



## BARTH SYNDROME FOUNDATION SERVES AS CATALYST FOR ADVANCES IN RESEARCH

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By Kate McCurdy, Vice President  
Science and Medicine

As of the spring of 2005, the Barth Syndrome Foundation, Inc. has funded a total of *fourteen* research grants for important scientific and medical work on various aspects of this complex disorder. These awards represent a financial commitment of nearly \$480,000. We are thrilled to have the talents and the dedication of so many outstanding scientists and physicians around the world focused on Barth syndrome.

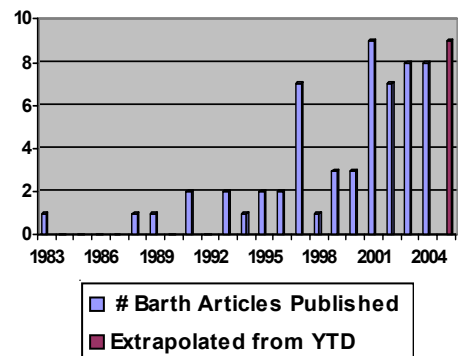
But the really critical element in all of this is the progress that is being made as a result. Not only has our grant program supported specific projects, but our conferences (held in 2000, 2002 and 2004) and our awareness programs have stimulated a great deal of excitement and attention on the disorder (refer to page 16 - "*Highlights of What is Known About Barth Syndrome, as of May 2005*"). Since the Barth Syndrome Foundation was established in late 2000, more professional articles about the syndrome have been published in top-notch, peer-reviewed journals than ever before (with the exception



Photograph by Kelly LaDuke

*One of the many 'faces' of Barth syndrome. Each issue we will present another 'face' of Barth syndrome.*

of 1997, just after the gene for Barth syndrome was discovered), as is evident in the chart below:



*(Continued on page 4)*

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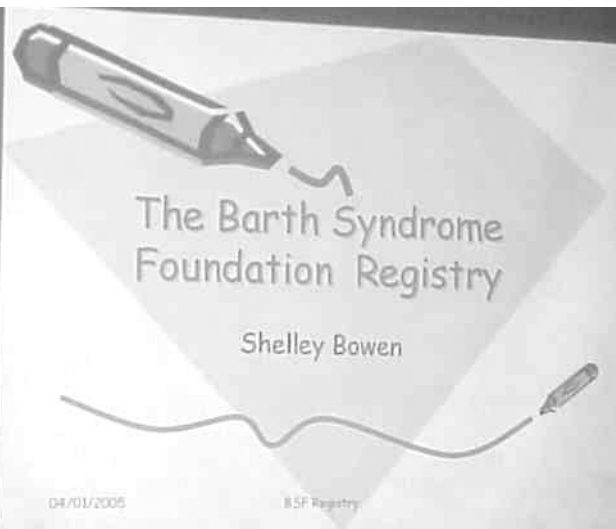
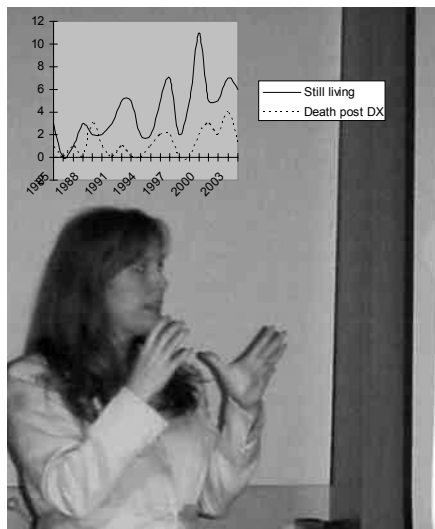
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*Our Spring Newsletter is usually focused on reporting our previous year's progress toward our goals, and we have a lot to report! With the help of all of our volunteers and supporters named on the back pages, we have moved ever closer to our vision, "A world in which no one will suffer or perish from Barth syndrome." We know that our success depends on the passion and participation of our families, volunteers, physicians, scientists and contributors, every one of whom we count as a friend. As the President of BSF, I want to thank you for the trust you have placed in this organization as we strive to make a difference in the lives of all those who have Barth syndrome. As a parent, I am grateful to be a part of such a warm, generous and caring community and awed at how it seems to continue to grow larger and more successful every year.*

*At the core of our organization is a growing group of committed volunteers – team leaders who are keeping us all focused, organized, and who truly do the heavy lifting that makes our growth and accomplishments possible. This year our teams have increased awareness among physicians and found many new Barth families and financial supporters around the world. We have begun to see our Canadian, UK, European and South African organizations thrive and our volunteer community expand to non-family members. For all of our volunteers and donors, as we take on even greater challenges, we will need your time and passion and support even more.*

*It has always been clear to me and to the Board of BSF that our best hope for the future can be found in science and medicine. And so in the coming months and years, we will re-double our efforts in this area, and then re-double them again. We need to increase research funding – both from BSF and other organizations. And we need to make certain that scientists have access to the most complete and comprehensive repositories of DNA, tissue and blood samples and longitudinal data from our rare population of affected boys and young men. These multi-year programs will help BSF become a more active scientific partner, enabling and encouraging research around the world.*

*As our Barth family has grown, so have our resources, our ambition and our hopes. Every year that we can turn our dreams into reality leads to a year of still bigger dreams. And every year forces us to stretch still further. 2005 is no different. Our vision remains the same. But with your help, our reach grows longer every year. And someday, maybe soon, I know that our goal will be within our grasp.*

*So thank you to all who helped turn our dreams for 2004 into reality. I hope that we can continue to count on you in 2005 and for as long as it takes to achieve our vision.*

*Gratefully,*

*Shelley Bowen*

# Year-End Report

## A SUMMARY OF BSF'S PROGRESS IN 2004

By Valerie ("Shelley") Bowen, President

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. Outlined below are those accomplishments that we would like to share with you, which fall under each one of our goals.

