Barth Syndrome Foundation®

NEWSLETTER

Volume 4, Issue 1

www.barthsyndrome.org

Five *NEW* Research Grants Awarded by BSF

Inside This Issue

By Kate McCurdy, Vice President, Science and Medicine

It is with great excitement that I announce that the Barth Syndrome Foundation, Inc. (BSF) has recently awarded five *new* research grants, with a total commitment of $173,760 over a two-year period, for work that will be conducted in laboratories around the world in order to advance knowledge about Barth syndrome. The BSF Board of Directors and our Scientific and Medical Advisory Board feel that these proposals are well worth our investment. Since 2002, BSF has now awarded ten scientific projects delving into various aspects of Barth syndrome – ranging from investigations into the underlying genetic and biochemical pathways of the disorder, to projects aimed at better comprehending the mechanisms resulting in the various clinical aspects of the syndrome, to work on creating animal models for the disorder. We are incredibly fortunate to have such breadth and depth of commitment toward understanding Barth syndrome.

(Continued on page 7)

Save the Date

BSF 2004 International Scientific & Family Conference

Come Join Us at Disney's Coronado Springs Resort

By Anna Dunn, Vice President & Family Liaison

Disney's Coronado Springs Resort
Lake Beuna Vista, FL
Centrally located to all of Disney's Theme Parks

On behalf of The Barth Syndrome Foundation, I would like to personally invite you to join us at Disney's Coronado Springs Resort to attend our 2004 Barth Syndrome Scientific and Family International Conference. This conference will provide two tracks of meetings so that the scientific/medical and lay communities can receive the most up-to-date information

(Continued on page 21)

Year-End Report

A Summary of BSF's Progress in 2003

By Valerie ("Shelley") Bowen, President
The Barth Syndrome Foundation, Inc.

It is our tradition at the end of each year to mark our progress toward the achievement of our goals and objectives. It helps us all appreciate how far we have come since we started BSF in 2000… and it helps us keep our focus on where we are going. It would be dangerous to become complacent and think that we had done enough, but we can all take great pride in our accomplishments so far.

We continue to accomplish these tasks with your help - a dedicated group of volunteers, scientific and medical advisors and contributors. We could not do it without you. We are making tremendous strides toward our vision, and the enthusiasm of our volunteers is infectious. If you would like to be more involved in the efforts of our group, I would strongly encourage you to consider volunteering. Together we can make next year even better than this, just as this year was better than the year before for all those affected by Barth syndrome.

In 2003, we revisited our Vision, Mission, Tagline, and Goals and Objectives that were created in the Fall of 2000. None of the revisions were radical – our original direction remains essentially unchanged. But the changes we have made reflect our dedication to learning and improving as we go. This is our road map to our future. In addition, we created a set of values for our organization to help guide our decisions and our day-to-day actions. In recent years we became aware that Barth syndrome affects men as well as boys, and that while extremely rare, Barth syndrome can affect females as well as males. We amended our tagline to include all those affected. Our revised Vision, Mission, Goals, Tagline and newly developed Values can be seen below. As is our custom, you can also find a summary of our accomplishments in 2003, organized under our major program goals.

Respectfully submitted,

(Continued on page 3)

Editior's Note:

This is the longest and most information laden issue of the BSF Newsletter yet! It's length is a reflection of the incredible growth in scientific and clinical research and attention now being paid to Barth syndrome, stimulated largely by the efforts of your foundation. We gave considerable thought to editing and reducing the content, but finally decided that these articles were all of critical importance to Barth families, their physicians, scientists and researchers and all of our many supporters and volunteers. We hope that you take the time to read the articles that are of greatest interest to you, and to be sure and pass them on to others who may find them of interest. There is something here for everyone! Additional copies are available. Contact ***Lsedefian@barthsyndrome.org***.

AMENDED VISION

Today, Barth syndrome is a rarely understood, frequently fatal, genetic disorder affecting boys. The Barth Syndrome Foundation's Vision is ... "A world in which no one will suffer or perish from Barth syndrome".

AMENDED MISSION

The Barth Syndrome Foundation's Mission is ... "To guide the search for a cure, to educate and support physicians, and to foster an informed and caring community for affected families".

AMENDED GOALS

Goal #1: To insure that all appropriate medical professionals are aware of Barth syndrome and have ready access to the tools to make a timely and accurate diagnosis.

- Created "How to Diagnose Barth Syndrome" document, which is available on the web and has been distributed at medical conferences
- Attended six professional conferences as exhibitors:
  - Children's Hospital of Philadelphia Cardiology 2003 - Orlando, Florida, February, 2003 (Jan Kugelmann, Steve Kugelmann, Shelley Bowen)
  - American Academy of Pediatrics - New Orleans, Louisiana October 2003 (Steve Kugelmann, David Mann, Shelia Mann)
  - American Heart Association - Orlando, Florida, November, 2003 (Steve Kugelmann, Lynda Croxton, Matthew Croxton, Shelley Bowen)
  - American Society of Hematology - San Diego, California, December, 2003 (Kate McCurdy, Mike Wilkins, Shelley Bowen)
  - The South African Genetics Conference - Durban, Natal, South Africa (Jeannette Thorpe, Allison Campbell-Gillies)
  - International Congress of Inborn Errors in Metabolism - Brisbane, Australia, September, 2003 (With the assistance of Dr. John Christadoulou BSF brochures and informational literature were provided to attendees about Barth syndrome and BSF)
- Made presentations at the following medical conferences:
  - Genetic Alliance Annual Conference, August 2003 (Kate McCurdy, Shelley Bowen)
  - Sarah Lawrence College for Human Genetics Program Seminar, October, 2003 (Kate McCurdy)
- Attended professional conferences as a participant:

(Continued on page 4)

For all correspondence, including information, please contact:

BOARD OF DIRECTORS:

Valerie (Shelley) Bowen
PRESIDENT
sbowen@barthsyndrome.org

Anna Maria Dunn
VICE PRESIDENT AND FAMILY LIAISON
adunn@barthsyndrome.org

Stephen Kugelmann
VICE PRESIDENT, AWARENESS
skugelmann@barthsyndrome.org

Katherine R. McCurdy
VICE PRESIDENT, SCIENCE AND MEDICINE
kmccurdy@barthsyndrome.org

Stephen B. McCurdy
VICE PRESIDENT, FINANCE AND DEVELOPMENT
smccurdy@barthsyndrome.org

Lynda M. Sedefian
SECRETARY AND NEWSLETTER EDITOR
lsedefian@barthsyndrome.org

Susan V. Wilkins
BOARD MEMBER
swilkins@barthsyndrome.org

ADDITIONAL CONTACTS:

Leonard Steinberg, EA, CMC
BOOKKEEPER

Michael Hope
WEBMASTER
mhope@barthsyndrome.org

Moira Masterson
GRANDPARENT LIAISON
mmasterson@barthsyndrome.org

BSF AFFILIATES

The Barth Syndrome Trust, United Kingdom & Europe
1 The Vikings
Hampshire
S051 5RG
United Kingdom
Telephone: +44(0)1794 518785
mdamin@barthsyndrome.org
www.barthsyndrome.org.uk

The Barth Syndrome Foundation, Canada
Canada Post P.O. Box #40
30 Kings Crescent
Ajax, Ontario L1S 3C2
Telephone: (905) 426-9126
inquiries@barthsyndrome.ca

2003 YEAR-END REPORT *(Continued from page 3)*

- Office of Rare Diseases Regional Meeting on "Gaining Access to Research Resources", January, 2003 (Kate McCurdy)
- National Heart, Lung and Blood Institute Public Interest Organization Meeting, February, 2003 (Kate McCurdy)
- NDRI "Genetics of Rare Disease – Window to Common Disorders" Conference, March, 2003 (Kate McCurdy)
- Sudden Arrhythmia Death Syndromes Foundation, Canada (Karen Gorden, Chris Hope)
- Sudden Arrhythmia Death Syndromes Foundation, USA (Steve Kugelmann, Shelia Mann)

- Increased visitors to the BSF website
  - 2003 total visits 59,057, a 106% increase over 2002
  - 2003 new (unique) visitors 14,129, a 106% increase
- Increased Family Membership by 16% in 2003
- Published two BSF newsletters

Goal #2*: *To stimulate the development of successful treatments for Barth syndrome, a multi-system disorder, and enable their delivery. [NEW GOAL]

- Families increased the sharing of useful medical information on treatments via BSF's Family listserv
- Physicians were able to correspond with each other directly about treatment issues via BSF's new Doctor's listserv

Goal #3: To encourage, guide and fund additional research to improve diagnosis and treatment, and ultimately to develop a cure for Barth syndrome.

- Funded 5 grants from the 2003 grant cycle:
  - **David C. Dale, M.D., Professor of Medicine**
    University of Washington
    "*Neutropenia in Barth Syndrome*"
  - **Mauro Degli Esposti, Ph.D., Senior Research Fellow, School of Biological Sciences**
    University of Manchester, UK
    "*Bid and Cardiolipin Metabolism: Impact on Neutropenia and Lymphoma Predisposition*"
  - **Taco W. Kuijpers, M.D., Ph.D., Professor of Pediatric Hematology, Immunology and Infectious Disease**
    Emma Children's Hospital, Amsterdam
    "*Neutrophil Function in Barth Syndrome in Relation to Annexin-V Binding and Cell Death"*
  - **Cathryn S. Mah, Ph.D., Assistant Professor, Pediatrics**
    University of Florida, Gainesville
    "Genetic Analysis of Barth syndrome"
  - **Yang Xu, M.D., Ph.D., Research Assistant Scientist**
    NYU Medical Center, New York
    "Is Tafazzin a Phopholipid Transacylase?"

Goal #4: To create a caring and informed community of Barth syndrome extended families actively involved in supporting each other and our organization.

- Used public relations and the media to increase awareness of BSF and Barth syndrome and to find new families

- January – South Bend Indiana Tribune "*Living with Barth – Child's rare ailment had no treatment"* by David Rumbach, featuring the Cook family
- February – Florida Today "*Dussich Dancers aid R.J.'s Cause"* by King Quillen, featuring the Kugelmann Family
- March – WPRY Radio *"Barth Syndrome Foundation – A Noble Cause in our Local Community"* - Melvin Parker interview with Shelley Bowen
- April – S Afr Med J. 2003 Apr, 93(4): 249:50 *"Little Known Killer: Barth Syndrome"* by C. Bateman featuring the Campbell-Gillies and Thorpe Families
- May – WCTV News Tallahassee Florida *"Barth Syndrome: Rare or Rarely Diagnosed"* interview by April Douglas featuring the Bowen Family
- June- September— Reader's Digest *"Saving Michael Bowen"* by Lynn Rosellini featuring Michael and Shelley Bowen
- June – Westchester Times (NY) *"The Times Applauds Carwash to benefit Barth Syndrome Foundation"* by Ava Crockett featuring the McCurdy Family
- June – Daily Local News West Chester (PA) *"Battling Barth Syndrome – West Chester Mother use Net to help in Fight"* by Tara Munkatchy featuring the Baffa Family
- August — Florida Today *"Fund-raiser supports Barth research"* by King Quillen featuring the Kugelmann family

- Developed translation services to support 13 different languages (translated and posted on the BSF website information about BSF and Barth syndrome in these languages)
- Created a website development team to keep website up-to-date and user friendly for members (Michael Hope, Lynn Elwood, Bill Knauer)
- Began *"Barth Educational Handbooks Project"* (educational assistance research project) to aid families seeking solutions on the day-to-day matters of education of affected children (Jon Rosenshine)
- Created a sibling support program (Alanna Layton)
- Created a peer-to-peer program to assist newly diagnosed families by providing assistance in navigation of the website, contacts, access to BTHS documents, thus transforming the new families into seasoned families within one year (Chris Hope)
- Created a program to insure timely release of information to families without access to the Internet (Chris Hope)
- Initiated the development of BSF family support materials regarding the day-to-day care of the various components of Barth syndrome (Karen Gordon)
- Expanded BSF listserv to serve five separate groups **(**Shelia Mann)
  - Entire group
  - Affected individuals
  - Grandparents
  - Physicians and Scientists
  - Siblings

Goal #5: To build and sustain a broad base of committed contributors who will provide the funds we need to achieve our vision.

- Raised $729,530 in over 630 separate contributions, a 122% increase over last year
- Received $500,000 from an anonymous, dedicated foundation

(Continued on page 6)

2003 Year-End Report *(Continued from page 5)*

- Received $50,000 from the Lebensfeld Foundation
- Raised $78,207 from solicitation letters sent by two Barth families to their friends and families
- Collected $27,350 in 2003 from the 2002 Ironman Fundraiser
- Received $17,000 from Dr. Paul and Allene Russell to fund the Educational Handbook Project
- Received $16,147 from a dinner in honor of the Baffa family
- Raised $14,826 from the 2nd annual BSF Golf Tournament in Merritt Island, Florida sponsored by Steve and Jan Kugelmann
- Received $4,398 in gracious gifts as memorials
- Received $3,200 from the Thunderbird car rally in Chattanooga, David and Shelia Mann members
- Received $2,673 in Corporate and Employer matching gifts
- Received $1,100 from various donors to support the 2004 BSF Family and Scientific/Medical Conference
- Received $770 from Dussich Dance Studio recital in honor of R.J. Kugelmann
- Received $650 from a carwash fund raiser sponsored by St. John's Church in Larchmont, NY, where Kate and Steve McCurdy are members

Goal #6: To inspire and make effective use of an organization dedicated to reaching our vision … "A world in which no one will suffer or perish from Barth syndrome".

- Increased distribution of BSF Newsletter from 500 copies (2001); to 1,300 copies (2002); to 2,300 copies (2003)
- Hosted two BSF volunteer workshops in 2003 and created volunteer groups focused on accelerating our progress in four key areas: Family Support; Awareness; Science and Medicine; and Fundraising
- Welcomed Steve Kugelmann as a new member of BSF's Board of Directors. Steve, as VP of Awareness, will focus on increasing awareness of Barth syndrome within the medical community.
- The Barth Syndrome Trust, UK officially obtained charity status in the UK in 2003 - Michaela Damin, President
- The Barth Syndrome Foundation, Canada has been formally incorporated and is close to obtaining charitable status in Canada - Cathy Ritter, President

VALUES

- We can make a difference in the lives of those affected by Barth syndrome, and we will actively seek to do so.
- We will insure that BSF means: Credibility, Integrity, Professionalism and Compassion.
- We will be accountable for our commitments and actions.
- We will be respectful of the time and talent we are offered and good stewards of the resources we are given.
- We value teamwork and collaboration and constantly seek to improve by learning from others.
- We believe that families and physicians should be able to make their own decisions about care and treatment, and we will help them by insuring access to the latest tools and information
- When representing BSF, we place the interests of all those affected by Barth syndrome above the interest of any individual.

AMENDED TAGLINE

"Saving lives through education, advances in treatment and pursuit of a cure for Barth syndrome"

FIVE *NEW* RESEARCH GRANTS AWARDED BY BSF

(Continued from Cover)

This year's projects will be carried out in laboratories in Seattle, WA; Manchester, England; Amsterdam, The Netherlands; Gainesville, FL; and New York, NY. The Principal Investigators for the work include two Ph.D.s, one M.D., and two M.D., Ph.D.s.

It is my privilege, on behalf of BSF, to congratulate those who have received these grants and to tell them how much we appreciate their interest and dedication to this fascinating and difficult disorder which is our cause. I also want to thank the talented scientists and physicians who volunteered their time to serve as reviewers of the applications that BSF received. Last, but certainly not least, I want to acknowledge the crucial role fulfilled by of all of our generous donors, without whom we simply could not fund these important projects. Together, we ***will*** make a difference.

The 2003 grants which have been awarded are the following:

Principal Investigator: David C. Dale, MD;
Professor of Medicine
Institution: University of Washington; Seattle, WA
Amount: $40,000
Time Period: 2 years
Title of Project: *Neutropenia in Barth Syndrome*

Abstract:

Patients with Barth syndrome (OMIM 302060) have dilated cardiomyopathy, skeletal myopathy, neutropenia and abnormal mitochondria. This syndrome is now attributable to mutations in the *G4.5* or *TAZ1* gene at locus Xq28. These mutations introduce stop codons resulting in truncation of tafazzin proteins, amino acid substitutions, or alternate splice sites in the *G4.5* gene. There is considerable heterogeneity in the clinical spectrum of abnormalities associated with these mutations. Most recent research on Barth syndrome has focused on the cardiac, genetic, and metabolic abnormalities associated with the disorder, and not on the patient's problem with neutropenia.

In 1983, Barth et al. described the clinical and laboratory abnormalities of a large pedigree with seven confirmed cases and a number of other, probably affected, individuals. The immediate cause for death in two patients, a full term infant and a child of 38 weeks, was septicemia attributed to neutropenia or agranulocytosis. The three new cases included in this report all had severe neutropenia, i.e., neutrophil counts less than $0.5x10^9$/L. These patients' neutrophil counts varied considerably, possibly related to the occurrence of inflammation or due to intrinsic aspects of the underlying disorders in neutrophil production and deployment. The original studies of this syndrome pointed to a defect in neutrophil formation as the primary reason for neutropenia and the susceptibility to infections in Barth syndrome patients. Other investigators as well as the Amsterdam group describing this syndrome, however, have not found consistent abnormalities in the marrow of these patients.

Patients with Barth syndrome have severe chronic neutropenia or SCN, i.e., blood neutrophil levels continually or intermittently less than $0.5x10^9$/L. With SCN, other blood cell counts are normal. Splenomegaly is generally not a feature of SCN and the neutropenia is probably attributable to a defect in cell production by the bone marrow.

Based on available data, we hypothesize that Barth syndrome is a condition caused by accelerated apoptosis of developing neutrophils, in some cases sufficiently severe to lead to fatal infections. Neutrophils are particularly vulnerable because they are in effect "pre-programmed" for an apoptotic death. We also hypothesize that in Barth syndrome, G-CSF is effective to blunt the apoptotic process throughout the stages of neutrophil development, and is therefore effective for treatment of this condition.

