18, 2005 - Mitochondrial Medicine 2005
- July 18, 2005 - 6th Annual Ohio Golf Outing, The Country Club, Pepper Pike, Ohio. For more information, call Stan Davis at 216-581-0000.
- July 21, 2005 - 8th Annual Pgh UMDF Golf Outing, Churchill Country Club. For more information, call Sandy at 412-793-8077.
- August 17, 2005 - 5th Annual Mito-What? Cruise in Bay City, MI.

UMDF Chapters & Groups

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CALIFORNIA

★Southern California Chapter

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OUTSIDE OF THE UNITED STATES

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New groups forming in Rhode Island and Denver. Interested in starting a group in your area? Contact melinda@umdf.org.

Attention all UMDF Members!! UMDF Database Under Construction



Dues Renewal Notices:

We ask for your patience during our transition period in upgrading the UMDF computer system and web site. If you have received a dues renewal notice and have already paid your dues, please email info@umdf.org or call Alisia at 412-793-8077. This will help our computer consultants alleviate such issues in the future.

In addition, we are currently unable to process networking requests. We hope to have a new and improved system operating during this quarter. Your patience is appreciated.

**The UMDF Office Staff
We're Here to Help You! 412-793-8077**

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If you have an event announcement or an idea for an article for the Mitochondrial News, please email kara@umdf.org. We want to hear from YOU!

For information on starting a fundraiser in your area, email sandy@umdf.org.



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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.

Deadline for next issue is 4/1/05