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

- a. Attended six medical conferences focused on a variety of sub-specialists:
  - i) 7<sup>th</sup> Annual Update on Pediatric Cardiovascular Disease hosted by the Children's Hospital of Philadelphia in Orlando, FL
  - ii) American College of Medical Genetics in Kissimmee, FL
  - iii) Sudden Arrhythmia Death Syndrome Conference in Salt Lake City, UT
  - iv) Child Neurology Society in Ottawa, Canada
  - v) American Heart Association in New Orleans, LA
  - vi) The Fifth International Symposium on Pediatric Cardiac Intensive Care in Miami, FL
- b. Presented a parent's perspective of Barth syndrome to Sarah Lawrence College for genetic counseling second year graduate students and University of Chicago school for genetic counselors
- c. Initiated Outreach Program designed to bring families together and promote awareness about Barth syndrome and BSF in regional medical centers
- d. Eight journal articles published as a direct result of the ten research grants awarded by BSF (see cover article)
- e. Hosted 2004 International Scientific/Medical & Family Conference
- f. Noted increase of website traffic:
  - i) 91,077 total hits in 2004, compared to 59,057 total hits in 2003
  - ii) 21,655 new visitors to our website in 2004, compared to 12,965 new visitors in 2003

(Continued on page 7)

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*BSF's newsletter is designed for educational purposes only and is not intended to serve as medical advice. The information provided within this newsletter should not be used for diagnosing or treating a health problem or disease. It is not a substitute for professional care. If you suspect you or your children may have Barth syndrome you should consult your health care provider.*

*All submissions and correspondence regarding the newsletter should be directed to Lynda Sedefian at: [lsedefian@barthsyndrome.org](mailto:lsedefian@barthsyndrome.org)*

# Barth Syndrome Foundation Serves as Catalyst for Advances in Research

(Continued from page 1)

It is impressive to note that eight of the articles that have been published in the last two years are the direct result of the ten research grants we awarded in the first two years of our grant program, and more are in the pipeline. Through experience, we all know just how crucial it is to have progress documented in highly-regarded journals so that the information can be accessed by everyone around the world.

I am pleased to provide summaries of the four grants that were awarded in our most recent grant application cycle, completed in January 2005. All four of these projects will move knowledge about Barth syndrome forward. We are very excited to add these projects to our list of supported research:

**Principal Investigator:** Willem Kulik, PhD  
**Institution:** Univ. of Amsterdam, Academic Medical Center; Amsterdam, The Netherlands

**Title of Project:** *Retro- and Prospective Measurement of the Incidence of Barth Syndrome in Cardiomyopathic Patients and Development of a Tool for BTHS Newborn Screening Using HPLC Tandem Mass Spectrometry*

**Amount:** \$37,000 / **Time Period:** 1 year

**Abstract:**

"Barth syndrome (BTHS) was first identified more than 20 years ago, but to date no systematic studies have been performed to determine its frequency in the general population or in high-risk groups. Estimates of the incidence of BTHS in newborn males range from as high as 1/100,000 to as low as 1/500,000. Although most children with BTHS manifest the typical characteristics of this disorder (hypotonia, cardiomyopathy, failure to thrive, neutropenia, muscle weakness and fatigue) some may have only one or two features, which can delay the diagnosis or lead to misdiagnosis. In addition, infants and children who die acutely from cardiomyopathy are often assumed to have viral myocarditis and may not always undergo a thorough diagnostic evaluation, making it likely that the diagnosis of BTHS will be missed. For these reasons, we believe that the true incidence and prevalence of BTHS are underestimated.

In order to better estimate the frequency of BTHS and to determine whether it is underdiagnosed, it is critical to develop sensitive and cost-effective diagnostic testing that can be used to screen a large number of patients. Certain tests, e.g. urine organic acid analysis or *TAZ* gene mutation analysis, are not ideal for screening purposes because of their high costs and methodological limitations. Elevated levels of 3-methylglutaconic acid are not specific to Barth syndrome as they can be seen in patients with other mitochondrial abnormalities. In addition, levels may not always be elevated in patients with *TAZ* mutations, and logistically urine samples are more difficult to collect than blood samples in infants. While *TAZ* gene analysis by mutation screening methods or DNA sequencing may be the most definitive test, the process is labor-intensive and costly. The most reliable biochemical test currently available to diagnosis BTHS is the HPLC tandem mass spectrometric (HPLC tandem MS) quantification of (monolyso)cardiolipin in blood cells and tissues developed by our laboratory. By establishing a collaboration between our laboratory and two major clinical centers for pediatric cardiology in the United States – Texas Children's Hospital in Houston, TX and Children's Hospital Boston in Boston, MA – we will investigate the frequency of BTHS in a group of high-risk individuals, namely pediatric patients who have been diagnosed with cardiomyopathy.

HPLC tandem MS analysis will be used to analyze the cardiolipin profile in lymphoblastoid cell lines and/or frozen tissue samples from pediatric patients with cardiomyopathy. Throughout the period of the grant, the same test will be used to prospectively test pediatric patients with cardiomyopathy at the two medical centers in whom consent for testing is obtained. The diagnosis of BTHS based on the characteristic cardiolipin profile will be confirmed by sequencing of the *TAZ* gene in our laboratory. Clinical features and *TAZ* mutation will be summarized descriptively. This project will determine whether BTHS is underdiagnosed in boys with cardiomyopathy, and it may also discover other defects in cardiolipin metabolism that cause cardiomyopathy. If the frequency of BTHS is found

(Continued from page 4)

to be significantly higher, the findings may help to promote disease awareness.

Additionally, we will perform pilot studies to determine the feasibility of expanding the HPLC tandem MS analysis of (monolyso)cardiolipin levels in blood spots. Although technically challenging, if successful this method has the potential to be a newborn screening test and could be used to determine the incidence of BTHS in the general population."

**Principal Investigator:** Mindong Ren, PhD

**Institution:** New York Univ. School of Medicine; New York, NY

**Title of Project:** *A Drosophila Model of Barth Syndrome*

**Amount:** \$40,000 / **Time Period:** 1 year

**Abstract:**

"Barth syndrome (OMIM #302060) is an X-linked inherited disorder characterized by cardioskeletal myopathy, neutropenia, abnormal mitochondria, and 3-methylglutaconic aciduria. It is associated with mutation in the tafazzin gene, a member of a superfamily encoding acyltransferases involved in phospholipid metabolism. Recent studies have shown that patients with Barth syndrome have a deficiency of cardiolipin, a polyglycerophospholipid present exclusively in mitochondria and required for their proper functioning, suggesting that tafazzin is involved in cardiolipin remodeling and the deficiency of cardiolipin underlies the clinical manifestations of Barth syndrome. What biochemical reaction tafazzin catalyzes and how the biochemical dysfunction leads to the tissue-specific pathophysiology associated with Barth syndrome are not known. In terms of the type of tafazzin mutation, the degree of cardiolipin deficiency, and the severity of the symptom, no specific genotype-phenotype correlation has been found, suggesting the existence of additional factors that modify disease expression.