The Severe Chronic Neutropenia International Registry (SCNIR) was begun in 1994 by an international group of researchers engaged in studying the various causes of severe chronic neutropenia. The Principal Investigator (PI) for this project is also the PI for the SCNIR. Through the Registry, we now have clinical information on the course and treatment for more than a thousand patients with various forms of severe chronic neutropenia, predominantly a pediatric population. Through the Registry, we have learned about the risk of leukemia in various forms of severe chronic neutropenia and analyzed the risks and benefits associated with treatment of severe chronic neutropenia with G-CSF, hematopoietic cell transplantation and other therapies. Currently, there are

(Continued on page 8)

(Continued from page 7)

seven patients with Barth syndrome in the Registry; enrollment of additional patients with and without neutropenia is feasible using our current mechanisms. Expanding the population in the SCNIR will provide a valuable base of information to guide clinical care and research on this syndrome.

The proposed research includes two aims:

(1) Expand the number of patients with Barth syndrome in the Severe Chronic Neutropenia Registry. Our goal will be to systematically describe neutropenia as a clinical consequence of Barth syndrome and, if possible, to establish genotype/phenotype relationships for neutropenia in this syndrome.

(2) Establish a cellular model of neutropenia in Barth syndrome which will be useful for understanding the cellular and molecular basis of mutant tafazzin-mediated neutropenia in Barth syndrome.

Principal Investigator: Dr. Mauro Degli Esposti, PhD; Lecturer in Molecular Toxicology
Institution: The University of Manchester; Manchester, UK
Amount: $30,000
Time Period: 1 year
Title of Project: *Bid and Cardiolipin Metabolism: Impact on Neutropenia and Lymphoma Predisposition*

Abstract:

One of the characteristic signs of Barth syndrome is neutropenia, a deficiency in neutrophils – the white blood cells that provide the major defense against pathogens (innate immunity). This deficiency causes recurrent infections and complicates the clinical profile, as well as the quality of life of Barth syndrome patients. This project will clarify whether neutropenia is linked to the severe deficiency in the mitochondrial lipid cardiolipin that originates from the genetic defect associated with Barth syndrome. I recently discovered that Bid, a tumor suppressor protein which is especially important for the differentiation of neutrophils, functions as a lipid transporter in the metabolism of cardiolipin. Following these findings, I formulated the hypothesis that Bid may be dysregulated in cells of Barth syndrome patients and thus compromise the normal differentiation of neutrophils leading to neutropenia and possibly predisposition to contract lymphomas – an insidious type of cancer.

In the proposed project, I shall study Bid expression in cell lines from Barth syndrome patients, then correlate these data with the expression of other proteins related to Bid (belonging to the Bcl-2 family) and with a detailed mass spectroscopy (MS) analysis of cardiolipin and other lipids. I'll next undertake genetic manipulation of the tafazzin gene that is defective in Bath syndrome. I will use a human cell line that is an established model for the differentiation of neutrophils and other myeloid cells to obtain modulated cardiolipin deficiency reproducing that observed in cells from Barth syndrome patients. Then I shall study in detail the correlation between this deficiency, Bid expression and differentiation of neutrophils. Once this novel cellular model will be established and fully characterized, I will undertake pilot studies to ameliorate cardiolipin remodeling with exogenous lipids and monitor the concomitant effect on Bid and various aspects of differentiation into the cells that confer innate immunity.

In sum, the proposed research will clarify the metabolic and genetic connection between the expression of tumor suppressor Bid and cardiolipin deficiency. It will also explore effective ways of restoring the homeostasis of both Bid and cardiolipin so as to ameliorate the conditions of Barth syndrome patients and reduce the risk of contracting lymphomas.

Principal Investigator: Taco W. Kuijpers, MD, PhD; Professor in Pediatric Immunology
Institution: Emma Children's Hospital / Academic Medical Center; Amsterdam, The Netherlands
Amount: $ 40,000
Time Period: 2 years
Title of Project: *Neutrophil Function in Barth Syndrome in Relation to Annexin-V Binding and Cell Death*

Abstract:

Barth syndrome (BTHS) is a rare X-linked disease characterized by a triad of dilated cardiomyopathy, skeletal myopathy, and neutropenia. Remodeling of tetraoleoyl-cardiolipin to tetralineoyl-cardiolipin, an important inner mitochondrial membrane component, is impaired in cultured skin fibroblasts. The disease is associated with mutations of the *TAZ* gene on Xq28. Untreated patients, all boys, often die in infancy or early childhood from septicemia or cardiac decompensation, although mildly affected patients may survive into adulthood. Neutrophil

(Continued on page 9)

function has never been studied. Whether the recent findings in BTHS of altered lipid modeling, in particular of cardiolipin, is causally related to the neutropenia or some myeloid defect remains to be determined.

Our preliminary findings indicate that BTHS patients have circulating neutrophils and eosinophils (but not monocytes or lymphocytes) that show Annexin-V binding, suggesting premature phosphatidylserine (PS) exposure due to early cell damage or apoptosis. The BTHS neutrophils contained very little if any cardiolipins. Reduced cardiolipin concentrations in normal cells have been suggested to be a feature of apoptosis and enhanced PS exposure. Unexpectedly, the neutrophils from BTHS patients did not show enhanced caspase activity, a hallmark of apoptosis, even though the cells were binding Annexin-V. Notwithstanding the lack of other features of apoptosis, PS exposed on the outerleaflet of the plasma membrane can be recognized by various receptors on human macrophages (i.e., the PS receptor, CD14, CD91). The assumption is that BTHS neutrophils will be recognized prematurely by macrophages resulting in early clearance and -as a consequence- a mild neutropenia.

When the BTHS neutrophils are not apoptotic, what is the role of cardiolipins in neutrophils and what is the relevance of the lipid alterations in BTHS with respect to the phenotype of the BTHS neutrophils regarding the clinical neutropenia? The study should address the enigmatic neutropenia in BTHS that can be considered relevant to the infections observed in BTHS patients. The relationship between high Annexin-V binding to the surface membrane of circulating BTHS neutrophils and neutropenia is an important focus. The identification of the ligand to which Annexin-V binds is the second focus of the study.

Hypothesis: In BTHS the plasma membrane of neutrophils is most likely disturbed in composition or symmetry, thus prematurely binding Annexin-V and contributing to the neutropenia in BTHS.

Principal Investigator: Cathryn S. Mah, PhD;
Research Assistant Professor of Pediatrics
Institution: University of Florida; Gainesville, FL
Amount: $40,000
Time Period: 2 years
Title of Project: *Genetic Analysis of Barth Syndrome*

Abstract:

Barth syndrome is an X-linked disease that is characterized by cardioskeletal myopathy, neutropenia, and 3-methylglutaconic aciduria. Currently, there is no known cure for Barth syndrome and treatment is palliative. Mutations in the *TAZ* (or *G4.5*) gene located at Xq28.12 have been shown to be responsible for Barth syndrome. The functions of the putative *TAZ* gene products(s), tafazzins, have not yet been clearly elucidated. Several studies have demonstrated respiratory chain abnormalities in muscle and fibroblast samples from Barth patients, which has been attributed, in part, to defective remodeling of cardiolipin in the mitochondrial inner membrane. Recently, Vaz et al. showed that a single splice-variant tafazzin protein affects cardiolipin metabolism in yeast, the first demonstration that tafazzins are involved in cardiolipin remodeling (Vaz, et al., 2003, J. Biol. Chem., Epub.).

To date, no clear correlations of age at onset and severity of cardiomyopathy, neutropenia, or 3-methylglutaconic aciduria have been made with the genotype of affected individuals, suggesting that additional factors may play a role in the pathogenesis of Barth syndrome. We propose to use gene array analysis to identify such potential modifier genes. To this end, we propose to examine the difference in global gene expression profiles resulting from the specific gain of function of *TAZ* activity in human fibroblasts. This gain of function will be mediated by recombinant adeno-associated virus (AAV) administration. We hypothesize that the specific gain in *TAZ* function in deficient cells will up- or down-regulate expression of genes that are involved in the mechanisms of *TAZ* function of molecules associated with downstream processes that are also likely to be involved in the pathogenesis of Barth syndrome.

The results of these studies should provide insights into other potential modifying genes of pathways that may play a role in Barth syndrome. Identified gene families may be not only pathognomonic for severe clinical presentation and progression, but could also provide candidate genetic determinants that would lead to the development of tools for screening and indicate appropriate palliative care. Identified genes could also prove to be potential targets for pharmacologic and/or gene therapeutic interventions and provide essential considerations when developing such therapies for Barth syndrome.

(Continued on page 10)

(Continued from page 9)

Principal Investigator: Yang Xu, MD, PhD; Research Assistant Scientist in the Department of Anesthesiology
Institution: New York University School of Medicine; New York, NY
Amount: $23,760
Time Period: 2 years
Title of Project: *Is Tafazzin a Phospholipid Transacylase?*

Abstract:

Over the past three years, significant progress has been made in understanding the pathologic mechanism of Barth syndrome (BTHS). The data support the Neuwald hypothesis, stating that tafazzin, the mutate gene of BTHS, is a phospholipid acyltransferase. Specifically, tafazzin appears to affect the fatty acid composition of the mitochondrial phospholipid cardiolipin. However, the exact enzymatic function of tafazzin has not been identified. We have obtained preliminary evidence suggesting that phospholipid transacylation (transfer of fatty acyl residues between phospholipids) is involved in the generation of specific fatty acid profiles in mitochondrial cardiolipin. The present proposal is designed to test the hypothesis that tafazzin is a phospholipid transacylase.

Our hypothesis is that the tafazzin gene encodes a phospholipid transacylase that is involved in the remodeling of cardiolipin. Therefore, tafazzin mutations result in alterations of the fatty acid pattern of cardiolipin. In order to test this hypothesis, we propose:

(1) To demonstrate whether or not transacylase activity is involved in cardiolipin remodeling in lymphoblast cell lines;

(2) To demonstrate whether this transacylase activity is deficient in lymphoblasts from BTHS patients; and

(3) To demonstrate which mRNA splice variant of lymphoblasts carries transacylase activity.

NIH Research Initiatives Seeking Applications

In addition to the vast investigator-initiated research that is supported by the National Institutes of Health (NIH), research in some specific areas is solicited by various NIH institutes from time to time. Applications for these usually are accepted for February 1, June 1 and October 1 deadlines every year. ***The following ongoing NIH initiatives are particularly relevant to Barth syndrome.***

Exploratory and Developmental Research Grants for Investigations in Rare Diseases (R21)
Initiative number: PA-03-171

Purpose: To encourage exploratory and developmental research projects by providing support for the early and conceptual stages of projects that represent novel approaches to the understanding, treating, and preventing rare diseases in the areas of heart, lung, and blood disease, as well as sleep disorders.
Please visit:
http://grants1.nih.gov/grants/guide/pa-files/PA-03-171.html **for more details.**

Chronic Illness Self-Management in Children
Initiative number: PA-03-159

Purpose: To solicit research related to improve self-management and quality of life in children and adolescents with chronic diseases. Children with a chronic illness and their families have a long-term responsibility for maintaining and promoting health and preventing complications of the chronic disease. Research related to sociocultural, environmental, and behavioral mechanisms as well as biological/technical factors that contribute to successful and ongoing self-management of particular chronic diseases in children is encouraged.
Please visit:
http://grants2.nih.gov/grants/guide/pa-files/PA-03-159.html **for more details.**

2004 REQUEST FOR RESEARCH PROPOSALS

The Barth Syndrome Foundation, Inc. (BSF) is pleased to announce the availability of funding for research on the natural history, biochemical basis, and treatment of Barth syndrome.

Background

Barth syndrome is a serious X-linked recessive condition associated with cardiomyopathy, neutropenia, skeletal muscle weakness, exercise intolerance, growth retardation, and diverse biochemical abnormalities (including defects in mitochondrial metabolism and phospholipid biosynthesis). Because many clinical and biochemical abnormalities of Barth syndrome remain poorly understood, we are seeking proposals for research that may shed light on any aspect of the syndrome. We are determined to find improved treatments – and ultimately a cure – for this rare and underdiagnosed disorder.

Types of Proposals Sought

We are most interested in providing "seed money" to be used by experienced investigators for the testing of initial hypotheses and collection of preliminary data leading to successful long-term funding by NIH and other major granting institutions. In addition, we are especially interested in attracting new investigators to the very interesting field of Barth syndrome research.

Funding

We anticipate awarding up to $150,000 in 2004, divided among several one- or two-year grants of up to $40,000 each. Funds will be available in January 2005, as soon as the successful grant applicants have been notified.

Process

Unlike prior years, in 2004 we will have a *one-stage* grant process. Applications should be of 10-15 pages in length and must follow the instructions listed on the BSF website. In general terms, detailed information about the specific aims, significance, research design and methods, personnel, and budget will be required, along with evidence of application to the relevant Institutional Review Board for any work involving human subjects. Completed proposals will be forwarded to the BSF Scientific and Medical Advisory Board (as well as outside reviewers, in certain cases) for evaluation. Based on the recommendations of the Scientific and Medical Advisory Board, the BSF Board of Directors will make the final funding decisions for the grant applications. Please consult our website, **www.barthsyndrome.org** for further guidelines and application details as well as a listing of grants that BSF has awarded to date.

Deadline

The deadline for submission of grant applications from interested investigators is **October 1, 2004**.

Contact Information

Kate McCurdy
Vice President, Science and Medicine
Barth Syndrome Foundation, Inc.
P.O. Box 618
Larchmont, NY 10538
kmccurdy@barthsyndrome.org

Clinical Work to be Done at BSF's 2004 International Scientific and Family Conference

By Valerie "Shelley" Bowen, President, BSF and Kate McCurdy, VP, Science and Medicine

Cardiology in Barth syndrome

We have long known cardiomyopathy to be a critical component of Barth syndrome. In recent months, we have grown increasingly aware that this disorder also may be linked to the *possibility* of serious arrhythmias. This concern came to light when several of our teenage and young adult members were identified as being at high risk for sudden cardiac death (SCD) upon electrophysiology studies. A fatal arrhythmia claimed the life of one of our children while he was at play on the school playground. It is unknown at this point if this is a tragic anomaly or a more frequent possibility.

As a result of this growing concern, Carolyn Spencer, M.D. and Randall Bryant, M.D. et al. will conduct a study to evaluate Barth children from the cardiac standpoint. They have received General Clinical Research Center (GCRC) approval and funding for this study at the University of Florida. This is a tremendous accomplishment. The GCRC was established through the National Institutes of Health (NIH). Both Dr. Spencer and Dr. Bryant are committed to our childrens' health and assisting all concerned to better understand this complex issue. To date, there has never been such a comprehensive study in the area of cardiology conducted on those with Barth syndrome.

Dr. Bryant has contacted a local pediatric cardiologist in the Orlando area to utilize his facility for this study while we are all in Orlando at our conference in July. Dr. Bryant will be assessing the EP aspect of this disorder, while Dr. Spencer will be assessing the cardiology function. Many of you may remember Dr. Spencer from the previous cardiology studies conducted in Baltimore, Maryland at our last meeting.

Neurology in Barth syndrome

At our previous conference, Tyler Reimschisel, M.D. conducted a series of brief, noninvasive neurology evaluations on those who have Barth syndrome. He presented his preliminary findings at the BSF scientific sessions the next day and is very interested in continuing his clinical investigation into the muscular and neurological aspects of Barth syndrome at the 2004 conference

Pedigrees in Barth syndrome

Rebecca Kern, M.C.G. and Iris Gonzalez, Ph.D. will once again tag-team in the area of genetics. While it may seem like finding a genetic mutation is the final answer, this could not be farther from the truth. It is important for families to know the exact genetic mutation that has been found in those in their family with Barth syndrome as well as to have a pedigree of other familial disorders. Common traits, which might be reflected in these pedigrees, could lead to investigation of more common disorders, ie; diabetes, strokes, Alzheimer's and so on. It is also equally important to understand all the various clinical manifestations of Barth syndrome. Some important common themes already have emerged; regardless of how seemingly insignificant some of the rest of these may appear in a single patient, common threads can lead to a better clinical description of this disorder.

Cognitive Development Project in Children with Barth syndrome

This project is designed to help understand the development of mathematics and related skills in

(Continued from page 12)

young children. One component of the project involves following the development of these skills in young children who may be at risk for math learning disability. One potential risk factor being explored is the diagnosis of Barth syndrome. This research on Barth syndrome is being carried out in collaboration with Dr. Richard Kelley, Director of Metabolism, Kennedy Krieger Institute.

We are currently recruiting children who have been diagnosed with Barth syndrome, and who are 5 to 9 years old. To participate, a child needs to be in kindergarten, first, second, or third grade. Participation will involve approximately 1 to 4 hours of psychological and academic achievement testing. The testing will occur at the Kennedy Krieger Institute in Baltimore, Maryland, or elsewhere, depending on your geographic region of residence. Following the testing, parents will be mailed a report of their child's test performance. There is no charge to the parent for any of this testing.

If you desire additional information, or if you would like to learn whether your child may enroll in this research project, please feel free to contact Dr. Michèle Mazzocco, Principal Investigator, at 443-923-4125 or Anne Henry, Research Assistant at 443-923-4121, or if you prefer email ***henrya@kennedykrieger.org*****.** If you are interested in more information about Barth syndrome please call Rebecca Kern at 443-923-2783.

Other clinics offered during the BSF International Conference, include the following:

- How to take apical pulses and blood pressure on a child with Barth syndrome
- CPR
- General Inquiries
- Educational consults
- Nutritional consults

Those registering to attend our BSF conference will be contacted with more information about these studies as well as appointments for these clinics. Appointments will be provided on a first come, first serve basis. In an effort to obtain the best possible appointment time, you should register for the BSF conference in a timely manner.

What is Barth Syndrome?

Barth syndrome is a rare but serious X-linked recessive disorder, in which the clinical effects of the *G4.5* (or *TAZ1)* gene mutation are manifested only in males. The characteristics of Barth syndrome include the following in varying degrees, even within the same family:

Cardiomyopathy**:** Heart muscle weakness. This, combined with a weakened ability of the white blood cells to fight infections, represents the greatest threat to boys with Barth syndrome.