The progress of current investigations into the molecular mechanisms underlying Barth syndrome has been hampered by the lack of animal models. Although tafazzin-null mutant yeast strains have been constructed and used to study the role of tafazzin in cardiolipin remodeling and mitochondrial

function, their usefulness is limited by their unicellular nature. We will generate a *Drosophila* model of Barth syndrome. Muscle is one of the most abundant *Drosophila* tissues and one of the most amenable to cell biological investigations. Accordingly, much of our knowledge of muscle development and function can be attributed to studies of *Drosophila*. Since cardioskeletal myopathy is the cardinal feature of Barth syndrome, these intrinsic advantages, together with the power of *Drosophila* genetics, make *Drosophila* a model of choice for investigating the role of tafazzin in muscle development and function as well as screening for modifiers of tafazzin function. To this end, we will pursue the following specific aims: 1) inactivation of the *Drosophila* tafazzin ortholog by imprecise P-element excision, 2) characterization of the phenotypes associated with the *Drosophila* tafazzin deletion, 3) rescue of the tafazzin deletion phenotypes by germline transformation, and 4) silencing of tafazzin expression by RNAi in transgenic flies."

**Principal Investigator:** Carolyn T. Spencer, MD

**Institution:** Univ. of Florida; Gainesville, FL

**Title of Project:** *Cardiac Functional and Electrophysiological Abnormalities of Barth Syndrome*

**Amount:** \$40,000 / **Time Period:** 2 years

**Abstract:**

"Barth syndrome is an X-linked disorder characterized by dilated cardiomyopathy, neutropenia, skeletal myopathy and growth delay. Clinical disease expression is variable, even within families. Mutations in the *TAZ* gene at Xq28 are responsible, leading to cardiolipin deficiency and mitochondrial dysfunction. To date, there has been no systematic evaluation of the cardiac phenotype in Barth syndrome. Recent reports suggest an increased incidence of arrhythmia, especially among adolescents and young adults (Spencer *et al.*, Pediatric Cardiology, 2005, accepted). This project is a longitudinal, observational study of a cohort of patients with Barth syndrome designed to evaluate the age-related risk of arrhythmia in addition to investigating the relationships of cardiac performance, skeletal myopathy, and biochemical correlates of disease severity. One of the questions

(Continued on page 6)

## Catalyst for Advances in Research ... (Continued from page 5)

to be evaluated in this clinical study is to determine if an age-related risk of cardiac rhythm disturbance is present and independent of the severity of cardiomyopathy. Secondly, the degree of cardiac dysfunction maybe related to other markers of disease severity, including neutropenia and degree of muscle myopathy. The aims are designed to answer these questions. The first specific aim will address analysis of cardiac rhythm abnormalities through non-invasive techniques. The second specific aim will investigate the type and degree of cardiomyopathy using detailed echocardiographic analysis. The third specific aim will address the degree of systemic disease severity using biochemical and hematological markers and quantitative muscle testing.

Patients will be enrolled initially at the University of Florida, and further data collection can be expanded to other sites. The initial phase of this study will take place over two years with the possibility of continued data collection. We anticipate that the results of this study will be valuable in guiding the medical care of patients with Barth syndrome, including screening for arrhythmias and the potential need for medical or device therapy for cardiac rhythm disturbance."

**Principal Investigator:** Arnold W. Strauss, MD

**Institution:** Vanderbilt Univ.; Nashville, TN

**Title of Project:** *Tafazzin Function in Animal Models of Barth Syndrome*

**Amount:** \$40,000 / **Time Period:** 1 year

### **Abstract:**

"Barth syndrome is an X-linked genetic disorder characterized by cardiomyopathy, skeletal myopathy and weakness, chronic fatigue, neutropenia, and organic aciduria that has high early mortality. This disorder is caused by mutations in the tafazzin (*TAZ*) gene that encodes a protein homologous to acyltransferases and is manifested by abnormal mitochondria that are deficient in cardiolipin, a key phospholipid. Thus, Barth syndrome is the prototype for mitochondrial phospholipid/cardiolipin biosynthetic and remodeling disorders and emphasizes the importance of this poorly studied pathway in mitochondrial function. The project will examine

the hypothesis that *TAZ* functions in the remodeling of cardiolipin and is essential in the generation of symmetric (C18:2)<sub>4</sub>(tetralinoleoyl)-cardiolipin that is critical for mitochondrial energy generation. To address this hypothesis, we used antisense-morpholino knockdown technology to create the first animal model of Barth syndrome in zebrafish. These *taz*-deficient embryos exhibit impaired overall and cardiac development, with bradycardia, edema, and high mortality. This suggests that *taz* is essential for normal vertebrate development, especially of the heart and cardiac pacemaker and conducting system. To test this second hypothesis, we will pursue the following aims: 1) assessment of function of Barth syndrome *taz* mutations and designed *taz* mutation predicted as essential for function, using rescue with these mutant *taz* mRNAs in the knockdown model, 2) delineation of zebrafish and murine *taz* mRNA and protein with subcellular localization. These studies will allow delineation of *taz* function both in mitochondrial energetics and vertebrate development and delineation of the effects of various *taz* mutations on its function. Understanding Barth syndrome pathogenesis, a mitochondrial phospholipid/cardiolipin biosynthetic and remodeling pathway defect has implications for defining this pathway's role in normal mitochondrial functions, such as energy generation, apoptosis, and development."

We at BSF are truly grateful to all those who have made these advances possible. This certainly includes the bench scientists and physicians who have worked so diligently on this disorder or who have reviewed the grant applications that we receive, but it also includes the boys and young men who have allowed their medical data and their biological samples to be used to advance knowledge. And it most definitely includes as well all those who have been so generous in providing the finances that are required in order to offer financial support for this work. We couldn't do it without all of you. There still is much more that needs to be learned, but this is a very good start.