Neutropenia**:** Reduction in the number of "neutrophils," a type of white blood cell that is extremely important in fighting bacterial infections. The neutropenia may or may not follow a regular cycle, but in either case, it puts Barth boys at an increased risk of serious infections.

Muscle Weakness and General Fatigue**:** All muscles in a Barth patient, including the heart, have a cellular deficiency which limits their ability to produce energy, causing extreme fatigue during activities requiring strength or stamina – from walking to writing to growing.

Growth Delay**:** Most boys with Barth syndrome are below-average in weight and height, often substantially so, until the late teenage years.

Early diagnosis is key to survival for Barth syndrome boys. Those in whom the diagnosis of Barth syndrome is missed have only a 30% chance of living through the first few years of life. With a proper diagnosis at an early age, however, these boys have an 85-90% chance of survival. This is why awareness of Barth syndrome is so important.

A Study of TAZ mRNAs in Barth Syndrome Individuals

Work by Iris L. Gonzalez, PhD (funded by BSF)

Iris L. Gonzalez, Ph.D.
Molecular Diagnostics Lab
Alfred I. duPont Hospital
Wilmington, DE

Many different mutations responsible for Barth syndrome have been identified in the *TAZ* gene. The publication that reported the discovery of this gene described what appeared to be a family of related proteins produced by the gene. Of note, there appeared to be two beginnings of the gene (like a story that you can start reading at either chapter 1 or at chapter 3); moreover, there was "alternative splicing", which means that various combinations of gene segments (called "exons") were used to produce this family of related proteins (this is like being able to read the story by reading different combinations of chapters).

The possibility that omitting gene segments could produce useful proteins was interesting in the context of genetic disease: could skipping of a mutated exon lead to a less severe disease? This possibility is contradicted by the finding that disease-causing mutations occur in all gene exons (except for exon 5) and that there is no correlation between the location of the mutation and the severity of Barth syndrome. I therefore wanted to re-examine the products made by the gene, looking at the readily accessible "TAZ mRNA", which is the intermediate product between gene and protein. mRNAs (extracted from white blood cells) from both normal individuals and from Barth syndrome individuals were included in the study.

RESULTS

I have found that when the actual gene products, the "mRNAs," are measured in cells the gene yields a much more limited repertoire of mRNAs than had been proposed earlier.

[1] There is only one beginning of the gene: there is no additional start site in exon 3 (or chapter 3) even though the gene sequence theoretically might allow that.

[2] I found that there are only four major products of the Barth gene, the most abundant of which is the one called "delta 5 mRNA", which means that exon 5 is skipped; the others are a full length product, a delta 7 mRNA and a delta 5/delta 7 mRNA. In addition, a variety of incompletely-spliced and alternatively-spliced products are found in lesser but significant amounts.

[3] It is not possible to obtain relative quantities of these mRNA products because they form hybrids called "heteroduplexes," which confound quantitation; however, a rough quantitation is possible by analyzing many randomly-selected clones of TAZ mRNAs.

[4] When analyzing the mRNAs of our Barth boys, I found differences depending on the type of mutation of the individual. Less TAZ mRNA was found when a frame-shifting mutation was present – this is due to a phenomenon called "nonsense-mediated decay", whereby the mRNAs break down because STOP codons are present. There was a normal amount of mRNA when the mutations only caused single amino acid changes or caused splicing alterations. This suggests that normal amounts of mutated protein may ultimately be made, but the protein is not functioning as it should.

[5] I found a variety of alternative splice sites (splicing at sites other than the normal ones), some of which would yield a lengthened mRNA product and lengthened but otherwise normal TAZ protein, and some of which would yield mRNA products with STOP codons, which would produce functionless shortened proteins or no protein at all. These alternatively spliced mRNAs are seen in individuals with or without Barth syndrome. The extent of function of the potential "lengthened but otherwise normal proteins" is not known, an important question because individuals with "splice site" mutations make significant amounts of these products.

(Continued on page 15)

TAZ mRNAs in Barth Syndrome

[6] The mystery of the often skipped gene segment (exon) 5 in which no disease-causing mutations have been found raises the question: "Is it a real exon?" Other researchers have reported that exon 5 is dispensable when protein function is tested in yeast. However, neither the normal yeast gene nor the normal rodent gene contains this segment, but a good number of human products do include it, which suggests that exon 5 may have an important role in humans. For that reason, I am currently looking at the *TAZ* gene and its mRNAs in other primates to determine how the DNA in exon 5 evolved into an exon. The possible function of exon 5 must be tested in cells of an organism that has exon 5, for example in human cells that have a frame-shifting or a STOP mutation earlier in the gene.

The main conclusion that one can draw from this work is that the TAZ protein family is actually small and may consist of only 1 or 2 members. This would mean that eventual therapies need to target only this limited number of proteins. Now it is important to learn exactly what the TAZ protein does, how it does its job, what parts of the molecule are important for its function(s), and how might we be able to alter the function of a defective molecule.

Cardiolipin – A Tough Nut To Crack

By Miriam L. Greenberg, Ph.D.

Miriam L. Greenberg, Ph.D., Professor, Dept. of Biological Sciences Wayne State Univ.

The original intent of this article was to discuss the difficulties of working with cardiolipin (CL), the phospholipid that is not properly remodeled in Barth syndrome. The difficulties inherent in measuring CL probably contribute to the under-diagnosis of Barth syndrome. However, as I began writing, I realized that people may not appreciate how important phospholipids are in general, and where they are found in our cells.

To really understand what CL does, it is important to know what phospholipids do, and that they are found in membranes, and so we need to know what membranes do. Therefore, I have started with a discussion of membranes, from which the story of CL develops.

Membranes are essential. All of our cells are surrounded by membranes, which are absolutely essential for cells to function properly. The reason is that membranes separate the cell from the outside, so that essential substances don't leak out, and toxic things from the environment don't easily get in. Membranes also play a very important role inside our cells. In each cell, individual compartments called organelles carry out specific jobs that include making large molecules (fats, nucleic acids etc.), breaking down these same molecules, generating energy, etc. These jobs have to be compartmentalized – it wouldn't be very efficient to make fats in the same place where fats were being broken down! In addition, different tools (enzymes) are necessary for different jobs – a compartment devoted to generating energy doesn't need enzymes for making fats! How are organelles compartmentalized? They are surrounded by membranes.

What are membranes? Membranes are composed primarily of two major components, phospholipids and proteins. Phospholipids have a "backbone" made of glycerol. Attached to one end of the glycerol is a phosphate. In addition, two fatty acids are connected to the glycerol backbone. There are different kinds of phospholipids, because different molecules can be attached to the phosphate. All cell membranes have 4 major types of phospholipids. In addition to these 4, there is a very unique phospholipid in the cell that is found only in one of the organelles. This organelle is called the mitochondrion, and it is responsible for producing energy. The mitochondrion is surrounded by a unique membrane. In addition to the 4 phospholipids found in all cell membranes, the mitochondrial membrane has a unique phospholipid – cardiolipin! Why is CL unique? The other phospholipids are composed of a single glycerol backbone with two fatty acids. But CL looks like a double phospholipid – two backbones each containing two fatty acids, connected by another molecule of glycerol. Thus, while all other

(Continued on page 16)

Cardiolipin – A Tough Nut To Crack

(Continued from page 15)

phospholipids have two fatty acids, CL has four. CL is unique in another way. The fatty acids in CL are different from those of the other phospholipids. Fatty acids can be saturated or unsaturated. There are more unsaturated fatty acids on CL than on the other phospholipids.

Why is CL important? We are only just beginning to learn why CL is important. One of the best ways to learn why a molecule is important is to study what happens when the molecule is absent. This type of study is often best done in "model" systems, i.e., organisms that can be easily manipulated in a laboratory. One of the best model organisms is yeast, the same yeast that we use for making bread and beer! Yeast cells are very similar to human cells in many ways, but they are much simpler to grow, and to do experiments with. We now have a yeast mutant cell, called *crd1,* that cannot make CL, and we have carried out many experiments with this mutant to understand the consequences of not having CL. We have learned that many mitochondrial functions are defective in the absence of CL. Respiratory control, the process whereby mitochondria generate energy, is defective. Mitochondria deficient in CL are less able to withstand the stresses of high temperature and volume changes. And CL-deficient mitochondria are defective in the ability to import proteins from other parts of the cell.

CL and Barth syndrome. There are two CL-related deficiencies in Barth syndrome. There is a reduced amount of total CL in Barth syndrome cells. In addition, the fatty acids that are present in the CL are not the unsaturated fatty acids normally present, i.e., linoleic acid. In order to understand the consequences of these deficiencies, we have turned once again to the yeast model system. We now have a yeast mutant that lacks the same gene that is missing in Barth syndrome. This yeast mutant, called *taz1*, has decreased total CL, and decreased unsaturated fatty acids in the CL, both hallmarks of Barth syndrome. We are actively engaged in experiments to understand the consequences of these defects to the cell.

How can CL be measured? As mentioned above, there are two CL deficiencies in Barth syndrome, decreased total CL and decreased linoleic acid in the CL. Therefore, definitive diagnosis involves measurement of total CL as well as CL fatty acid content. Neither measurement is a standard clinical test at this time. To measure CL, membranes are extracted from cells in chloroform/methanol, which dissolves lipids. The solvent will then contain all the membrane phospholipids. Of all the major phospholipids, CL is the least abundant. That means that to get accurate measurements, you need a lot of cells to start with. Now that you have a mixture of phospholipids, how do you determine how much CL is present? You have to use a procedure to separate the phospholipids. This is called chromatography. After the individual phospholipids are separated, they can be quantified, and the levels of CL in a patient's sample can be compared to levels in normal control samples. This procedure tells us the relative amount of CL, but it does not tell us anything about the fatty acids present in the CL.

The second test, to identify the fatty acids present in CL, requires further analysis. Two procedures are currently used to identify the fatty acids. About 13 years ago, Dr. Michael Schlame developed a technique that enabled the identification of fatty acids using a chromatography procedure called HPLC (high performance liquid chromatography). (This procedure is published in *Analytical Biochemistry* 195:290-295, 1991). This is a very innovative technique. However, it is very labor intensive and requires very sophisticated procedures that do not lend themselves easily to automation in a clinical setting. More recently, Fredoen Valianpour, a student in the Amsterdam group of Peter Barth and Ronald Wanders, worked out another technique to quantify the fatty acids of CL using a procedure called electrospray ionization mass spectrometry (ESI-MS). In ESI-MS, electrically charged droplets containing the molecule to be studied are prepared. The droplets enter a vacuum that evaporates the solvent, reducing the droplet size. This causes the charged molecules within the droplet to disintegrate and release molecules that are volatilized, accelerated by an electromagnetic field, and analyzed according to the ratio of mass/charge. Fredoen showed that this procedure can be utilized to identify the fatty acids in CL (as published in *Clinical Chemistry,* 48:1390-1397, 2002). These two procedures, while extremely useful, are labor intensive, require sophisticated instruments, and do not at this point lend themselves to automation.

Summary. The identification of a CL remodeling defect in Barth syndrome by Peter Vreken and co-workers opened the door to clinical diagnosis of the disorder, and to experimentation to understand the cause of the pathology. Two factors most likely contribute to the under-diagnosis of Barth syndrome. One is that the association of Barth syndrome with defective CL remodeling has been made only recently. As research on CL-associated defects continues, more clinicians will become aware of Barth syndrome. Second, the biochemical tests to measure CL and associated fatty acids are complex and not routine. Improvements in this area and/or the more widespread implementation of current procedures will no doubt simplify diagnosis of Barth syndrome.

From Gene to Function

By Frédéric M. Vaz, Ph.D.

Frédéric M. Vaz, Ph.D.
Academic Medical Center
University of Amsterdam

After the finding of Peter Vreken and Fredoen Valianpour that Barth syndrome patients have a deficiency of the mitochondrial phospholipid cardiolipin, and the suggestion of Neuwald that the tafazzin protein is involved in the remodeling of phospholipids, it appeared that the unraveling of the function of the tafazzin gene was nearby. Unfortunately, the function of Tafazzin still remains unknown. This considerably impedes our understanding of Barth syndrome and our efforts to develop an adequate treatment strategy. Our project, which is supported by the Barth Syndrome Foundation, called "Resolution of the Function of the TAZ-gene and Characterization of its Gene Products" aims to do just that; determine the exact function of Tafazzin.

The Tafazzin gene, however, complicates things because it produces several different mRNAs. mRNAs (where m stands for messenger, RNA for ribonucleic acid) are templates that bear the information needed to produce proteins, which exert their function in the cell. The process where *one* gene produces several different mRNAs (and potentially proteins) is called alternative splicing. Already at the time the tafazzin gene was identified it was found that this gene can give rise to at least 12 different proteins, which all could have different functions!

To investigate the function(s) of these different tafazzin proteins we selected a model system; namely Baker's yeast. Baker's yeast also has a gene that resembles the human tafazzin gene and by genetic manipulations we disrupted this gene, thereby creating a "Barth syndrome yeast". Like Barth syndrome patients, this Barth syndrome yeast also has cardiolipin deficiency. Additionally, the Barth syndrome yeast accumulates precursors of cardiolipin in the remodeling process, monolysocardiolipins. This finding is another indication that Tafazzin is involved in the remodeling of cardiolipin.

By separately introducing the twelve human tafazzin mRNAs that potentially produce the different tafazzin proteins into the Barth syndrome yeast, we investigated which tafazzin protein could restore the cardiolipin deficiency and alleviate the accumulation of monolysocardiolipins. As it turned out, only one of the twelve mRNAs we tested encoded a tafazzin protein, which was able to normalize both cardiolipin and monolysocardiolipin levels. This is the first *direct* evidence that tafazzin indeed is involved in cardiolipin metabolism. Although we have not excluded that the remaining tafazzins could play other roles in phospholipid metabolism, it appears that only one tafazzin protein is involved in the remodeling of cardiolipin. Again we are closer to the elucidation of the function of tafazzin, but it still remains elusive!

We also want to use the Barth syndrome yeast to generate large amounts of the 'correct' human tafazzin and isolate this protein. By adding potential substrates (cardiolipins, monolysocardiolipins and other substances needed for remodeling) to this purified protein, we hope to investigate the function of tafazzin in more detail. Another point of discussion is the localization of tafazzin in the cell. Although it seems logical to assume that tafazzin is present in mitochondria (since cardiolipin is a mitochondrial phospholipid) this still has not been demonstrated experimentally. Our recent experiments, however, suggest that tafazzin indeed is a mitochondrial protein.

In addition to the functional studies described above, we are in the process of ameliorating our assays to accurately diagnose Barth syndrome on the basis of the cardiolipin profile. We have analyzed the cardiolipin profile of several types of blood cells and tissues of healthy and Barth syndrome individuals. A surprising finding was that also in (human) Barth syndrome, monolysocardiolipins accumulate, especially in the most affected tissues, heart and muscle. But also in lymphocytes and cultured lymphoblasts of Barth syndrome patients, monolyso-cardiolipins accumulate and, in addition to the cardiolipin deficiency, this can be used as an additional diagnostic parameter to identify Barth syndrome patients. In fact, measurement of the cardiolipin/monolysocardiolipin ratio in lymphocytes is superior to the measurement of cardiolipin in platelets as used by us an others before.

We hope that our efforts and those of other Barth syndrome researchers will improve the diagnostic accuracy and speed so that early diagnosis and subsequent treatment is possible. Hopefully, the more fundamental research will result in a better understanding of the underlying defect in Barth syndrome, which will provide clues for the development of a therapy.

The Molecular Mechanism of Barth Syndrome

By Grant Hatch, Ph.D.

Grant Hatch, Ph.D.
Director, Lipid Lipoprotein & Atherosclerosis Group
University of Manitoba
Winnepeg, Canada

Phospholipids, or phosphorus containing fats, are important structural components of biological membranes. One of these phospholipids is cardiolipin. Cardiolipin is an important phospholipid found in all cells of the body that need to make energy. Cardiolipin is responsible for activating enzymes or proteins that make the energy for our bodies to perform various functions including muscle contraction or even beating of the heart. Like other phospholipids, cardiolipin contains long chain fatty acids that may come from the diet. The types of fatty acids that are found in cardiolipin make up its so-called "composition". Both the amount of cardiolipin and its composition seem to be important for activating the enzymes or proteins that help make the energy. The composition of cardiolipin seems to be regulated by remodeling pathways in which certain saturated fatty acids are removed and then replaced with other unsaturated fatty acids such as linoleic acid. In Barth syndrome it appears that the cardiolipin levels are reduced and monolysocardiolipin, a cardiolipin breakdown product, accumulates. This is due to a deficiency in the Barth syndrome gene product TAZ. Analysis of the gene reveals that TAZ codes for an acyltransferase. Acyltransferases are enzymes that remodel phospholipids. Therefore, a reduced ability to synthesize and remodel cardiolipin as well as other phospholipids could be one of the underlying molecular mechanisms, among others, responsible for Barth syndrome.

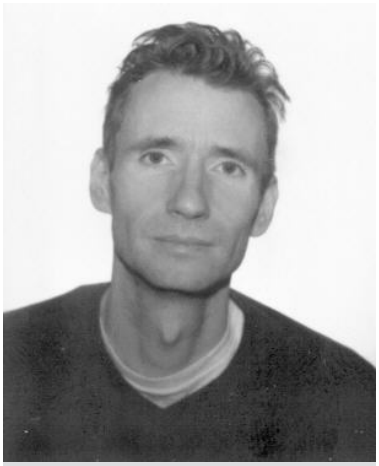
The Barth syndrome gene *TAZ* belongs to a large family of acyltransferases that are involved in glycerolipid biosynthesis and remodeling. Work from Dr. Barth and Dr. Wanders' laboratories have identified a potential defective remodeling of the phospholipid cardiolipin and this is correlated with a reduction in cardiolipin levels and accumulation of monolysocardiolipin. A recent study from Dr. Schlame and Dr. Kelley's laboratories has suggested that the tafazzin gene product may be a transacylase although the activity of the tafazzin gene product itself has not been directly identified. Recently it was also shown by Dr. Barth and Dr. Wanders' laboratory that the TAZ messenger RNA, which codes for proteins, is modified and this modified form of the TAZ messenger RNA may code for the functional Barth syndrome protein.

We have recently characterized the expression of the TAZ messenger RNA in the mouse and some human, non-Barth syndrome, cell lines. Only two tafazzin messenger RNAs, both lacking exon 5, were expressed in mouse tissues. Only four tafazzin messenger RNAs were expressed in the human cell lines. We have also observed the presence of a novel fifth motif (an area in the Barth syndrome protein), identified as critical for the glycerolphosphate acyltransferase family, in human TAZ. Glycerolphosphate acyltransferases are important enzymes in lipid synthesis. The presence of a mutation in this region in Barth syndrome patients indicates that this motif is essential for tafazzin function and indicates a greater complexity in lipid metabolism than we first imagined. More evidence seems to suggest that when we overexpress the modified form of the TAZ messenger RNA in cells, we begin to see effects on other lipid metabolism pathways, possibly as compensatory mechanisms. This may also be true in Barth syndrome cells in which the protein is defective. We are beginning to characterize these changes in the hope that they will lead to some insight into the metabolic changes that are occurring in Barth syndrome cells.

The Barth Syndrome Foundation has been with us since the beginning of this project and we gratefully acknowledge their support.

Links Between Lipids and Barth Syndrome Symptoms

By Michael Schlame, M.D.



Michael Schlame, MD
Dept. of Anesthesiology
NYU School of Medicine

The American Heart Association (AHA) has given our laboratory $210,000 to do research related to Barth syndrome. Funding of the project, entitled "The biochemical basis of Barth syndrome", began in January 2003 and is expected to continue until the end of 2005. The overall goal of the project is to understand the metabolic defect that is present in children with Barth syndrome.

During the last BSF Conference in Baltimore, discussions centered around the idea that Barth syndrome is caused by a gene of lipid metabolism. At the time we had just learned that one of the lipids affected by the disease is cardiolipin. At that meeting the question was raised as to whether cardiolipin is the only "sick" lipid or whether other lipids are affected as well. Furthermore, we asked why Barth boys are unable to maintain a normal lipid profile and why does the presence of abnormal lipids cause so many apparently unrelated symptoms in heart, muscles, and blood, which together make up the typical features of Barth syndrome.

In its first year, the AHA-funded research provided answers to some of these questions, albeit not to all of them. While it supported the key concept of the inborn error of lipid metabolism in Barth syndrome, it challenged some of the fine points of our disease model. For instance, evidence is getting stronger that several lipid defects co-exist in children with Barth syndrome. Thus, the Barth gene seems to participate in the formation of more than one lipid. Perhaps the entire lipid metabolism is affected, and abnormal lipids may be scattered around many different structures in the cell. This idea could help to rationalize why Barth syndrome is associated with so many different symptoms.

"...The past year has witnessed an enormous increase in information about the pathophysiology of Barth syndrome. This progress is the result of a concerted effort by the Barth Syndrome Foundation ... to fund basic research."

However, the main effort of the AHA-funded initiative concerned the molecular mechanism of tafazzin, the enzyme that is derived from the Barth gene. It appears that tafazzin is part of a complex network that moves fatty acids from one molecule to another. In particular, fatty acids can move between different types of lipids, of which they are an important structural element. This process may help to generate lipids with a distinct composition of fatty acids, i.e. it may ensure that certain lipids associate with specific fatty acids. This research is of foremost importance because it goes directly to the molecular origin of Barth syndrome. If we will ever develop a specific drug for Barth syndrome, this drug will most likely interfere with the traffic of fatty acids inside the cell.

Which role do lipids play with respect to the actual symptoms of Barth syndrome? In other words, how does an inborn error of lipid metabolism turn into heart disease or muscle weakness? And how are all the other problems, big and small, which patients with Barth syndrome experience daily, related to lipids? In the beginning we thought that children with severe Barth syndrome ought to have more abnormal lipids than children with a milder form of the disease. However, we found the same cardiolipin deficiency in all Barth boys, regardless of whether they had mild or severe symptoms, regardless of whether they had primarily heart disease, growth-related problems, or abnormal blood counts. Therefore Barth syndrome cannot be explained on the basis of cardiolipin deficiency alone. Instead we believe that Barth syndrome, just like many other genetic diseases, is influenced by developmental and environmental factors. Disease-modifying factors have received a lot of attention lately in relation to such prevalent conditions as diabetes or obesity. Thus we have to look beyond cardiolipin if we want to understand Barth syndrome.

In conclusion, the past year has witnessed an enormous increase in information about the pathophysiology of Barth syndrome. This progress is the result of a concerted effort by the Barth Syndrome Foundation and the AHA to fund basic research. Several research groups around the globe have also contributed to this progress. We hope to build on this momentum in the following years.

Educational Consultant Awarded Grant by BSF

By Jonathan Rosenshine, Educational Consultant

Jon Rosenshine
Educational Consultant

Dear BSF Children, Parents and Community:

Over the past couple of years, I have been extremely lucky to get to know Will McCurdy and his family. In his 9th grade year, Will needed some extra tutoring in English, and my friend Eileen Juico recruited me to begin seeing him. Because of Will's extraordinary intelligence and character, I consider my work with him to be one of my most rewarding teaching experiences in my 12 years as an educator. I am constantly amazed by his strength, energized by his passion for ideas, and humbled by the love I see in his family. From the stories I have heard and from reading the daily listserv, the whole BSF community seems to me to be made up of boys like Will and families like the McCurdys.

I was, therefore, very excited at the prospect of doing educational research and consulting work this year for the Barth Syndrome Foundation. While the immediate health and safety of the boys who suffer from Barth syndrome remain the most important concerns on everyone's mind, many parents have expressed the need for support in their efforts to meet the special educational needs of their children. My goal this year is to produce four handbooks that will be useful guides and resources for those concerned with educating your children.

The handbook for the parents will be designed to inform parents of their children's legal rights, of other parents' experiences with their children's educations, and of educational solutions that have worked for some BSF students. It will also give parents guidance on how best to advocate for their children. The handbook for the students will be designed to help them learn better how to advocate for themselves. The handbook for the teachers will be designed to educate them both on the nature of Barth syndrome and on how they can best teach and support a student who has Barth syndrome. Finally, the handbook for the school administrators will be designed not only to educate them on the nature of Barth syndrome but also to insure that they are aware of the laws under which children with Barth syndrome are protected.

My research began in the fall as I started following the listserv discussions and perusing the listserv archives for postings that are directly relevant to educational issues. I have been learning about the challenges you all face, and I have been taking notes on the creative solutions you have found that have helped the students through their challenges. Also, I have been educating myself further regarding federal laws that protect students with disabilities such as the Americans with Disabilities Act (ADA), Section 504 of The Rehabilitation Act of 1973, the Family Educational Rights and Privacy Act (FERPA), and the Individuals with Disabilities Education Act (IDEA) of 1997.

Recently, some BSF parents have agreed to help me in my research by filling out a survey I designed to help me gather more information about parents' experiences in their children's educations. Next, I hope to produce a similar questionnaire for the students themselves, so I can hear directly from them about their educational challenges and successes. If you are a BSF parent learning about this survey for the first time and you would like to participate in the survey, please contact me at ***jonrosenshine@yahoo.com***, and I will make sure that you are included in the research. Furthermore, if you have any ideas, questions, or feedback on my research and my project to write the handbooks, please feel free to contact me at the above e-mail address.

I feel honored by the Barth Syndrome Foundation for the trust they have put in me to take on this project. I hope very much that the handbooks will be of some use to you all when they are finished at the end of the summer of 2004. I very much look forward to communicating with students and families directly, and I am especially excited to meet more of the BSF community at the Orlando conference in July.

2004 International Conference

(Continued from cover)

about the disorder and approaches to clinical treatment for Barth syndrome. All Barth syndrome scientists, researchers, educators and Barth family members (including siblings and grandparents), and other interested individuals are invited to attend. This conference will provide a sharing and learning experience on Barth syndrome for all!

The Scientific and Medical Meetings

Dr. Richard I. Kelley, M.D., Ph.D. will be hosting the scientific/medical portion of this conference. All interested physicians and scientists are invited and encouraged to attend these meetings. The unanimous opinion of all paticipants at our last conference was that the mixture of scientific/medical and family meetings was very motivating. We will once again follow this format due to its huge success!

The scientific and medical meetings will include sessions on current and future Barth research on *G4.5* gene product expression, cardiolipin metabolism, development of models for various aspects of Barth syndrome, and future strategies for Barth scientific research. Also covered will be discussions of the clinical aspects of Barth syndrome, including the natural history of the disorder, pathology and functional abnormalities of the heart, neutrophils and skeletal muscles, disease models, clinical biochemistry, genetic findings, cognitive developments and educational insights.

Scientists, researchers and clinicians interested in the many facets of Barth syndrome will collectively share their most up-to-date information on Barth syndrome and further stimulate research. This format was highly successful for us in the 2002 Barth Syndrome Scientific Conference meetings.

The family meetings will consist of presentations on cardiology, neurology, hematology (neutropenia), nutrition, and day-to-day practical medical concerns. There will be discussions of psychosocial and educational issues pertaining to Barth syndrome consisting of sessions on coping day-to-day (tips from professionals and other parents), educational insights, how to advocate for your child, and how the entire family is affected (including siblings). Barth families will also have the opportunity to learn about the latest Barth syndrome research, as well as what they can do to facilitate the progress. Along with these sessions, individual clinics for those affected by Barth syndrome will be offered, which were also highly successful at our 2002 conference. New to this year's conference, BSF will be sponsoring a Sibling Workshop on July 10th, 9am – noon, for all Barth siblings ages 8 and up. This workshop will be conducted by Don Myers, Director of the Sibling Support Project.

The 2004 Barth Syndrome Scientific and Family International Conference will take place at Disney's Coronado Springs Resort in Lake Buena Vista, Florida on *July 8th- 12th, 2004*. Our special BSF room rates are $115.00 (plus tax) per night. Be sure to reserve a room at #407-939-1020 **ASAP**. A limited number of rooms have been reserved on a first call, first serve basis. Disney's Coronado Springs Resort is situated around a 15-acre shimmering lake, Lago Dorado. It offers vast walking nature trails, five themed pools with water slides, hot tubs, childrens' themed playgrounds, and most importantly it is wheelchair accessible. Free bus transportation to all Disney theme parks is readily available at the front entrance.

If you have any questions in regards to our upcoming conference, please do not hesitate to contact Anna Dunn, Vice President and Family Liaison, at ***adunn@barthsyndrome.org***. Please fill out the *BSF 2004 Conference Registration Form* **ASAP** directly from

(Continued on page 22)

our website at ***www.barthsyndrome.org*****,** and be sure to frequently revisit for all the latest information pertaining to this conference!

Important steps to take prior to the 2004 Conference:

1. Reserve your vacation time to come to Disney's Coronado Springs Resort for BSF's 2004 Scientific/ Family Conference.

2. Fill out the registration form located at BSF's website, ***www.barthsyndrome.org*****.**

3. Call the Coronado Springs Resort today at **407-939-1020** (from all locations) and reserve your room at $115.00 (plus tax) special rate. Mention that you are reserving rooms for the Barth Syndrome Scientific/Family Conference.

4. Barth families, ask your son's physicians to reserve their schedule in advance if they are interested in attending the scientific/medical portion of this conference.

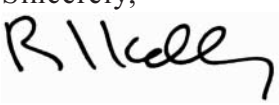
5. Barth families, be sure to register your Barth siblings 8 years of age and up for our Sibling Workshop on our website, ***www.barthsyndrome.org***.

We need you all to join and share your piece of the Barth syndrome puzzle so that we can move one step closer to a potential treatment, and ultimately one day a cure. I look forward to seeing you there. This upcoming conference is a golden opportunity to unite as "one family" and obtain the most up-to-date information on Barth syndrome from various distinguished scientists/ researchers/educators. Together let us visualize the hope for a better tomorrow for our Barth children, and future generations, so that one day, we can confidently say, ***"... no one will suffer or perish from Barth syndrome".***

Dear Colleagues,

On July 10 and 11, 2004, The Barth Syndrome Foundation, Inc. (BSF) will sponsor a meeting of medical professionals, scientists and families to review and discuss recent discoveries relating to Barth syndrome and to address important issues in the management of this complex disorder. It will be held at the Coronado Springs Resort in Orlando, Florida. The meetings will follow the same basic format as the Fall 2002 Barth Syndrome conference, with parallel meetings of scientists and families on Saturday and Sunday, as well as clinics for the children and families with a number of Barth syndrome specialists and researchers during the several days preceding the meetings. On Monday, clinical specialty groups will meet to work on the establishment of treatment guidelines. Although Barth syndrome has been known to geneticists and neurologists for almost 25 years, compared to other equally rare syndromes, still very little has been published on the spectrum of problems in Barth syndrome and, in particular, on practical aspects of the day-to-day care of patients with the disorder. We hope that this meeting will provide a forum for the exchange of such practical information, for the many important "tips of the trade" that never seem to find their way into the pages of medical journals. In addition, with further exciting discoveries about the abnormalities in phospholipid metabolism in Barth syndrome, we are bringing together what we hope will be the critical mass of scientific expertise needed to launch the next generation of Barth syndrome research, to bring us ultimately to a definitive treatment for this disease.We hope that many practitioners and research scientists alike will participate in this valuable opportunity to both learn and to teach. Please check the BSF website at ***www.barthsyndrome.org*** for further details (soon), or call one of us directly if you have any questions. We hope to see you there.

Sincerely,



Richard I. Kelley. M.D., Ph.D.
Professor of Pediatrics
Johns Hopkins University
Director, Division of Metabolism
Kennedy Krieger Institute
(443) 923-2782

Valerie (Shelley) Bowen
President
The Barth Syndrome Foundation, Inc.
(800) 223-1128

Articles Relevant to Barth Syndrome Published in Professional Journals Since Last Newsletter

Esposti MD. **The mitochondrial battlefield and membrane lipids during cell death signalling.** Ital J Biochem 2003; 52(1):43-50.

Bateman C. **Little known killer: Barth syndrome.** S Afr Med J 2003 April; 93(4):249-50.

Stein SM, Dale DC. **Molecular basis and therapy of disorders associated with chronic neutropenia.** Curr Allergy Asthma Rep. 2003 Sept; 3(5):385-8.

Esposti MD, Cristea IM, Gaskell SJ, Nakao Y, Dive C. **Proapoptotic Bid binds to monolyso-cardiolipin, a new molecular connection between mitochondrial membranes and cell death.** Cell Death and Differentiation 2003; 10:1300-9.

Vaz FM, Houtkooper RH, Valianpour F, Barth PG, Wanders RJ. **Only one splice variant of the human TAZ gene encodes a functional protein with a role in cardiolipin metabolism.** J Biol Chem 2003 Oct 31; 278(44):43089-94. Epub 2003 Aug 20.

Schlame M, Kelley RI, Feigenbaum A, Towbin JA, Heerdt PM, Schieble T, Wanders RJA, DiMauro S, Blanck TJJ. **Phospholipid abnormalities in children with Barth syndrome.** J Amer Coll Card 2003 Dec 3; 42(11):1994-9.

Versluys B, Bowen VM, McCurdy K, Mann S, Cantlay A, Newbury-Ecob R, Kern I, Goulden N, Steward C. **X-linked organic aciduria: an important cause of severe chronic and cyclic neutropenia in males.** ASH abstract of poster session 77-1. Dec 2003.

Xu Y, Kelley RI, Blanck TJ, Schlame M. **Remodeling of cardiolipin by phospholipid transacylation.** J Biol Chem 2003 Dec 19; 278(51):51380-5. Epub 2003 Oct 9.

DiMarco JP. **Implantable Cardioverter-Defibrillators.** Review Article. N Engl J Med 2003 Nov 6; 349:1836-47.

Rugolotto S, Prioli MD, Toniolo D, Pellegrino P, Catuogno S, Burlina AB. **Long-term treatment of Barth syndrome with pantothenic acid: a retrospective study.** Mol Genet Metab 2003 Dec; 80(4):408-11.

Maianski NA, Maianski NA, Kuijpers TW, Roos D. **Apoptosis of neutrophils.** Acta Haematol 2004; 111(1-2):56-66.

Gu Z, Valianpour F, Chen S, Vaz FM, Hakkaart GA, Wanders RJA, and Greenberg ML. **Aberrant cardiolipin metabolism in the yeast taz1 mutant: a model for Barth syndrome.** Mol Microbiol 2004; 55:149-58.

Maianski NA, Geissler J, Srinivasula SM, Alnemri ES, Roos D, Kuijpers TW. **Functional characterization of mitochondrial in neutrophils: a role restricted to apoptosis.** Cell Death Differ 2004 Feb; 11(2):143-53.

Kuijpers TW, Maianski NA, Tool AT, Becker K, Plecko B, Valianpour F, Wanders RJ, Pereira R, Van Hove J, Verhoeven AJ, Roos D, Baas F, Barth PG. **Neutrophils in Barth syndrome (BTHS) avidly bind Annexin-V in the absence of apoptosis.** Blood 2004 Feb 5. Epub ahead of print.