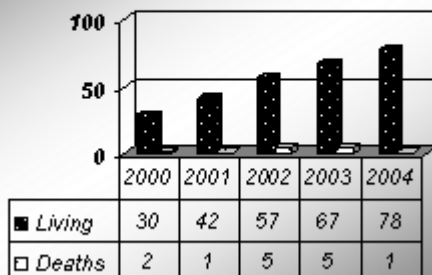
*(See page 19 for specific dates of BSF's 2006 International Scientific/Medical & Family Conference, when we will reconvene to discuss research efforts and how to further advance knowledge about the natural history, biochemical basis, gene product function and treatment of Barth syndrome.)*

# Year-End Report ... A Summary of BSF's Progress in 2004 *(Continued from page 3)*

**Goal 2.** *To stimulate the development of successful treatments for Barth syndrome (a multi-system disorder) and enable their delivery.*

- a. First multi-disciplinary clinic for Barth syndrome was held in Bristol, England on June 18, 2004
- b. Hosted 2 days of multi-disciplinary clinics at the 2004 conference in Orlando, Florida for all affected individuals (31 affected individuals were present)

**Number of People Affected by Barth Syndrome by Year**



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

- a. Awarded four research grants for the 2004 Grant cycle for a total of \$157,000 over a two-year period (see cover article)

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

- a. Hosted 2004 BSF Family Conference (141 family members present)
  - i) Sponsored the recording of DVD's of the entire conference for families and scientists
- b. Registry increased to (79) living individuals worldwide in 2004; and (67) known deceased through 2004
- c. One child diagnosed in utero

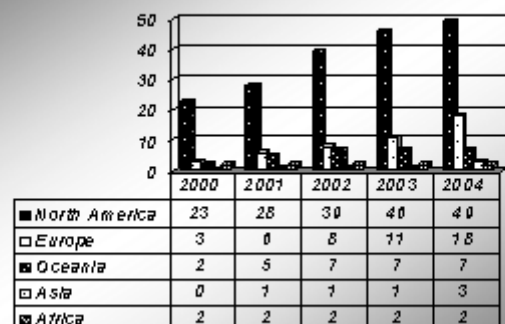
**Goal 5.** *To build and sustain a broad base of committed contributors who will provide the funds we need to achieve our vision.*

- a. Hosted multiple fund raising events and broke a record on the number of donors as a result of our grass roots fund raising efforts (see "Fund Raising for BSF", pg. 18 of this issue).

**Goal 6.** *To inspire and make effective use of an organization dedicated to reaching our vision.*

- a. Attended the 2004 Genetic Alliance Conference in Arlington, VA
- b. Hosted BSF Volunteer Enrichment Workshop to aid in fulfilling BSF goals and objectives (28 volunteers present)
- c. Restructured our volunteer organization
- d. Joined the National Health Council as a Voluntary Health Agency, meeting 41 standards of excellence to become a member of the organization
- e. Signed on to the Open Access to research petition which is in support of providing open access to information about Federally funded research in the U.S.
- f. Canada filed articles of incorporation
- g. Participated as a Public Interest Organization (PIO) in the 2004 National Heart Lung and Blood Institute (NHLBI) annual meeting
- h. Shelley Bowen appointed as Executive Director of BSF in August, 2004

**Number of People Affected by Barth Syndrome by Continent**



# BARTH SYNDROME FOUNDATION'S 2004 FINANCIAL REPORT

By Steve McCurdy, BSF Chairman and CFO

We ended the year with a solid balance sheet – over \$813,000 in Fund Balances available for future years' programs. These Fund Balances are securely invested in insured bank certificates of deposit which mature at different times over the next two years so that we will always have funds available to run BSF. These Fund Balances provide us with insurance against any shortfall in fund raising and at our current rate of spending equates to almost two years of budgeted expense. We do not want to have to use them, of course, but knowing that they are there does allow us to be more ambitious in our program planning!

The Barth Syndrome Foundation, Inc.				
Statement of Financial Position				
At December 31				
	2004	2003	2002	
<b>Assets</b>				
Investment Assets	\$ 934,593	\$ 942,028	\$ 385,522	
Other Assets	\$ -	\$ 1,450	\$ 29,597	
<b>Total Assets</b>	<b>\$ 934,593</b>	<b>\$ 943,478</b>	<b>\$ 415,119</b>	
<b>Liabilities</b>	<b>\$ 121,557</b>	<b>\$ 22,600</b>	<b>\$ 76,859</b>	
<b>Net Assets</b>				
Unrestricted	\$ 796,036	\$ 903,878	\$ 312,182	
Temporarily Restricted	\$ 17,000	\$ 17,000	\$ 29,038	
<b>Total Net Assets</b>	<b>\$ 813,036</b>	<b>\$ 920,878</b>	<b>\$ 341,220</b>	
<b>Total Liabilities and Net Assets</b>	<b>\$ 934,593</b>	<b>\$ 943,478</b>	<b>\$ 415,119</b>	

As I look at other, similar rare disorder organizations, very few are fortunate enough to enjoy such a sizeable reserve. Thanks to our anonymous donor, our own fund raising activities and careful management, we have been incredibly blessed. But a quick review of our Statement of Activities (what non-profits call their income statement) reveals the challenges ahead.

During 2004, BSF raised almost \$340,000. If you exclude the large contributions from our generous anonymous donor in past years, this is more money than we have ever raised before and an accomplishment worth heralding. Our largest single donation in 2004 was for \$50,000, and we had more than 500 individuals, corporations and foundations contribute \$50 or more to our programs... more than

63 people contributed \$1,000 or more. We also earned over \$17,000 in interest on our investments. It was a very good year on the revenue side!

Where did we spend our money? Seventy eight percent (78%) of our total expenses went toward our programs:

- In 2004 we awarded almost \$174,000 in research grants to five separate investigators who are advancing our knowledge and understanding of the genetic and biochemical pathways of the disorder, the clinical manifestations and treatment of Barth syndrome and creating animal models for future research efforts.
- Many of you attended our BSF Conference in Orlando in July. That Conference cost over \$133,000 to run. We paid for conference rooms, food, travel and accommodations for our speakers and for the recording and production of the presentations on DVDs which are helping us educate families, physicians and scientists who were unable to attend.
- Representatives of BSF attended six medical conferences in 2004, setting up the BSF Booth and distributing brochures, information and increasing awareness of Barth syndrome among those who will find, treat and someday perhaps cure this disease. Our awareness programs cost over \$15,000.
- We invested in volunteer development and family outreach both in the United States and internationally.