Presentations Given About Barth Syndrome by Scientists and Medical Professionals in 2003

- Miriam L. Greenberg, Ph.D.; "Aberrant Cardiolipin Metabolism in the Yeast *taz1* mutant: A Model for Barth Syndrome"; 6th Yeast Lipids Meeting; Colmar, France; May 2003.
- Colin Steward, M.R.C.P., Ph.D., F.R.C.P.C.H.; "Development of a UK Diagnostic Service for Barth Syndrome"; Clinical Molecular Genetics Society Spring Meeting 2003; May 2003.
- Miriam L. Greenberg, Ph.D.; "The Role of Cardiolipin in Mitochondrial Function: Implications for Barth Syndrome"; Gordon Research Conference on Molecular and Cellular Biology of Lipids; July 2003.
- Iris L. Gonzalez, Ph.D.; [her preliminary Barth research results]; A.I. DuPont Hospital for Children Genetics Symposium; September 2003.
- Tyler Reimschisel, M.D.; "Neurological Manifestations of Barth Syndrome"; International Congress on Inborn Errors of Metabolism; Brisbane, Australia; September 2003.
- Grant Hatch, Ph.D.; "Barth Syndrome: a Childhood Disease of Phospholipid Remodeling?"; Children's Hospital Oakland Research Institute Research Seminar; Oakland, CA; September 2003.
- Miriam L. Greenberg, Ph.D.; [seminar on her work on Barth syndrome]; Bratislava; September 2003.
- Grant Hatch, Ph.D.; "Regulation of Cardiolipin Metabolism in Barth Syndrome"; 28th Annual Canadian Lipoprotein Conference; Muskoka, Ontario; October 2003.
- Michael Schlame, M.D.; "The role of cardiolipin in mitochondria"; Department of Biochemistry and Molecular Biology, University of Bari [lecture series entitled "Conversations on Biochemistry"]; Bari, Italy, March 2003.
- Michael Schlame, M.D.; "The role of cardiolipin in mitochondria"; Department of Biochemistry, University of Rome; Rome, Italy, March 2003.

WWW.BARTHSYNDROME.ORG

To read more about previous presentations given on Barth syndrome, visit:
http://www.barthsyndrome.org/new/conference_presentations_MD.html

Dr. Richard I. Kelley Receives "Art of Listening Award" From Genetic Alliance

By Valerie ("Shelley") Bowen, President

Richard I. Kelley, M.D., Ph.D.

In April of 2003 the Genetic Alliance (GA) announced awards that were to be given at their 2003 annual conference. The ***"Art of Listening Award"*** celebrates a health care professional who takes the time to listen and understand, thereby profoundly easing the difficult, often frustrating journey faced by individuals and families dealing with the uncertainties and ambiguities of a genetic condition.

The GA received several letters in recommendation of Dr. Richard Kelley, M.D., Ph.D. - Director, Div. of Metabolism, Kennedy Krieger Institute (KKI); Professor., Dept. of Pediatrics, Johns Hopkins University; and Chairman, BSF Scientific & Medical Advisory Board (SMAB), for his outstanding contributions to BSF and our families. In July, we learned that Dr. Kelley would in fact be the recipient of this prestigious award. I began to research this quiet man who seems to never sleep, and in this process my respect for his work and the man himself deepened. I contacted Hugo Moser, M.D., Dir. of the Neurogenetics Dept. at KKI who said to me "... *He works in the clinic near Lancaster, PA every week. There is a large population of Amish children who have maple syrup urine disease in this region. This is one of the most difficult disorders to manage in medicine. However, through Dr. Kelley's work and the process of educating these families this population has the lowest percentage of individuals requiring hospitalization. This is truly because of Dr. Kelley's commitment to educating the families about this disorder. He is a remarkable man. It is his goal to educate those around him in the process of caring for his patients. Two nights a week he does not have a bed when he is in Baltimore; he lives in his lab and takes short naps to sustain himself. I don't know when he sleeps. I don't know what drives him or how he does what he does. What I can say is they don't make them like him anymore.*"

While we at BSF know Dr. Kelley's merit and contributions to our group, it was an honor to see him receive this award in the presence of other lay leaders who represent various disorders from around the world. Throughout the evening individuals approached Dr. Kelley and introduced themselves. "*Dr. Kelley, I don't know if you remember me but when my child was diagnosed I called you about his condition and you took the time to speak with me about this*." As the President of BSF and the parent of a child with Barth syndrome, I am well aware of how much Dr. Kelley has meant to my family and our extended BSF families. It was incredible to see how many other lives he has touched beyond BSF by simply offering an ear and a curious mind.

During Dr. Kelley's brief speech he spoke about how much a physician can learn from listening to parents. He spoke about his work with the Clinic for Special Children, a clinic which serves Old Order Amish, Mennonite, and other families with children who suffer from genetic diseases such as glutaric aciduria (GA1), maple syrup urine disease (MSUD), Crigler-Najjar syndrome (CNS), and medium-chain acyl-CoA dehydrogenase deficiency (MCADD). It is a non-profit clinic started by Dr. Kelley and his partner D. Holmes Morton, MD. Dr. Kelley stated:

"*The Amish are often misunderstood people. They are quiet and unassuming. When I began my work with the Amish I learned about the importance of the Amish Bible. In the Bible a record was made of each child who was born with maple syrup urine disease but not as the disorder. The entry would read `Special Child'. These Bibles were full of Special Children. That is how we came to name the clinic. I would say to you tonight that each of you has a Special Child*."

The same could be said about Dr. Kelley ... he is a quiet and unassuming man. He *is* a "Special Doctor". We all know how rare Dr. Kelley is in the world of science and medicine. Many of us have gone years without the ability to speak to a physician about questions, concerns or recommendations of the next step to take. As an active member of the Genetic Alliance, I am frequently reminded how very fortunate we are to have such a gracious man to lead BSF's SMAB and assist our families in time of need. We are blessed to have the talents of Dr. Kelley, who is most deserving of this award. On behalf of BSF, we thank you for all you do!

BSF Collaborates at Genetic Alliance Conference, Washington D.C.

By Valerie ("Shelley") Bowen, President, BSF

Shelley Bowen, Kate McCurdy, and Dr. Richard I. Kelley

Kate McCurdy and I were proud to represent BSF not only as attendees but also as speakers at the Genetic Alliance's (GA) annual conference in August of 2003. I served on the conference committee for the group and had the pleasure of getting to know many lay leaders of advocacy groups in the process. It was an honor to be a part of such an undertaking. Steve Groft, Director of the Office of Rare Diseases, a division of the National Institute of Health, recommended that Kate McCurdy be afforded the opportunity to speak on the topic of Conference Planning, a presentation which focused on the importance of providing sound science at these conferences and using the conference as a vehicle to foster collaborative research through and amongst scientists and physicians. Practical tips, resources and sharing of personal experiences and advice were offered to guide participants to identify realistic goals, recruit presenters and attendees and produce a meeting that meets the needs of all involved. Kate's presentation was informative and invaluable to those in attendance.

Currently there are 7,000 rare disorders, for which only 1,000 of these rare disorders have focus groups representing their cause. For some time now I have realized a common theme among leaders of lay advocacy groups. "*Our disorder is under-diagnosed. We need accelerated research to better understand the complexities of our disorder*." Sound familiar? Nearly two years ago I shared a concern with Genetic Alliance that there were many groups such as ours that only represent few affected members. I felt it was imperative to demonstrate a collective concern about common needs and to demonstrate how many people are actually affected/impacted by various rare/genetic disorders. I put a plan together for what is now known as the *Human Helix on the Mall* - the gathering of as many affected individuals — those directly affected by genetic conditions, their communities, health professionals, researchers, policy-makers and educators — to create a *Human Helix on the Mall* in Washington D.C. I felt the collective voice of many would resonate a common theme ... that we need continued funding for genetic research, targeted treatments and accurate diagnosis.

The"*Human Helix*" idea was unveiled at the GA meeting with profound enthusiasm. In fact there were leaders from the genetic community from Canada, Germany and Australia who wanted to take this idea home and do this internationally. On Saturday night after Dr. Kelley received the *Art of Listening Award,* Dr. Francis Collins got up on the platform and sang a song, "This is a Song for All the Good People", a celebration of our common thread, DNA. During the song tables began to rise holding hands and before we knew it the entire room was standing holding hands, demonstrating their commitment to this project. It was an amazing site to see. I was humbled to think that this project could have such an impact. The proposed date for this event will be in the Spring of 2006. I will continue to keep you all posted on the development. I think the quote of the weekend had to be delivered by Dr. Eric Lander of The Whitehead Institute, "*The sum of all rare disorders is common*."

Kate and I learned a great deal. As a part of small discussion groups with Dr. Francis Collins and other highly esteemed leaders in research, we were able to discuss our concerns about Barth syndrome and how best to propel a better understanding about the disorder we represent. At the final ceremony we were humbled by Penny Kyler, a Public Health Analyst of the Genetic Services Branch of Maternal and Child Health Bureau, Health Resources and Services Administration, when she publicly acknowledged BSF as an exceptional group.

Barth Syndrome Foundation's 2003 Financial Report

By Steve McCurdy, BSF Chief Financial Officer

The year 2003 was a terrific year for your foundation, and this financial report reflects that success. Following this report are a summary Statement of our Revenue and Expenditures and a Balance Sheet for The Barth Syndrome Foundation, Inc. for the fiscal year ending December 31, 2003. Our financial statements are audited by Buckley, Sitzman and Nielsen, CPAs in Lincoln, NE, and we submit them to the IRS and the 10 states in which we are registered. They are also available on our website (***www.barthsyndrome.org***) and through such US organizations as Guidestar.org – a major source of information on charities in the United States.

No matter how you look at it, 2003 was a record year.

- We raised more money, than ever before, $729,530, including our largest single donation to date of $500,000!
- We committed almost $150,000 to five multi-year research grants awarded in 2003, with $77,715 spent in 2003 and the remainder due in 2004. Elsewhere in this newsletter you will see that we have committed an additional $175,000 to research in the second round of research grants awarded in 2004.
- We spent $52,884 on other programs including education and awareness. In addition to maintaining our website and publishing our newsletter, brochures and other materials, we sent BSF representatives to six scientific and medical conferences which also required that we purchase our own professional Barth Syndrome Foundation display board. This will serve us well in use at many conferences to come.
- We spent an additional $27,083 on general and administrative expenses ranging from insurance to printing and postage, dues for organizations like the Genetic Alliance and travel for our annual planning conference (Steinhatchee) for our lead volunteers.
- And we finished the year with net assets of over $943,478!

Charity watchdogs, including many of the states in which we are registered and groups like Guidestar.org, rate orgaizations on their efficiency in fund raising and the % of their expenses that go toward programs vs. administration and fund raising. In each of these categories we receive very high ratings: less than .5% of every dollar we raise goes to fund raising and more than 81% of our expenses go toward our programs. The primary reason for our success in each of these areas is that we are an all-volunteer organization. BSF has no paid employees. All of the members of our Board and all of our volunteers (both family members and professionals) who dedicate many hours each week to our cause are compensated only in their, and our, hearts.

At the end of 2003, your Board accepted, with reluctance, the resignation of our Treasurer, Mike Wilkins. Mike has been responsible for setting up and maintaining our financial records and has led us through two clean audits. However, as our operations and finances have grown, Mike felt that it was best to bring in some professional assistance. So as of February 1st, we have hired Leonard Steinberg, a Certified Management Consultant and a specialist in non-profits and small business, to serve as our bookkeeper and advisor. Leonard has served as controller and CFO for several non-profits, teaches accounting and has consulted with BSF on the structuring of our financial record keeping initially. We are looking forward to working with Leonard and gaining the benefit of his experience, and we offer our sincere thanks to Mike Wilkins for his dedication and excellent work. If you ever get tired of being a Doc, Mike, you can always get a job as a Treasurer!

In 2004, we can expect to accelerate many of our programs still further. We will attend more scientific and medical conferences, increasing awareness about Barth syndrome within these communities. We are working with several other groups in the Genetic Alliance to establish a Blood and Tissue Bank that will be an invaluable aid to researchers. We have commissioned the creation of an educational handbook specifically designed to assist parents and educators with the special educational needs of their affected children, and we will be holding the 2nd International BSF Scientific and Family Conference from

(Continued on page 28)

BSF's 2003 Financial Report

(Continued from page 27)

July 8th-12th, 2004, at Disney's Coronado Springs Resort in Lake Buena Vista, Florida. This conference is expected to include a series of clinics specifically designed for our Barth kids, and should be an invaluable benefit to all those families who can attend.

As BSF continues to grow, seeking even more ways to help our families by increasing awareness, stimulating research and assisting the physicians caring for our children, our programs become more varied and in some cases more complex. We are committed to maintaining the same dedication to professionalism, good judgment and care for those affected by Barth syndrome as we have from our beginning. We will continue to be good stewards of our assets, both financial and volunteer. Our principle constraints to growth continue to be the number of hours that our dedicated group of volunteers – family members, scientists and physicians - can contribute. We have been very fortunate that our volunteer base continues to grow as we find more ways to reach out to find and assist affected families. As the father of a young man who continues to struggle with Barth syndrome, I am eternally grateful to all of you who stand with us and I am increasingly optimistic that life will improve because of your dedication and support.

Barth Syndrome Foundation, Inc.
Statement of Financial Position
as of December 31

	2003	2002
Assets		
Current Assets	$ 942,028	$ 385,522
Other Assets	$ 1,450	$ 29, 597
Total Assets	**$ 943,478**	**$ 415,119**
Total Liabilities	**$ 22,600**	**$ 76,899**
Net Assets		
Unrestricted	$ 903,878	$ 312,182
Temporarily Restricted	$ 17,000	$ 29,038
Total Net Assets	**$ 920,878**	**$ 341,220**
Total Liabilities and Net Assets	**$ 943,478**	**$ 418,119**

Barth Syndrome Foundation, Inc.
Statement of Activities
For the Year Ended December 31

	2003	2002
Support and Revenue		
Contributions	$ 729,530	$ 328,344
Other	$ 11,157	$ 3,682
Total Support and Revenue	**$ 740,687**	**$ 332,026**
Expenses		
Program Services	$ 130,600	$ 111,808
Management & General	$ 27,083	$ 14,331
Fund Raising	$ 3,346	$ 6,571
Total Expenses	**$ 161,029**	**$ 132,710**
Change in Net Assets	$ 579,658	$ 199,316
Net Assets, Beginning of Period	$ 341,220	$ 141,904
Net Assets, End of Period	**$ 920,878**	**$ 341,220**

A Milestone Year For BSF Development

By Steve McCurdy, CFO and Vice President, Finance and Development

The best measures of BSF's progress toward our Vision are those that mark increasing awareness within the medical community, deepening understanding of the causes of Barth syndrome and more rapid progress toward development of effective treatments and a cure, and most of all, clear improvements in the quality of our childrens' daily lives and a future full of hope and opportunity for all of them. BSF registered progress

(Continued from page 28)

(with a long way still to go) in every category in 2003 including fund raising – which along with a growing cadre of dedicated volunteers provides a critical resource to accelerate our progress in the future. There are two stories here:

- Our incredible good fortune in raising almost $730,000 in more than 630 individual contributions in 2004
- Supporting the fund raising efforts of three men entered in the 2004 Wisconsin Ironman Race who will be raising money for BSF around the world

First, our eternal thanks to all of the volunteers who led fund raising events in 2004 and the growing list of contributors who supported them. Our contributors are thanked by name on the inside of the back cover of this newsletter. You have all made more of a difference than you may realize! The efforts of our volunteers are noted in Shelley's list of 2004 Accomplishments elsewhere in this newsletter, but bear repeating here:

- The Wilkins and McCurdys who continue to bring their friends and families into the Barth circle with annual letters and updates, and raised over $78,000 in 2003 in the most efficient way possible for BSF.
- Gary Rodbell and John Steigerwald, BSF's own Ironmen, raced in the 2002 Florida Ironman Triathlon and were still collecting money in early 2003. Joined by Tim Monetti, they will be racing for BSF again in 2004 in Wisconsin.
- Paul and Allene Russell, Will McCurdy's grandparents, have made a special donation to fund development of the "Barth Educational Handbooks Project" to be written by Jon Rosenshine. This should be an invaluable guide for all those assisting boys with Barth syndrome from grades K-12.
- Bill Fagan and the "Friends of the Baffa Family" who put on a magnificent evening of dinner, auctions and dancing to honor the Baffa family and raise funds and awareness for BSF.
- Jan and Steve Kugelmann and the many sponsors and golfers who made the 2nd Annual Barth Syndrome Golf Tournament in Merritt Island, Florida a great success and an event to look forward to for the pros and the duffers!
- The four families who lost loved ones in 2003 and asked that in lieu of flowers, their friends make donations to BSF. We gratefully acknowledge the Rosiek, Lochner, Monahan and Towles families. Our thoughts and thanks are with you.
- David and Shelia Mann and the Thunderbirds in Chattanooga, TN who have raised money for BSF at their car rally for the second year.
- The Dussich Dance Studio in Florida who dedicated their performance to R.J Kugelman and BSF, and the youth group at St. John's Church in Larchmont, NY who raised money for BSF by washing cars… in the rain!
- The many companies that generously match their employee's charitable gifts, and the employees who remembered to include their matching forms in their gifts to BSF.
- The growing list of contributors to the upcoming BSF International Scientific and Family Conference scheduled for July, 2004.

The Barth Syndrome Foundation would like to make a special acknowledgment of the generosity of three foundations that have created a special place in their funding plans for BSF. The Lebensfeld Foundation in Exchange Place, New Jersey, the Lied Foundation Trust in Las Vegas, Nevada, and our Anonymous Benefactor have all made significant contributions to BSF in 2003. Their contributions, along with those mentioned above have insured that BSF is able to sustain a strong, credible and growing research grant program, and to expand our programs to develop improved treatment for those affected and informational support to their families. Although our Anonymous Benefactor prefers to remain just that, everyone should appreciate the sustained support that this foundation has offered BSF from our earliest days. They were "there for us" early, when it meant so much, and they are still "there for us" today as we begin to make real progress toward our Vision.

As the parent of a young man with Barth syndrome, I am so grateful to all of our generous contributors and volunteers. You are enabling us all to move forward with increased confidence to a future where no one need suffer from the debilitating effects of Barth syndrome.

Thank You! Please keep us foremost in your plans for 2004!

Janus Charity Challenge

IRONMAN NORTH AMERICA

BSF ANNOUNCES ...WITH GREAT EXCITEMENT ...

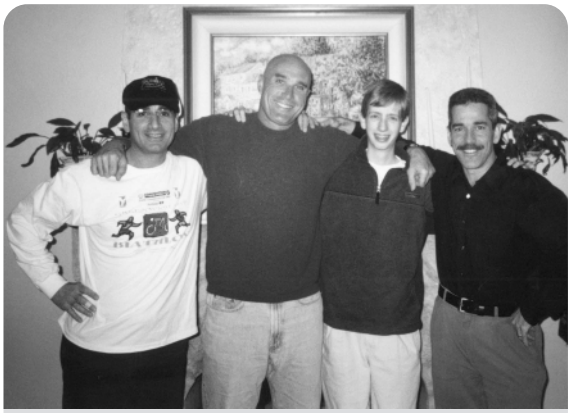
THE RETURN OF OUR IRONMEN!