About 17% of our total expenses were general and administrative in nature - the same proportion as in the previous year. These covered accounting and auditors, office and Board expenses, insurance, dues & conferences, publications, state filing costs, etc.

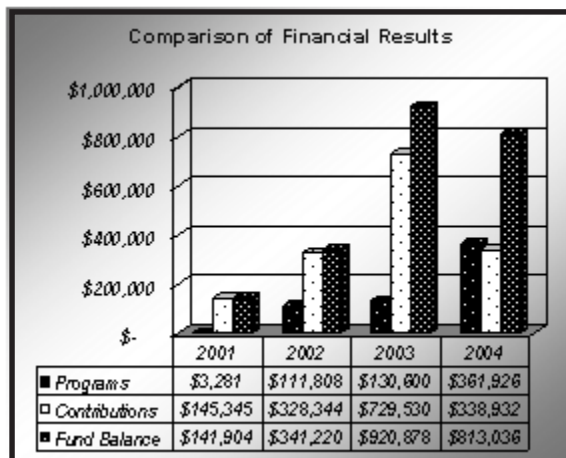
(Continued on page 9)



The Barth Syndrome Foundation, Inc. Statement of Activities For the Years Ended December 31			
	2004	2003	2002
<b>Public Support and Revenue</b>			
Contributions	\$ 338,932	\$ 729,530	\$ 328,344
Other	\$ 17,380	\$ 11,157	\$ 3,682
<b>Total Support and Revenue</b>	<b>\$ 356,282</b>	<b>\$ 740,687</b>	<b>\$ 332,026</b>
<b>Expenses</b>			
Program Services	\$ 361,926	\$ 130,600	\$ 111,808
Management and General	\$ 79,547	\$ 27,083	\$ 14,331
Fund Raising	\$ 22,651	\$ 3,346	\$ 6,571
<b>Total Expenses</b>	<b>\$ 464,124</b>	<b>\$ 161,029</b>	<b>\$ 132,710</b>
<b>Change in Net Assets</b>	<b>\$ (107,842)</b>	<b>\$ 579,658</b>	<b>\$ 199,316</b>
<b>Net Assets - Beginning of Period</b>	<b>\$ 920,878</b>	<b>\$ 341,220</b>	<b>\$ 141,904</b>
<b>Net Assets - End of Period</b>	<b>\$ 813,036</b>	<b>\$ 920,878</b>	<b>\$ 341,220</b>

And finally, BSF spent about 5% of our expenses raising money. Sometimes our fund raising costs are borne by our fund raisers – things like mailing costs. But the costs of larger and more complex events such as the Annual BSF Golf Tournament are picked up by BSF. All of our fund raising activities in 2004 raised far more than they cost.

But if you look further, you will see that we spent more than \$464,000 in 2004, a net deficit of expenses over revenue of almost \$108,000. This deficit was funded by a reduction in our Fund Balance. In effect, we dipped into our savings account in 2004 because we spent more than we earned. The Board manages BSF's finances closely, approving every program and expenditure. The BSF Conference is put on once every two years, and created a significant demand for funds in 2004. While this \$133,000 event will not occur in 2005, we have already begun to plan its funding for 2006.



## 2005 Budgets

BSF's 2005 Budget anticipates approximately \$416,000 in expenses, including approximately \$300,000 in program expenses. Not included as yet are expenses related to the start-up of the BSF Blood and Tissue Bank and Medical Database (a more formalized Registry). These programs are being studied and budgets are not yet available, but it is clear that these programs, which are critical to the success of future research and development of improved treatments, will be expensive. As mentioned above, we must also begin raising funds to help cover the cost of our July 2006 BSF conference. BSF is becoming a more powerful force on our behalf. But as it does so, more and more people are coming to depend on it and its programs. When we start up the Blood and Tissue Bank and Medical Database, they must continue to operate every year. We cannot decide to fund them one year, but not the next. To be prudent, we will need to be confident that we have sufficient funding sources from year to year. Our future success is now even more determined by our ability to raise money.

Our Development committee has received commitments from people who have raised funds for BSF in the past to raise \$200,000 in 2005. This leaves a shortfall in fund raising of at least \$216,000 for 2005. And while we typically also enjoy a few large, unbudgeted contributions each year, we cannot count on these to make up the deficit we see in 2005. **Clearly, BSF needs additional help to close our budget deficit in 2005!**

All in all, however, 2004 was an important year for The Barth Syndrome Foundation. We enhanced and grew our programs, grew our volunteer base, found more families, increased our focus on our medical and scientific agenda, and raised more money from grass roots sources than ever before. Our financial position is strong and our future is bright! We can all be proud of what we have accomplished... and after celebrating let's get back to work. Our kids are counting on us.



# OPPORTUNITIES TO PARTICIPATE IN ONGOING RESEARCH

## UNIVERSITY OF FLORIDA

Drs. Carolyn Spencer, Barry Byrne, and Randall Bryant are continuing their data collection on the cardiac and clinical findings in Barth syndrome. Many of you participated in this data collection in Orlando at BSF 2004 conference. Dr. Spencer has been awarded a BSF research grant, and this grant includes some travel money for families to go to the University of Florida to continue to participate in this project (both returning families and new families). If you would like to discuss a potential visit to the University of Florida, please contact Dr. Spencer at [cspencer@pedcard.ufl.edu](mailto:cspencer@pedcard.ufl.edu).

It may be possible to provide international families a stipend although it would not fully cover the cost. These families can also contact Dr. Spencer if interested. If travel to the U.S. is not possible but you would like to include your son's data, then you (or your child's cardiologist) may also contact Dr. Spencer at the above e-mail address.

## KENNEDY KREIGER INSTITUTE

The Cognitive Development Project is designed to help us understand the development of cognitive and academic skills in young children. One component of the project involves following the development of these skills in young children with Barth syndrome. We are currently recruiting children who are either in Kindergarten, First, Second or Third grade and who have Barth syndrome.

Participation will involve several hours of psychological and academic achievement testing, over one or two days. The testing will include measures of reading, mathematics, spatial reasoning, and other problem solving skills. Parents may receive a summary of their child's test performance following each evaluation, if requested. The testing will occur at the Kennedy Krieger Institute in Baltimore, Maryland, or elsewhere, depending on your geographic region of residence. There is no charge to you for any of this testing.

If you desire more information, or if you wish to enroll your child in this project, please contact Dr. Michele Mazzocco, Principal Investigator of this research project, at (443) 923-4125, or Anne Henry, Research Assistant, at (443) 923-4121. If you prefer, you may also e-mail us at [henrya@kennedykrieger.org](mailto:henrya@kennedykrieger.org). There are no significant risks to participation, nor any direct medical benefits. Minor risks include finding some of the activities too challenging or too easy.



## 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.

### Tools for Zebrafish Research

(Initiative number: PAR-05-080)

Purpose: To encourage investigator-initiated applications designed to exploit the power of the zebrafish as a vertebrate model for biomedical and behavior research. **Please visit:** <http://grants.nih.gov/grants/guide/pa-files/PAR-05-080.html> for more details.

### Chronic Fatigue Pathophysiology and Treatment

(Initiative number: PA-05-030)

Purpose: To support investigator-initiated research on the epidemiology, diagnosis, pathophysiology, and treatment of chronic fatigue syndrome (CFS) in diverse groups and across the life span. **Please visit:** <http://grants.nih.gov/grants/guide/pa-files/PA-05-030.html> for more details.

## **2005 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, gene product function, and treatment of Barth syndrome.*

### **Background**

Barth syndrome is a serious X-linked recessive condition associated with cardiomyopathy, neutropenia, skeletal muscle weakness and hypoplasia, 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 2005, divided among several one- or two-year grants of up to \$40,000 each. Funds will be available in January 2006, as soon as the successful grant applicants have been notified.

### **Process**

The Barth Syndrome Foundation, Inc. has 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 and/or the Animal Use and Protection Committee for any work involving animal projects. 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](http://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 **Friday, September 30, 2005.**

### **Contact Information**

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

# THE INTERPRETATION OF GENETIC TESTING RESULTS FOR BARTH SYNDROME

Karla R. Bowles, PhD, FACMG, John Welsh Cardiovascular Diagnostic Laboratory  
Department of Pediatrics (Cardiology), Baylor College of Medicine, Houston, TX



When many individuals participate in genetic testing, they often assume that the results will give them a concrete answer. Unfortunately, this is often not the case.

Genetic testing is complex and can give results that are difficult to interpret by both medical professionals and patients. Before undertaking genetic testing, it is important to distinguish between a clinical diagnosis and a genetic diagnosis. A clinical diagnosis is made by the patient's physician(s) based upon the symptoms of the patient and the results of all tests that have been done on behalf of the patient. This testing may include, but is not limited to, blood tests, biochemical analysis, analysis of heart function, etc. Thus, many aspects of the patient are evaluated when making a clinical diagnosis.

A genetic diagnosis is predominantly based upon the results obtained by examining a patient's genetic material, which can be either DNA or mRNA. In the case of Barth syndrome, most genetic testing begins by performing DNA sequencing analysis on the patient's *TAZ* (*G4.5*) gene, which is the gene for Barth syndrome. This testing has four possible outcomes:

1. A disease-causing mutation is identified in the patient.
2. An alteration in the patient's DNA is identified, but this alteration does not cause Barth syndrome.
3. An alteration in the patient's DNA is identified, but there is not enough information to determine if this alteration causes Barth syndrome.
4. No disease-causing mutations are identified in the patient's DNA.

In the first case, if a disease-causing DNA mutation is identified in a male individual clinically diagnosed with Barth syndrome, then the results of the genetic testing support this clinical diagnosis. If a disease-causing mutation is identified in a male who currently does not have clinical symptoms of Barth syndrome (for example a brother of a patient with Barth syndrome), then we would consider this individual to be at extremely high risk for developing Barth syndrome.

A second possible outcome of genetic testing is the identification of a DNA change that is known not to result in disease. Every person's genetic material is different, with the exception of identical twins/triplets/etc. Thus, when we sequence an individual's DNA, we often find minor changes. The vast majority of these changes do not cause disease. Some of these changes may be responsible for normal variations in the general population, such as differences in eye color, while other DNA changes have no effect at all. Many of these "harmless" DNA changes have been documented in the scientific literature. Thus, when we identify one of these DNA changes in a diagnostic laboratory, we are able to reference the scientific literature and determine that it is not associated with disease.