Gary Rodbell and John Steigerwald are now joined by Tim Monetti, and will be racing in the Wisconsin Ironman Triathlon on September 12, 2004, and participating in the Janus Charity Challenge on behalf of The Barth Syndrome Foundation and Barth families around the world to raise money for our programs!

Many of you may remember that incredibly long day on October 9, 2002 when Gary and John swam 2.4 miles, then biked a 112 mile race, and finally ran a 26.2 mile marathon. They finished in just over 16 and 14 hours respectively, and raised over $79,000 for BSF. BSF families followed their progress on-line as Will McCurdy and Michael Bowen paced them through the course (from inside a warm dry car driven by their Dads) and radioed back to Shelley who kept our global community informed.

Well obviously, these Ironmen have not had enough. Their goal is to raise as close to $200,000 as they can get before their race in September. And the BSF community is stepping up to help them. If they succeed in raising the most of any team in the race, Janus Capital will contribute an additional $10,000 to BSF! We will be reporting Gary, John and Tim's progress on-line again from Madison, Wisconsin on September 12th.

We are asking every family around the world to help out!!



From L-R: Gary Rodbell, John Steigerwald, Will McCurdy and Tim Monetti

In support of BSF, Gary, John and Tim, BSF's Ironmen, will be competing in the 2004 Wisconsin Ironman Triathlon.

Let's all join in and support these guys!!

For those who already have fund raising efforts planned, please consider designating the funds you raise to be included in the Janus Charity Challenge. Your efforts can help these guys reach their goal and yours as well. If you have not yet given any thought to fund raising for BSF, **PLEASE DO SO NOW!** This is a golden opportunity to build on a major athletic event and to help BSF and all those affected by Barth syndrome.

It takes enormous dedication, training and sacrifice to prepare for and complete a Triathlon. Life for many of our boys must often seem like a Triathlon every day. Gary, John and Tim are unusual guys, but their struggle to get through each day of training offers them a unique perspective on our Barth boys who struggle to get through each day of their lives. Gary put it simply and eloquently when he wrote of his friend Will – *"He understands what it means to not give up. To keep going no matter how tired and lousy you feel. And so I am training and running this race for him."* Help Gary, John and Tim to achieve their goal. To learn more about how you can help, please contact Steve McCurdy at ***smccurdy@barthsyndrome.org***.

The Barth Syndrome Foundation, Inc. (BSF) appreciates your contribution. Your gift helps us continue our programs designed to increase awareness, support and educate families and physicians, and fund research. Please visit our website at *www.barthsyndrome.org* for more information. All gifts are tax-deductible to the fullest extent permitted by the law. The official registration and financial information of BSF may be obtained from the Pennsylvania Dept. of State by calling toll-free, within PA, 1-800-732-0999. Registration does not imply endorsement. BSF's Florida registration number is SC-12347. One Hundred percent of your contribution will be received by BSF. Please forward all contributions to: The Barth Syndrome Foundation, Inc., P.O. 618, Larchmont, New York 10538

BSF Affiliate Officially Established in the UK

By Michaela Damin, Chairperson, BSF - UK

Michaela Damin, Chairperson
Barth Syndrome Trust
UK and Europe

The past year has been a busy one for us and 2004 promises to be even busier! On November 21, 2003, the Barth Syndrome Trust gained official charity status in the UK. This is the equivalent of a non-profit status in the US.

As a mother of two young boys, one of whom has Barth syndrome, my days are pretty full! People often say I need more hours in the day; my standard response has become that I need more hours in the night! When everyone has gone to bed, I can sit down and immerse myself in this incredibly rewarding work.

As a family, we count ourselves incredibly lucky to have a diagnosis for our son, to have medical specialists and educators dedicated to helping him. But what about those families out there who have yet to be diagnosed? What of the families who need help with specific regional issues such as education and healthcare? What of the families who need to be able to pick up the phone and chat to another person nearby? If we, as an organisation, can help in the quest to raise awareness about Barth syndrome, this will lead to more accurate and timely diagnoses and intervention. As we find new families, we can provide a friendly shoulder to lean on when times get tough. But it does not end there… we need to help direct those families to accurate and reliable information, we need to give them some extra tools to care for their boys. So what are we doing in 2004? These are some of the things we are working on:

Family Support:
Families in the UK and other European countries will often find that their medical system operates entirely differently than that in the States. The educational system and the social or state services operate differently from country to country. We will direct families to appropriate centres of help locally.

In the UK, we are very pleased to announce that the first multi-disciplinary clinic will soon be up and running for individuals with Barth syndrome. This is being organised in Bristol by Dr. Colin Steward, amongst others, and those attending will have the opportunity to be seen by a variety of skilled experts ranging from haematology to cardiology to genetics, etc. These clinics will be run once a year and it will be an ideal opportunity to have access to a wide range of specialists "under one roof" so to speak. It will also be a chance for the families and the boys themselves to meet each other at least once a year.

Awareness:
We will be working on increasing awareness amongst doctors and scientists in the UK and Europe. We will network with major hospitals and other groups such as umbrella organisations for rare disorders, genetic interest groups, etc. We have created our website (***www.barthsyndrome.org.uk***) and we will continue to update it regularly.

(Continued on page 32)

BARTH SYNDROME TRUST
UNITED KINGDOM & EUROPE

Barth Syndrome Trust

Registered Charity Number 1100835
(An Affiliate of The Barth Syndrome Foundation, Inc.)

Mrs. Michaela Damin – Chairperson
1 The Vikings
Hampshire
S051 5RG
United Kingdom
Telephone: +44 (0)1794 518785
E-mail: ***mdamin@barthsyndrome.org***
Website: ***www.barthsyndrome.org.uk***

(Continued from page 31)

Fundraising:

Last year we organised several fundraising events such as jumble sales, a coffee morning, raffles, etc. Now that we have our charity number and can receive tax efficient donations, we have some more plans for fundraising:

In March 2004, several volunteers from Disney throughout UK and Europe will be running the Rome Marathon and raising funds for the Barth Syndrome Trust. This effort is being spearheaded by Isabelle Lemettre and we are very grateful to her and her colleagues.

In June 2004, our Treasurer, Jerome Bigara has entered for a half marathon in his local town and we will be (walking!) alongside him with our boys.We have many other plans for the upcoming year and we are hoping to have some fun whilst raising money for our favourite cause. Even my neighbours regularly hoard all their unwanted Christmas and birthday presents for me to sell at an event – we now have 2 outside sheds to store all the stuff! It seems that I have managed to drag everyone I know into doing something for us! And everyone has been so wonderful in coming forward to help in any way they can – thank you all!

Above all, whilst we are committed to provide an efficient and professional service to all our families and all the doctors and scientists involved, I am always reminded of the fact that I too know what it's like to find out that my child has Barth syndrome. I know how alone and worried I sometimes feel. I know what it is like to have a child with a disorder that very few of my friends really understand, one that I hardly understand myself at the best of times. But I also know that having the support of other families and caring doctors has helped us during the most difficult of times. And, knowing that we are all doing something to help, however small it may be, brings great hope for the future.

Lastly, I would like to thank our trustees, our doctors, all the board members of BSF and all the individuals who have donated so generously of their time, expertise and money – we could not do this without your help!

An Update From The Barth Syndrome Foundation of Canada

Catharine Lynn Ritter, President, BSF Canada

L-R: Karen Gordon, Christine Hope, Lynn Elwood, Michaela Damin (UK), and Cathy Ritter

Increasing awareness was on the agenda when Karen Gordon and Chris Hope attended the SADS (Sudden Arrhythmia Death Syndrome) conference in Toronto this past fall.

Plans are currently underway to further increase awareness as members of the board of BSF Canada plan to attend three additional conferences between Toronto and Ottawa in the upcoming year.

It's official! We have received the Letters Patent making Barth Syndrome of Canada, Inc. official, and the not-for-profit charity status won't be far behind!

It has been a busy time for the Barth Syndrome Foundation of Canada, with a great deal of time and effort being spent toward pursuing our incorporation and not-for profit status. With these issues resolved, we will now be able to forge full steam ahead in promoting awareness of this disorder as well as supporting Canadian families.

Our members have been busy working with the international group on many fronts and as such attended two workshops in Steinhatchee, Florida. Family support, awareness, fund-raising, and the upcoming conference at Disney's Coronado Springs Resort in Florida have been the areas of focus. Plans for both the medical and family components of the conference are well underway and it promises to be an informative and empowering occasion. I strongly urge everyone to register and attend this event if at all possible.

As a result of a brain storming session at the last workshop, BSF Canada held its first fundraising effort this past December with the selling of poinsettias. It was a huge success as we almost doubled our initial goal of selling 100 plants. My living room became a sea of flowers as box after box was delivered! I cannot describe the emotion that I felt as I saw 'Barth Syndrome Foundation of Canada" printed on the boxes. Not only did this event prove to be a successful fundraiser, but it also increased awareness of Barth syndrome among many people of our community.

As awareness increases, it will be even more important to support those families attempting to find a diagnosis as well as those who become part of our organization. The upcoming year promises to be another busy one as we all work toward our Vision that ***"... not one more person shall perish from Barth syndrome".***

Cathy Ritter and her aunt Audrey Hintze organize fundraiser for BSF Canada

Awareness Program Takes to the Road

Stephen Kugelmann, Vice President, Awareness

L-R: David and Shelia Mann join Steve Kugelmann,VP of Awareness, to represent BSF at the American Academy of Pediatrics in New Orleans, LA

First and foremost, I am humbled by the BSF Board's invitation to become a Board member responsible for the awareness campaign. It has been a year now since we aggressively started the awareness drive to the physicians, researchers, clinicians, specialists and nursing staff. And what a spectacular year it has been!

Late in 2002, the BSF board approved a plan to purchase a "trade show" style exhibit with banners depicting the common symptoms of Barth syndrome. The banners included pictures of some of the boys and put a personal appeal to the display. Brochures were printed describing the clinical aspects of the disease in detail and extra newsletters were printed for distribution. Reservations were made to attend several conferences throughout the year.

Our first conference was the Children's Hospital of Philadelphia (CHOP) 6th Annual Cardiology Symposium at Walt Disney World in Orlando, Florida. With over 400 physicians and staff present the exhibit was very busy. Over 100 packages of our literature were distributed in the 3 days of the exhibit. Less than 5% of those visiting the booth had ever heard of Barth syndrome. We knew this was going to be an uphill battle.

The next conference that we attended was the SADS (Sudden Arrhythmia Death Syndrome) conferences in Toronto, Canada, and Atlanta, Georgia. With the growing concern that this disorder may be linked to the *possibility* of serious arrhythmias, this conference seemed like the perfect place to be. Both of these conferences had a concentrated group of cardiologists, electrophysiologists and staff. Once again, most had never heard of Barth syndrome.

The SADS conference was followed by three back-to-back conferences where we had purchased or were granted non-profit booth space. First we attended the American Academy of Pediatrics in New Orleans, La., then the American Heart Association in Orlando, Fl., followed by the American Society of Hematology in San Diego, Ca. The logistics of attending these conferences was very challenging. However, at each and every one, we made contact with a physician that thought they were caring or have cared for a child with Barth syndrome. That is priceless information.

In addition to the aforementioned conferences, several presentations were delivered to the medical community by our BSF family members, as well as presentations to local community groups and schools. BSF literature was on display at the International Congress of Inborn Errors of Metabolism in Australia and the American Society of Human Genetics in Los Angeles, Ca. BSF was recognized by the media in an article which appeared in the June 2003 issue of the Reader's Digest entitled, "*Saving Michael Bowen*". Furthermore, we had fundraising events that raised much needed money and awareness, simultaneously.

Shelley Bowen poses with son Michael and daughter Alanna during an interview with Reader's Digest.
"Saving Michael Bowen", their intimate journey with
Barth syndrome was distributed to 95 million readers worldwide.

The combined efforts of our volunteer base this past year resulted in nine new Barth syndrome cases either being diagnosed or joining our extended family. "*Saving lives through education, advances in treatment and pursuit of a cure for Barth syndrome*" ... a common goal we all share. Awareness is key to meeting this goal. If you are interested in assisting the BSF Awareness Committee in any capacity, feel free to contact me directly at ***skugelmann@barthsyndrome.org*****.** Your support is needed, whether it is on a local or an international level. I look forward to the day when one can walk into the office of a pediatrician, cardiologist, hematologist or neurologist and not have to bring the Barth Syndrome Resource Notebook. We are making progress!

Heat Strokes in Florida Raise Funds for BSF

By Jan Kugelmann
Committee Chair, Grassroots Fundraising

On Labor Day weekend 130 of our friends and family braved the hot Florida sun and played 18 holes of golf at the Savannahs Golf Course in Merritt Island. This was the 2nd Barth Syndrome Golf Tournament that was successfully executed in the peak of hurricane season! Many of the players were return golfers from the first tournament and have stated that their Labor Day weekend will be planned around the annual Barth Syndrome Golf Tournament. This event surpassed last year's proceeds and raised over $20,000 for BSF in cash, prizes and donations.

The combination of community support and friendship are ever present throughout the duration of the event. Family and friends passionate about R.J. and eager to support the Barth Syndrome Foundation come together to solicit donations and raise money for our cause.

Forty-five companies and individuals paid to have their name advertised along the course by sponsoring a hole. Hole sponsorships were $100 for a Par and $250 for a Birdie. $500 bought an Eagle sponsor and eight companies generously supported our effort. Those companies included Lockheed Martin, Mike Erdman Motors, EDG & Associates, Inc., Premium Assignment Corporation, Jones, Edmunds & Associates, United Space Alliance, Perini Building Company and Merritt Island Printing Company.

(Left to Right): BSF dads Michael Bowen and Mike Wilkins join supporters Charlene and Lowell Walker as they get ready to T-off in support of the 2nd Barth Syndrome Golf Tournament.

Approximately 82 local businesses and individuals donated items for auction and prizes including free rounds of golf, Oakley sunglasses, tickets to Universal Studios, passes to Kennedy Space Center and a champagne party for 50 in the VIP room aboard the Sterling Casino cruise ship out of Port Canaveral.

Even in tough economic times contributions were greater than expected. Kugelmann family members traveled from Atlanta, Georgia to participate and Mike Wilkins, fellow BSF family member from Lincoln, Nebraska risked missing the Nebraska Cornhuskers game to join in the fun. The sunburned and tired golfers, along with the volunteers concluded the day at the 19th hole, a.k.a. The Kings Duck Inn where prizes were awarded. A well-earned lunch was served and strokes were forgotten!

BSF'S Calendar of Events for the Rest of 2004

BSF's 2004
International Scientific/Medical and Family Conference
July 8-12, 2004

Wed., July 7: New Family Orientation - PM

Thurs., July 8: Barth Syndrome Clinics

Fri., July 9: Barth Syndrome Clinics
Registration for All - PM

Sat., July 10: Family Sessions
Scientific/Medical Sessions

Sun., July 11: Family Sessions
Scientific/Medical Sessions

Mon., July 12: BSF Closing Meeting
Working Sessions for Treatment Guidelines

Deadline for Submission of 2004 BSF Research Grant Applications

October 1, 2004

BSF's Attendance at Medical Conferences

February 26-29, 2004 - Children's Hospital of Philadelphia (CHOP); Orlando, Florida

March 5-6, 2004 - American College of Genetics; Kissimmee, Florida

August 27-28, 2004 - Sudden Arrhythmia Death Syndrome (SADS); Salt Lake City, Utah

October 13-16, 2004 - Child Neurology Society Annual Meeting; Ottowa, Ontario

November 7-9, 2004 - American Heart Association; New Orleans, Louisiana

BSF, Inc.
Board of Directors' Meetings
April 13, 2004
July 25, 2004
October 19, 2004

BSF Board of Directors will attend the Genetic Alliance's Annual Conference
July 23-25, 2004

BSF, Inc.
Executive Committee Meetings
March 30, 2004
May 18, 2004
June 3, 2004
August 17, 2004
September 21, 2004
November 16, 2004

"Birth of Barth" Month

BSF has decided to concentrate on a specific month each year to recognize BSF and all that it stands for - and we have chosen the month of ***May*** to do so. The "Birth of Barth" will be a yearly opportunity to aggressively raise money from activities such as fundraisers, charity drives and donations from family members, employers, etc. There will be a "heart warmer" theme which will be in the form of a small pin that can be worn on the collar or lapel to commemorate BSF throughout this month! This pin will be sent to any and all, and, attached will be a donation form for efforts of raising funds for BSF. If interested, please contact ***jkugelmann@barthsyndrome.org***

Rome Marathon
March 28, 2004

Disney volunteers throughout UK and Europe will participate in this marathon to raise funds for BS Trust. This fundraiser is being spearheaded by Isabelle Lemettre.

St Alban's Half Marathon
June 13, 2004
Jerome Doherty-Bigara, Treasurer, Barth Syndrome Trust, will be participating in this marathon to support BS Trust.

Wisconsin Ironman Triaththlon
September 12, 2004
Let's all support Gary, John and Tim, BSF's ***Ironmen****, and make this an international phenomenon!!!*

Steinhatchee Workshop Fosters Interaction Amongst Attendees

By Jeannette Thorpe, South African Ambassador, BSF

1st Row (L-R)*: Cathy Ritter, Jeannette Thorpe, Rosemary Baffa, Lynn Elwood, Shelley Bowen*

2nd Row (L-R)*: Lynda Sedefian, Chris Hope,Anna Dunn, Kate McCurdy, Karen Gordon*

3rd Row (L-R)*: Jan Kugelmann, Shelia Mann, Sue Wilkins, Michaela Damin*

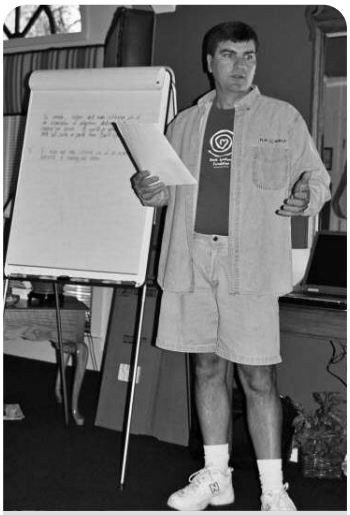
4th Row (L-R)*: Steve Kugelmann, David Mann,Tom Monahan, Mike Wilkins, Michael Bowen*

"Courage is the finest of human qualities because it guarantees all the others"

~ Winston Churchill

A pretty apt saying for the group of very dedicated, hard working and life-loving individuals that gathered for the third BSF Workshop, held from the 21st – 23rd November 2003 at the Steinhatchee Landings in Steinhatchee, Florida.