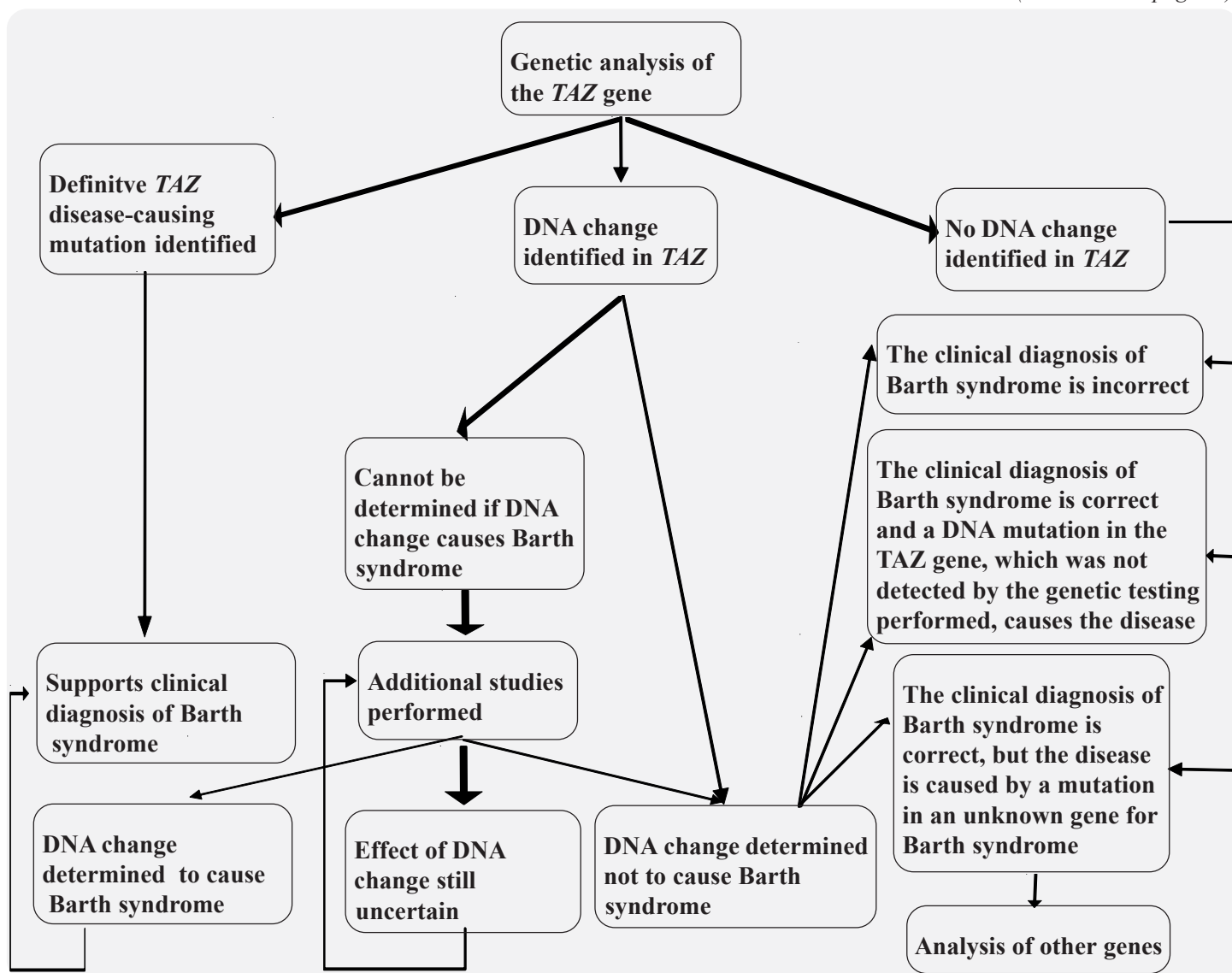
A third possible outcome of genetic testing is that we identify an alteration in a patient's DNA, but we cannot determine if that alteration causes disease. This is usually the most difficult result of genetic testing for patients and their family members to understand. To many, it would seem that if a patient has a clinical diagnosis of Barth syndrome and a DNA change is identified in the *TAZ* gene, then that DNA change must be the cause of the disease. However, this is often not the case. Multiple sequence changes, which do not cause Barth syndrome, have already been identified in the *TAZ* gene. These DNA changes are found in the general

(Continued from page 12)

healthy population and represent natural variations in DNA sequence that do not cause disease. Many of these sequence changes can be found in the scientific literature, on-line databases, and private laboratory databases. However, this list of “normal” sequence variations is incomplete. When we identify certain sequence changes in patients with Barth syndrome that have never been identified in either other patients with Barth syndrome or in healthy individuals from the general population, we cannot be certain if these DNA changes cause Barth syndrome or if they are natural sequence variations that do not cause disease. In addition, some sequence changes published as “mutations” in the scientific literature have not been definitively proven to cause Barth syndrome and require cautious interpretation in the diagnostic laboratory setting. Additional studies may provide information that can

help us determine whether or not these DNA changes cause Barth syndrome. For example, if we sequence a large number of patients from the general population and identify a sequence change in several healthy male individuals, then we would assume that this sequence change does not cause Barth syndrome. However, if we sequence a sufficient number of family members of a patient with Barth syndrome and find that a sequence change is only identified in males with Barth syndrome, their mothers, and possibly other female relatives, and not identified in older healthy male relatives, then this would provide evidence that this sequence change may be a disease-causing mutation. Furthermore, if a sequence change is identified in a male with Barth syndrome, but not in his mother, then this would provide strong evidence that the sequence change is a new disease-causing

(Continued on page 14)



## The Interpretation of Genetic Testing

(continued from page 13)

mutation that occurred either during the development on the mother's egg or during fetal development. Unfortunately, the significance of many of these DNA changes may remain unclear for an indefinite amount of time.

Finally, genetic testing may fail to identify a disease-causing mutation in the *TAZ* gene. However, it is important to note that a "negative" result or an "inconclusive" genetic testing result, as just discussed above, does not necessarily mean that the clinical diagnosis of Barth syndrome is incorrect. Although we strive to offer the best genetic test possible for Barth syndrome, we must also design the test to be affordable to patients. Because of this, the currently available diagnostic tests probably do not detect all possible disease-causing mutations. It is possible that some patients with a definitive clinical diagnosis of Barth syndrome have a mutation in the *TAZ* gene which cannot be detected by the genetic tests that are currently available. In addition, we cannot exclude the possibility that mutations in an unknown gene may also result in clinical symptoms consistent with Barth syndrome. The diagnosis of "Barth syndrome" is a clinical diagnosis based upon the clinical symptoms of the patient. If a disease-causing *TAZ* DNA mutation is identified in a patient with Barth syndrome, then this would support the diagnosis of Barth syndrome. However, genetic testing cannot definitively exclude the clinical diagnosis of Barth syndrome. Thus, for a patient with a definite clinical diagnosis of Barth syndrome, if the results of the *TAZ* genetic testing are negative or inconclusive, the clinical diagnosis of Barth syndrome can still be correct. Genetic testing for *TAZ* mutations is only one out of many pieces of information that physicians can use to make a diagnosis. The exclusion of the diagnosis of "Barth syndrome" based on only the results of genetic testing would be inappropriate. The results of genetic testing, whether they be positive, negative, or inconclusive, must be correlated with other medical data from the patient in order to determine whether or not a patient has Barth syndrome.



## 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.



The Cardiomyopathy and Heart Failure Program at the  
Children's Hospital of Philadelphia

Announces

Barth Syndrome Multidisciplinary Clinics:

\* January 13, 2005 \* April 14, 2005 \* July 14, 2005

Interested families should contact Genotra Byus, Program  
Administrator at (215) 590-6051, for more information.