The participants were divided into four focus groups (*Awareness*: Steve Kugelmann, Lynda Sedefian, Mike Wilkins, Lynn Elwood and Jeannette Thorpe; *Family Support*: Anna Dunn, Shelley Bowen, Shelia Mann, Michaela Damin and Karen Gordon; *Science and Medicine*: Kate McCurdy, Rosemary Baffa, Cathy Ritter, Michael Bowen and Sue Wilkins; and *Fundraising:* David Mann, Tom Monahan, Jan Kugelmann and Chris Hope). After a full day of intense brainstorming each focus group came up with a comprehensive action plan which was then presented to the rest of the attendees for comment.



Steve Kugelmann
VP, Awareness

AWARENESS

There is an urgent need to make this disorder well known in the medical as well as the public arenas. This group is to spearhead educational programs aimed firstly at those physicians who would be more likely to see a child displaying characteristics of Barth syndrome (pediatric cardiologists, hematologists, neurologists, electrophysiologists, and geneticists, etc.); and then moving on to the non-physician professionals (nurses, occupational/physical therapists, echo technicians, dentists, teachers, psychologists, nutritionists, pharmacists, etc.) and the general public. Since active awareness campaigning has begun, there has not only been an increase in the number of visitors to our website but also an increase in the number of children being diagnosed with Barth syndrome.

Anna Dunn
VP & Family Liaison

FAMILY SUPPORT

This focus group divided family support into three specific areas: education/information; services/ registry; and membership.

(Continued on page 38)

Workshop Fosters Interaction

(Continued from page 32)

Shelia Mann
Family Support

Education/Information: The goal is to provide families with all the basic information needed to advocate for our children.

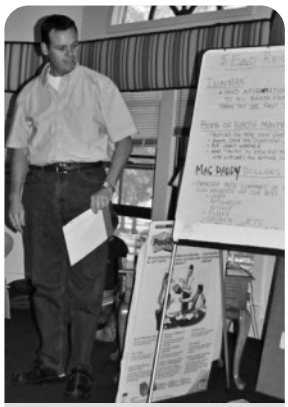
Services/Registry: A full list of services available will be outlined as well as a plan to access these services. Phone calls will be made to families to assist them and guidelines will be provided to those families who do not have Internet connection at home on how to use their local library for Internet access. The registry continues to be a key focus and it is CRUCIAL that all affected families participate. The registry will have IRB approval. Physicians will use this registry to access information. Please note that all information provided to the registry is dealt with utmost discretion and privacy. Consent will be required each time information needs to be accessed.

Membership is a huge task and one that will be continually maintained.

Kate McCurdy, VP
Science & Medicine

SCIENCE & MEDICINE

There are many science and medical initiatives that BSF has undertaken, some of them long-term in nature. This focus group discussed ways for BSF to help advance research through our grant program, involvement in the new BSF registry, establishment of a Barth blood and tissue bank, and fostering relationships with large funding agencies. There also was great interest in supporting the physicians who take care of our children. Toward this end, work will be done to help create Barth treatment guidelines. All of our initiatives will be furthered by putting together a top-notch, stimulating agenda at the scientific and medical meetings at our upcoming conference in July and by assembling wonderful speakers and interested participants with a broad spectrum of specialties.



David Mann ...
making fundraising
FUN !

FUNDRAISING

This is an area that many shy away from. However, without funding the Barth Syndrome Foundation would not be able to exist, let alone move forward to our ultimate goal. The goal of this capable and willing fundraising committee was to develop fund-raising activities that all BSF families could participate in. Our very able (and fit!!) Ironmen have once again generously offered their support. We are hoping that families all over the world will use this event to raise money for BSF. More detail on this will be sent to the families. This event will take place in September 2004 and will be our first international fundraiser. Another creative idea was starting a "Birth of Barth Month". This would consist of an active month ... (*May* has been chosen)...of fundraising (sounds like fun!). Some ideas: garage sales, car washes, dinner parties, golf days, competitions, etc.

Karen Gordon
Family Support

Rome may not have been built in one day, but I tell you what, we certainly moved mountains in two!! We could really use your help – no matter how small!! PLEASE contact Shelley Bowen at ***sbowen@barthsyndrome.org*** and let us know which focus group would interest you: Awareness, Family Support, Science and Medicine, or Fundraising (or all!).

I would like to take this opportunity of thanking every BSF workshop participant for taking time away from their families to attend this workshop, for their incredible strength and courage and endless determination.

(Continued on page 39)

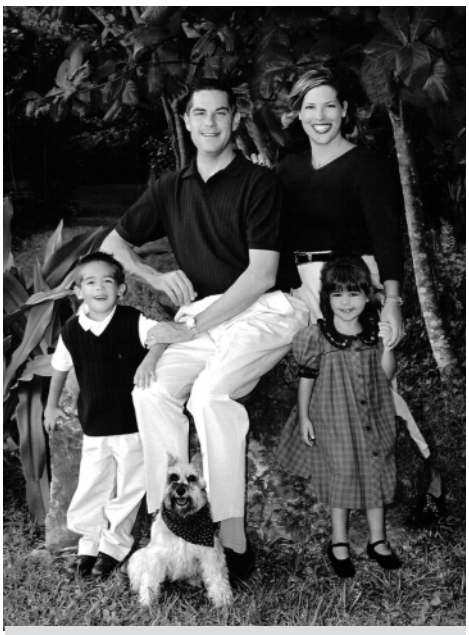
(Continued from page 38)

It was an honor and privilege working with you and I look forward to working with many other members in the near future! Let's move those mountains!!!

Jeannette Thorpe
South African Ambassador

BSF Offers New Hope

By Julie Fairchild, Wellington, Florida



Jake (son), Dewayne (Dad) , Julie (Mom) and Grace (daugher)

Jacob Fairchild was born November 15th 1998. Jake was a normal baby, or so we thought as first time parents. Jake did have one problem, he didn't eat well. Jake never ate more than 2-3 oz. of milk at a time.

Our pediatrician said Jake had poor muscle tone and sent him to physical therapy and a neurologist without diagnosis. When Jake was 14 months old he became lethargic, he would lie on the floor and cry, breathing heavily. After this, our pediatrician sent us to a cardiologist. Jake was admitted to PICU for 10 days and diagnosed with dilated cardiomyopathy.

After our hospital stay, we went to another hospital for additional testing and to see a geneticist. No answers were found. After 23 days Jake was sent home with a feeding tube and medication. We then discovered my 1st cousin's son Andrew had the same heart condition as an infant, but never actually received a diagnosis. His heart has recovered but he still suffers from low muscle tone.

Jake's heart slowly recovered to a normal low function, and we thought we were out of the woods! However, just after Jake's 4th birthday, he was rushed to another hospital. His heart function had declined again. The doctors argued with me and said there was no way his heart was ever functioning on the low side of normal.

Over the next few months Jake was doing all right except for occasional "episodes" characterized by lethargy, and sweating. We kept taking him to the cardiologist but they couldn't give us an answer. He wore a holter monitor for a month to see if he had an arrhythmia, but one was not found. One of the doctors mentioned Barth syndrome to me but we dismissed it because Jake's white blood count had not been low. In June he had another episode and that was the last straw for us . We decided to go to Boston Children's Hospital to find an answer. A heart biopsy uncovered nothing. However, the 3-methylglutaconic acid did come back high. Barth syndrome was again mentioned.

A visit to the same geneticist who found nothing before resulted in Jake being tested for Barth syndrome. While he gave us the information, it was up to me to get the blood drawn and sent! We searched the Internet and found the Barth Syndrome Foundation and read everything we could. Why wasn't our doctor managing this? Days later we got the diagnosis; we were relieved, yet concerned. After 14 years, Andrew (my cousin's son) also had a positive diagnosis. Now we have hope that Jake's heart can recover. He can have a normal life. Jake is doing well now; he goes to preschool, karate, swims, and plays T-ball. We want him to be normal. We do not want him labeled. We are excited to be a part of the Barth Syndrome Foundation and interested in helping to find a cure. It's critical we all participate and give all the information we have to help find a diagnosis.

The Journey of A Loving Grandparent

By Carolyn Gravitt
Grandmother of Benjamin & English Mann

Carolyn Gravitt

Little did we know on January 16, 1997, that we had been chosen to have a very special child given to us. While we knew things were somewhat "different", we blindly went through the joys of a new baby until that fateful day 3 weeks later when our world shattered. The next few months were pretty dismal since the possibility of Barth syndrome was looming in our faces and the only information we could find was not positive. We felt alone and vulnerable. We searched, not so much for answers, but for any glimmer of information that might suggest our special baby had a chance. We felt desperate. So few physicians and no laymen knew of Barth syndrome.

We wondered about the possibility of taking our baby to Amsterdam to see Dr. Barth and whether he was well enough for such a long trip. As our desperation continued, we learned of a physician in Texas who knew of Barth syndrome. We hurriedly made plans to take our baby there. In the meantime, we learned about our wonderful Dr. Kelley at Johns Hopkins. The first conversation with him was our first indication that there truly was someone out there who knew what was happening with our special baby. We will never forget his kindness, his understanding, the information he provided and the encouragement we received. He was our first inkling of hope.

We also learned that he had plans for bringing together families with Barth boys. So, with hopeful expectations, we went off to Baltimore in 2000. What an impressive group! In those short three days, the Barth Syndrome Foundation was born.

We found families whose experiences were the same as ours, who had experienced the isolation, lack of information, and prospects of little hope for our boys.

We left Baltimore as a different family. Our "family" had increased instantaneously. No longer were we isolated and alone. Someone else had experienced the same issues we were dealing with. We could share our fears, our hopes and our frustrations of not knowing. We learned about treatments, ideas and trials experienced with other boys.

We had access to physicians who understood the Barth processes and how our boys are affected and who were willing to discuss these issues with us. This was quite a step from being the educator who relentlessly explained Barth syndrome to caregivers and tried to educate them so they could treat our baby.

What does Barth syndrome and the Barth Syndrome Foundation mean to me? I have watched two parents work relentlessly to support the disease and the Foundation while becoming the best parents I have ever known. I have watched a big sister adjust to life with a special brother as she learns how to be a "Barth mother" if that becomes her fate. I have watched a "Barth boy" capture the hearts of everyone he meets. I have watched tireless efforts of parents and caregivers as they nurture the Foundation and each other. I have watched the members of the Foundation reach out to new families so that they don't experience the aloneness we felt in the beginning. I have seen the Foundation meet special needs as when the grandparents' group was created.

But most of all, the Foundation is hope. The Foundation is the hope we didn't have, the support we need when the difficult times come. It is the sharing and celebrating in times of joy. It is knowing we are no longer alone and that by working together, our boys and our families will reap the rewards.

His Determination To Succeed Prevailed

By John Wilkins, Lincoln, NE

John Wilkins celebrates the moment of receiving his hard-earned GED

"I'm happy to tell you that last July I completed and passed the GED - the General Educational Diploma exam. I'm now a high school graduate!"

For several reasons my family and I decided it would work best for me to homeschool through high school, with the help of a great tutor and my mom. We used the University of Nebraska Independent Study High School cirriculum. After 5 years, I had finished all of the core requirements and only had elective courses left. I decided I wanted to take the GED exams.

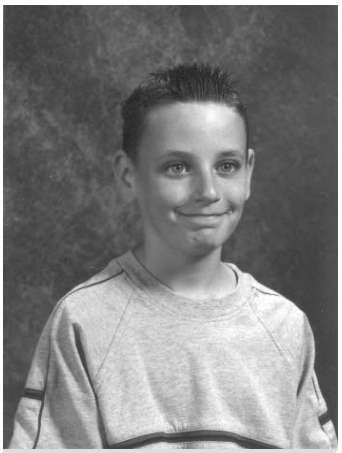
The GED involves taking 5 exams, one each in math, social studies, science, literature and writing. I decided to take one exam each week, starting early in the summer. We were also planning my sister's wedding, so it was a busy summer. There are many different kinds of books you can get to help you study for the GED—we found the Kaplan book to be the most helpful. They go over each subject and also have a couple of practice exams.

I am proud to say I passed each exam on the first try and actually did quite well on each one! I got the letter telling me this two days before the wedding. After my sister and brother-in-law got home from their honeymoon, we had a great graduation party to celebrate.

Right now, I am continuing my part time job. I have also been accepted into a Microcomputer Technology program. I will start my first class on March 31st - Fundamentals of Microcomputers. It's very exciting !!

In Memoriam

To My Best Friend Tim
November 28, '89 - September 19, '03



Timothy P. Rosiek

Tim was truly a joy to have in my life, not to mention so many others. He was a loving and caring person. He always wanted to please and he would do anything to make you happy. Nothing was to extreme to him when it came to making you laugh or smile.

As I have learned in recent months, he was a true friend, that he had touched many lives, and what a joy he was to be around. Not just with his peers but the adults in his life as well. Some say he made them feel important and really knew who they were. As for me, I already knew that.

Tim and I could talk about anything from school to all the things life can bring. He was very curious about life, especially his own knowing he had a serious illness. That never got him down though. He did everything he wanted, within his own limitations.

He loved his animals, many cats and a dog, Mayzee. That was his favorite thing to do, sit in the yard and play with them. He took very good care of them also and they seemed to love him. Some days I would look out and see him covered with cats. What a picture that was. I'm sure they miss him.

I feel I not only lost a terrific son, but one of my best friends as well. Life right now seems bleak and empty without him, but I know in time it will get easier to cope with. It is somewhat comforting to know he is with his younger brother Mikey. I can see them together as they were when they were little ... getting into whatever they could.

We have lost a special person, a loving son, grandson and nephew, a true friend and animal advocate. He will be deeply missed by all, and especially me.

All my love,
Cheryl Rosiek (Mom)

The Power of Kindness *(Contributions Received Since May 2003)*

Special Thanks to Our "Angels" Who Have Made Significant Donations

Atwood, Brian/Lynn Edminster
Anonymous
Barad, Seth/Amy
Blumenthal, Richard/Cynthia
Cusack, Tom/Carrie
Davis, Martha
Doherty, James/Kimberly
Evoy, Larry/Sara
Fennelly, Nancy
Fowler, David/Susan
Geary, Ann
Hart, Dana
House, David/Jan
Kavetas, Mrs. Harry - The Harry L. Kavetas Family Fund
Kelly, Al/Peggy
Kugelmann, Peter/Karen
Lindsey, Mr. and Mrs. John - Sara and John Lindsey Foundation
Lummis, P. Bradley/Gaylord
Lummis, William
Malkin, Scott/Laura
Martin Electronics
McCurdy, Steve/Kate
McKown, Chris/Abby
Osnos, Susan
Pierson, Dr. Richard/Allene
Polish White Eagles
Russell, Dr. Paul/Allene
Sam's Club Foundation
The Hartford Insurance Co.
The Lebensfeld Foundation
Thunder Valley Mustang Club
Vaisman, Beth/Natan
Wilkins, Dr. Mike/Sue

Contributions of $50 and Above

AAMCO Tansmission of Merritt Island
Abbonizio, Leita
Alderman, Thomas/Lisa
Alexander, Edward
Allman, Peter/Maureen
American Express Fdtn.
American Express Gift Matching
Anderson, Wayne/Suzy
Andrews, David/Ellen
Aurley, Louis/Rita
B.P.O.E Lodge # 1851
Baffa, David/Shasta
Baffa, Mary
Baffa, Theodore
Bancroft, Rev. Frank
Barlow, Steven/Rebecca
Bater, Jennifer N.
Bates, William/Mary Anne
Benzie Area Church of Christ
Bergquist, Clay
Bernard, Tina
Bernhard, Susan
Berry, Rick/Carla
Bevilacqua, Mr./Mrs. Carmen
Big World Enterprizes
Blackman, Sandra
Black's Spray Service, Inc.
Blaise Window Tinting, DBA Blaise Truck & Auto Acc
Block, David/Sharon
Blumenthal Children
Blumenthal, Arthur/Roberta
Blumenthal, Martin/Sally
Bodary, Michael/Lisa
Bogan, James/Margaret
Bogert, Amy
Bogert, Nicholas/Sally
Bond, Louis/Kimberly
Booth, Mark/Patricia
Boris, Marc/Mary Pat
Borst, Joseph
Borst, Mary Susan
Boschi, John/Anne
Bowen, Shelley/Michael
Brabbs, Kelly/Madelyn
Bradley, Robert/Margaret
Bradshaw, John/Susan
Brenner, Andrew/Kathleen
Brevard Home Furnishings Gallery Inc
Brevard Mutual Insurance Agency Corp.
Brewer, Gerilyn
Broome, Jay - Bro Rock, Inc
Brown, Marcia/Tom
Bruton, Charles
Buckley, Mary/Joseph
Burke, Thomas/Rose
Burmeister, Charles/Marita
Burtis, Cleo
Butcher, Ineke
Byrd, Todd/Michelle
Calabrese, Frederick/Ann
Calabrese, Joanne
Calabrese, John/Kathleen
Calabrese, Santo/Donielle
Callahan, Paul/Mary - CNS Ceramics
Cargill-Horizon Milling
Carr, Glenn/Susanne
Carroll, Ann/Robert
Clinch, Peter
Coastal Instrument & Supply Co., Inc.
Colloredo, Scott
Conchar-Grenafege, Cynthia
Connell, Kathy/Wayne
Correia, Brian/Patricia
Cosenzo, Denise
Crittenden, Gary/Catherine
Crossan, John/Jeanne
Crowley, Peter/Gretchen
Cullison, James/Margaret
Cunniffe, Bernie/Rosemarie - Precision Engraving Group
Cunniffe, Francis/Helen
Cunniffe, Peter/Jodi
Damin, Nori
DeCarlo, Susan
Decker, Thomas/Jennifer
Despins, Luc/Suzanne
Diamond, Dr. Kimberly
DiBernardinis, Gary/Donna Marie
Digiovanni, Eugene/Teresa
DiLello, Thomas - Mapace Enterprises DBA Curves for Women
Dix, Glenda/Lee
Dobrosky, Thomas/Paula
Doherty, Henry
Doherty, Henry/Allyson
Doherty-Bigara, Jerome
Doherty-Bigara, Family (Mauritius)
Donahue, John
Donnelly, Kevin/Beth
Downey, William/Lois
Dunn, Anna/Mark
Draddy, Mary Patricia
Drinkwater, Paul
Dunlap, Maureen - PartyLite
Eadeh, Ernest/Leslie
EDG & Associates
Egan, Michael/Constance
Elwood, Lynn/Rick
Erie, Dawn
Ewald, Raymond/Judith
Falcone, Philip/Anne
Field, Michael/Kathleen
Fields, Wendy/Brenda
Fishwick, John/Jeanne
Fitzgerald, Joan
Florence, David/Elizabeth
Fracassa, Moria
Frank, Joel/Marie
Franklin, Peter/Dorothy
Friendly Feathers
Gallagher, James/MaryJane
Gallagher, Martin/Colleen
Gardiner, Timothy /Nancy
Garrett Hill Auto Service, Inc
Garrity, Jonathan/Caroline
Garvey, Joseph/Joanne
Geeser, Gerald
Geib, Michael/Christine
Geithner, Peter/Deborah
Genthner, Harold
Gerwig, Elizabeth
Giacomucci, Susan
Glasgow, Merrill/Elizabeth
GLOW Title & Escrow
Golden, Louis
Gontko, Bernard
Gonzalez, Dr. Iris
Goodmon, Randal
Goodwin, William/Virginia
Gordon, Karen/Dave
Graham, James/Linda
Grant, Alec/Catherine
Green, Cheryl
Gress, Emil/Natalie
Griffon, Rodney/Karen
Grohol, Dr. William
Gurr, Clifton/Sheila
Haas, Rod /Wendy
Hagan, John/Christine
Haines, Austin/Linda
Haltiwanger, R. Curtis/Dona
Hamdan, Dr. Firas
Hanlon, Gregory/Elizabeth
Hanlon, Michael/Stephanie
Hazen, Edward /Elizabeth
Heinsinger, Robert/Marylou
Hepp, Timothy
Hingle, Carl
Hintze, Audrey
Hobbs Pharm. United, Inc
Hobson, Lisa Masterson
Hoffman, Paul/Michele
Holmes, Pam
Hope, Chris/Michael
Houlette, Mark/Elizabeth
Howell, David/Patrica
Hsieh, David/Priscilla
Huck, Charlotte
Hudson, Thomas/Nancy
Iapicco, Steve
If It's Water, Inc
Ingersoll, Jared
Isaac, Paul/Karen
Island Surf and Skate LLC
Janiec, Stephen/Diane
Jessiman, Dr. Andrew/Joan
Jobes, Shirley
Johnson, Tom - Mastercrafters
Jones, Edmunds & Assoc.
Kane, Vera/Arthur
Kasinkas, George
Kealey, Sr, Patrick/MaryJane
Kearns, Richard
Kelley, Dr. Richard/Alice
Kelly, John/Anne
Kelly's Security Service, Inc
Kennedy, Halisey/Holly
King, Robert/Barbara
Kinnan, Kevin/Kimberly
Kirk, Joseph/Rebecca
Kirsch, Martin/Kathleen
Kittleson, Clay/Holly
Klockner, Daniel/Nancy
Komancheck, James
Kordel, Chester/Rita
Kring, DDS, H. Roderic
Krueger, Mary
Kugelmann, Mary Irene
Kugelmann, Matt/Lori
Kugelmann, Mike/Catherine
Kugelmann, Steve/Jan
Kugelmann, Tom/Hanh
Kugelmann, Warren/Maria
Kugelmann Land Surveying
Landis, Steven/Cindy
Laneko Engineering Co.
Lee, Gayle
Lemons, Wallace/Hazel
Leon, Susan - The Leon/Fredman Family
Linen, Jonathan
Lockheed Martin & Friends
Lukinovich, Barbara
Lyon, Robert
Lyons, Douglas
M2 Constructors, Inc
MacDonald, William/Barbara
Mancini, William/Janet
Mann, Allen/Rosa
Mann, David/Shelia
Mannal, Dr. Richard/Karen
Mariani, Dominick/Catherine
Marsh, Bette
MaryKathleen O'Leary, and Robert Mulhern
Masterson, Moira
Matthias, Michael/Linda
Maynard, Dr. Edwin/Elizabeth
McAllister, Paul/Tara
McBride, Jr., Michael/Donna
McCabe, Fr. James
McConaughy, James/Beverly
McCormack, Joseph
McCurdy, John/Sharon
McCurdy, William/Virginia
McFee, Wendy/Jmel Wilson
McIntosh, Will
McKenna, Mary/Kevin
McMahon, Tracy
McQuaig, Michael/Brenda
Merlino, Jr., Samuel
Merritt Island Breakfast Rotary Club
Meyer, Stephanie/Jim - Ace Electric
Miccioli, Anthony - Timeless Dwellings
Michaud, Steven/Yoko
Microsoft Matching Gifts Program
Mixter, Stephen/Elizabeth
Moerman, John/Rosemary
Mollica, Jeremy/Alison
Mollichella, D.
Moncure, John
Montanaro, Louis/Theresa
Moore, Michael
Moore, Mr. and Mrs N. (Lorna)
Morales, John
Motzkin, Robert
Mueller, Henry
Muldowney, James/Margaret
Mulvey and Flanagan, P.C., Attorneys at Law
Murphy, Donald/Jane
Murray, Jon/Toni-Anne
Neal, Vickie/John
Neff, George/Elizabeth
Nelson, Dr. Miles
Newman, Randy
Nosek, Denise/William
Nygaard, Wilma
O'Brian, David/Karen
Olson, Ken/Tina
Olson, Richard/Sharon
Olson, Tom/Maria
Ordonez, Albert/Kimberly
Ossorio 1, Inc
Pagano, James - Fully Involved Lawn Service
Palandrani, David/Gina
Palmer, Kirk/Lori
Panaccio, Jeanette
Paolizzi, Vincent/Celeste
Paradise Ford
Parkhurst, Charles/Hilary
Pellerite, Philip/Debra
Penny, Lisa
Perini Building Company, Inc
Perkins, Phyllis
Philip, Katharine/Robert Shults
Phillips, Bruce

The Power of Kindness

Phillips, Jr., Kenneth/ Margaret
Phillips, Kenneth/Margaret
Phillips, Sharon
Pickell, Robert/Ellen
Pierce, Frederick/Lorraine
Pietrini, Andrew/Pam Mari
Plumez, Jean Paul/ Jacqueline
Porta, Joseph
Priest, Albert/Karin
Prieto, Omar Urdaneta
Pringle, Matthew/Julie
Purcell, Robert/Jaqueline
Rader, Carol
Rafter, Marianne - McGrory Glass, Inc
Ranck, David/Tina
Randzin, Alan/Elizabeth
Reid, Thomas/Toni
Remensnyder, Dr. John/ Mary
Rementer, Edward/Laura
Rigsby, Robert
Rigney, John
Ritter, Cathy/Chris
Rivers, Edward/Angelina
Roberts, John/Elizabeth
Rodden, Stephen/Anna
Rogers, Jimmy/Susan
Rosiek, Henry/Wanda
Rosiek, Susan
Rothman, Peter/Amy
Rowe, Mrs. M.
Russell, Sara/Paul
Russo, Bobby/Dottie
Russo, Martin/Mary
Rye, Brian/Tanya
Sagorski, Douglas/Suzanne
Sallie Mae Employee Contribution Programs
Sanborn, Noel/Virginia
Sanchez, Miguel/Carmen
Sauer, Robert/Elizabeth
Sautner, Robert/Sarah
Sawtell, Joseph/Deborah
Schantzen, John/Sandy
Schneider, Gregory/Nancy
Schwartz, Mark/Marie
Schwarz, Stefan
Scoville's Auto Machine
SD Martin Financial Services, Inc
Security Systems Specialists, Inc
Lynda Sedefian
Segal, Mary Lycett
Shields, Frank/Mary
Sipler, Edward/ MaryElizabeth
SKN Data Research, Inc
Sleeper, Emmy-Lou
Smith, Jeffrey/Janet
Smith, Jeffrey/Judi
Smiths Aerospace Electronic Systems (Employees)
Snedeker, Frances/Robert
Solomon, Mike
Sportsline
Spotts, Frank - Big Frank's Tire
St. John's Episcopal Youth Group
Stenson, Martin/Marie
Stenson, Martin/Sylvia
Stenson, Mrs. Mary
Stevenson, Robert/Sharon
Strauch, Catherine/Joel
Strisko, Randy
Sullivan, Thomas/Jean
Sure to Pure
Sutherlin Cadillac, Mike
Erdman Motors, Inc
Sverdrup Technology, Inc
Teufel, June
Tezel, Kurt/Patricia
Tulchin, Nora/David
Unigraphics Solutions, Inc
United Space Alliance
Universal Drywall and Plastering, Inc
van Loo, Joke/Albert
Varner, Judy
Varner, Paula
Varner, Tom/Beth
Viebranz, Alfred/Elaine
Volpi, Vincent/Susan
Waite, Joel/MaryFrances
Walker, Doug/Gina
Ward, Anne/Barry
Warfield, Paul/Elizabeth
Waterman, Christopher/ Marcy
Waters, Martin/Helen
Weiner, Steven
Welsh, William/Denise
Wendling, Paul
Whitcombe, Andrew/Lisa
Wilborn, Amy/T.D.
Wilkins, E. Joanne
Wilkins, Muriel
Wilkins, Sue/Dr. Mike
Williams, Kathleen
Wilson, James
Wilson, Tim/Ruth
Wing King Five (DBA Beef O'Brady's)
Winski, Edward/Jane
Winston, Laura
Worst, David/Karen
Zerilli, Sam/Eileen
Zervanos, John/Patricia
Zierk, Gail/Tom
Zorthian, Gregory/Robin

Special Contributions of Time and Advice

Suzy Anderson
MaryEllen Angelone
Frank Baffa
Mary Baffa
Rosemary Baffa
Dr. Peter Barth
Nancye Beulow
Carmen Bevilaqua
Jerome Bigara
Dr. Mary Ann Bonilla
Michael Bowen
Michael Bowen, Jr
Dr. Randall Bryant
Les Buckley, CPA
Jacquie Butera
Lara Burnazian
Dr. Barry Byrne
Tony Carlson
Robert Carter, Esq
Kate Casidine
Dr. John Christodoulou
Sonia Collings
Carol Cook
Dr. Gerald Cox
Linda Croxton
Matthew Croxton
Alexandra Coutinho
Dr. David Dale
Marco/Michaela Damin
Nori Damin
Dr. Salvatore DiMauro
Jerome Doherty-Bigara
Jason Downard
Mark Dunn
Holly Edsel
Lynn Elwood
Dr. Mauro Degli Esposti
Bill Fagan
Julie Fairchild
Dr. Annette Feigenbaum
Dr. Alan Friedman
Helena Fruendt
Doug Ganz
Dr. Iris Gonzalez
Karen Gordon
Carolyn Gravitt
Dr. Miriam Greenberg
Dr. Stephen Groft
Darlene Guasco
Dr. Grant Hatch
Lawton Hawkins
Maggie Hoffman
Susan Hone
Christine/Michael Hope
Eileen Juico
Dr. Edward Kaye
Dr. Richard Kelley
Rebecca Kern
Bill Knauer
Dr. Philip Koeffler
Jan Kugelmann
Dr. Taco Kuijpers
Kelly LaDuke
Alice Land, SADS FDTN.
Alanna Layton
Isabelle Lemettre
Joyce Lochner
Dr. Cathryn Mah
Shelia/David Mann
Annick Manton
Yuriko Maruno
Moira Masterson
Eileen McMahon, RD
Steve Michaud
Tom Monahan
Tim Monetti
Theresa Montenero
Sharon Olson
Mary Lou Pagano
Jim Pagano
Melvin Parker, WPRY
Dr. Catherine Parrish
Dr. Gail Pearson
Gwyn O Price
Bryce Reece
Carolina Reece
Deanna-Lynn Reilley
Cathy Ritter
Gary & Colette Rodbell
Jon Rosenshine
Dr. Michael Ruelf
Mary Beth Salerno
Dr. Michael Schlame
Raghad Schroeder
Anne Segal
Cathy Sherman
Dr. Geoff Sherwood
Dr. Carolyn Spencer
Dr. Giovanna Spinella
Dr. Jules Spotts
John & Linda Steigerwald
Leonard Steinberg
Steinhatchee Landings
Leonard Steinberg, EA,CMC
Dr. Colin Steward
Dr. Joan Stoner
Dr. Arnold Strauss
Dr. Kathryn Taubert
Sharon Terry
Jeannette Thorpe
Ginny Torncello
Pavla Tousova
Dr. Jeffrey Towbin
Suman Vallabhbhai, CPA
Dr. George Van Hare
Joke van Loo
Dr. Frederic Vaz
Dr. Ronald Wanders
John Wilkins
Dr. Michael Wilkins
Dr. Yang Xu

In-Kind Donations

Frank Baffa
Basket of Love Florist
Baskets by Baker
Bath Cottage
Big Frank's Tire and Wheel
Blockbuster Regional Office
Carol Youmans
Carrabba's Italian Grill
Carousel Florist
Carroll Distributing Co.
Carvel Ice Cream Bakery #855
Casa Del Rey
Casey's Flags
Catholic Parish of Overton and Oakley
Charlie & Jake Brewery & Grill
Charles Connor, DMD
Chili's
Coconuts of Cocoa Beach
Community Educators Credit Union
Courtyard on the Grove
Cracker Barrel
Dairy Queen
Disney, Hammersmith Offices, London
Domino's Pizza
Donut Connection
Durango's Steakhouse
ED Italian Restaurant
Erdman, Mike
Fazoli's
Frankie's Wings & Things
Freida's Kritter Boutique
Gerding, Bill/Laurie
Gregory's Hair Studio
Heaven on Earth Day Spa
Herbal Body Therapy
Island Reflections
J & J Sporting Goods, Inc
Jenny's Auto Parts II, Inc
Jim Thompson's Golf World
Kash 'n Karry
Kennedy Space Center Visitor Complex
Kinder, Judy
Kings Duck Inn
LaBella Spa
Merritt Island Printing Co.
Ocean Potion
Orlando Princess
Pamela's Garden
Pear Tree
Penny Lane Computers
Pinch A Penny Pools
Porky's Bar-B-Que
Portsmouth Stake Relief Society
Pro Health
Quiet Flight Surf Shop
R.J. Gator's
Red Lobster
Richard's Paint Mfg. Co. Inc
Rockledge Gardens
Royal's Beachwear
Sam's Executive Golf
Save A Lot
Schenck Distributing
Selman, Jack
Smoke Rings
Space Coast Crafters
Steak and Shake
Sterling Casino Cruise Line
Suntree Country Club
The Village Ice Cream Shop
The Village Gourmet
Tires Plus
Travis Hardware
Turtle Creek Golf Club
U. S. 1 Golf Center
Village Perks
Wacky Hut
Wal-Mart #771
Walter's Orchids
Winner Auto Center
Bill Wright, Perry Pepsi

Peter's Visit to the South of France

Peter walks beside Pont d'Arc (close to the village Salavas, region Ardeche river) to witness the "Himalaya"

I am Peter van Loo, from the Netherlands. The Barth Syndrome Foundation asked me to write about my trip to Southern France with my school. Our journey started on October 6, 2003 at midnight. We gathered at the bus station in Heerde and after 30 minutes waiting the busses arrived. We watched several movies in the bus on our way to Southern France. Each 3 hours we had a stop for 20 minutes and at 13.30 h we had a lunch stop for 60 minutes. Finally we arrived in Salavas, Ardeche, on our camping at 16.00 h and we had to put up our tents. When all tents were built, more or less solid, we were split up in four groups. Each group got a bag with something to put on the French bread and each 2 persons got tins with different kinds of meals, like hotchpotch, kale, smoked sausage. Each morning we got one French bread per person.

Tuesday and Wednesday we had survival activities. We all had to do four different kinds of activities, but the groups did them in different order. My group had to do some mountain climbing on Tuesday morning and an orientation exercise on Tuesday afternoon. On Wednesday my group rafted down the river in kayaks in the morning and went on mountain bikes in the afternoon. I wasn't able to participate in those activities, but I watched the kayaks at the finishing point on Tuesday. On Wednesday I made a walk besides the river to watch the kayaks again and witnessed the "Himalaya" - start of kayaks. When people do the Himalaya –start with a kayak, they pull up the boat on a steep hill, enter the boat and others give the boat a push. The boat is sliding down the hill and falls into the water from a height of more than 6 feet.

We had to warm our own meals above the campfires at the end of both days. Wednesday evening we travelled again with our bus to Avignon. There we had to rebuild our tents again, which wasn't easy because it was dark already. Thursday we had a more tasteful breakfast with coffee, juice, croissant and pistolet (petit pain), some jam and some butter. Thursday and Friday we visited various museums in Arles and Avignon. This was interesting and fun too, but quite different than survival activities. You can read more on ***http://www.petervanloo.tk.***

Saving lives through education, advances in treatment and pursuit of a cure for Barth syndrome

Barth Syndrome Foundation®

The Barth Syndrome Foundation, Inc.
www.barthsyndrome.org

P.O. Box 974
Perry, Florida 32348
Phone: (850) 223-1128

info@barthsyndrome.org