The Children's Hospital of Philadelphia  
A pediatric healthcare network

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# HIGHLIGHTS: What is Known about Barth Syndrome, as of May 2005

**1981 and 1983: Peter G. Barth, pediatric neurologist in The Netherlands, et al., first fully described “An X-linked mitochondrial disease affecting cardiac muscle, skeletal muscle and neutrophil leucocytes.”**

*An X-linked mitochondrial disease affecting cardiac muscle, skeletal muscle and neutrophil leucocytes.*

~ Barth PG, Scholte HR, Berden JA, Van dK-VMJM, Luyt-Houwen IE, Van tV-KET, Van dHJJ, Sobotka-Plojhar MA

**1991: Richard I. Kelley et al. found 3-methylglutaconic aciduria to be a biochemical marker for Barth syndrome.**

*X-linked dilated cardiomyopathy with neutropenia, growth retardation and 3-methylglutaconic aciduria.*

~ Kelley RI, Cheatham JP, Clark BJ, Nigro MA, Powell BR, Sherwood GW, Sladky JT, Swisher WP

**1995: Gerald F. Cox et al. reported that G-CSF can be used successfully to treat Barth neutropenia.**

*Correction of neutropenia in Barth syndrome by G-CSF.*

~ Cox GF, Pulsipher M, Rothenberg M, Korson M, Kelley RI

**1996: Silva Bione et al. discovered the gene on distal arm of Xq28 (called TAZ1 or G4.5; proteins encoded by the gene called tafazzins).**

*A novel X-linked gene, G4.5, is responsible for Barth syndrome.*

~ Bione S, D’Adamo P, Maestrini E, Gedeon AK, Bolhuis PA, Toniolo D

**1997: Adwani et al. documented heart transplantation as being successful in Barth patient.**

*Heart transplantation for Barth syndrome.*

~ Adwani SS, Whitehead BF, Rees PG, Morris A, Turnball DM, Elliott MJ, de Leval MR

**1997: Andrew F. Newald hypothesized that tafazzin is acyltransferase involved in phospholipid biosynthesis.**

*Barth syndrome may be due to an acyltransferase deficiency.*

~ Neuwald, AF

**1998: Shown by Orstavik et al. that female carriers of BTHS are healthy due to extremely skewed pattern of X-chromosome inactivation.**

*X-chromosome inactivation in carriers of Barth syndrome.* ~ Orstavik KH, Orstavik RE, Naumova AK, D’Adamo P, Gedeon A, Bolhuis PA, Barth PG, Toniolo D

**2000: Peter Vreken et al. demonstrated that tafazzin is involved in cardiolipin remodeling in Barth fibroblasts.**

*Defective remodeling of cardiolipin and phosphatidyl-glycerol in Barth syndrome.* ~ Vreken P, Valianpour F, Nijtmans LG, Grivell LA, Plecko B, Wanders RJA, Barth PG

**2001: Michele Mazzocco et al. published preliminary data suggesting a cognitive phenotype for Barth syndrome, including lower visual spatial skills.**

*Preliminary evidence for a cognitive phenotype in Barth syndrome.*

~ Mazzocco MM, Kelley RI

**2002: Michael Schlame et al. found tetralinoleoyl-cardiolipin to be nearly absent in platelets, fibroblasts and muscle from Barth patients.**

*Deficiency of tetralinoleoyl-cardiolipin in Barth syndrome.* ~ Schlame M, Towbin JA, Heerdt PM, Jehle R, DiMauro S, Blanck TJJ

**2003: Miriam Greenberg et al. constructed a taz1 yeast mutant model.**

*Aberrant cardiolipin metabolism in the yeast taz1 mutant: a model for Barth syndrome.* ~ Gu Z, Valianpour F, Chen S, Vaz FM, Hakkaart GA, Wanders RJA, Greenberg ML



*Shelley Bowen visits with Arnold Strauss, M.D., at his lab located at the Vanderbilt Children's Hospital in Nashville, TN.*

**2004: Arnold W. Strauss et al., and Mauro Degli Esposti et al., independently created zebrafish knock-in models of Barth syndrome; Strauss demonstrated that G4.5 gene is essential for normal cardiac development in zebrafish.**

**2004: Iris L. Gonzalez presented data in 2004 that was then published in 2005 that only two functional forms of G4.5 mRNA exist (delta 5 and full-length) in humans; also noted that exon 5 does not exist in yeast or rodents and that the full ability to splice developed only after evolutionary split from Old World monkeys, but is important to humans.**

*Barth syndrome: TAZ gene mutations, mRNAs, and evolution.* ~ Gonzalez IL

**2005: Carolyn T. Spencer et al. documented the risk of serious arrhythmias and sudden cardiac death in adolescent Barth patients.**

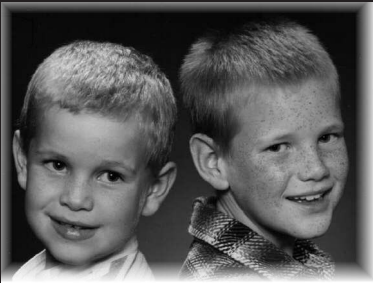
*Ventricular arrhythmia in the X-linked cardiomyopathy Barth Syndrome. Pediatric Cardiology, (accepted for Spring 2005 publication).*

~ Spencer CT, Byrne BJ, Gewitz MH, Wechsler SB, Kao AC, Gerstenfeld EP, Merliss AD, Bryant RM

**Currently, Drosophila and mouse models of Barth syndrome are being developed.**







# 2005 CALENDAR OF EVENTS



## January 2005

January 20 Four new grants awarded for Research into Barth syndrome

January 25 BSF Board of Directors' Meeting

## February 2005

February 8-9 Participation in NHLBI's Public Interest Organization Meeting; Bethesda, MD

February 10-12 Participation in National Health Council's 2005 Voluntary Health Leadership Meeting; Tucson, AZ

February 11 BSF Special Board Meeting/Executive Committee Meeting

February 16-20 BSF booth at 8th Annual Update in Pediatric Cardiovascular Disease Meeting; Orlando, FL

## March 2005

March 4 Barth Syndrome Trust Board of Directors' Meeting

March 6 BSF of Canada Annual Meeting

March 13-15 Participation in NHLBI/ORD Working Group on Cardiomyopathies in Children with Rare Diseases; Bethesda, MD

March 17 BSF Executive Committee Meeting

March 17-20 BSF booth at 2005 American College of Human Genetics Annual Clinical Genetics Meeting; Dallas TX

March 21 BSF of Canada Board Meeting

## April 2005

April 5 BSF Board of Directors' Meeting

April 12 -30 Europe Outreach

April 15 European Mainland Conference; AMC, Amsterdam, Netherlands

April 18 BSF of Canada Board Meeting

## May 2005

May 1-2 **Barth Syndrome Awareness Month**  
Barth Syndrome Trust Workshop; Hampshire, UK

May 9 BSF of Canada Board Meeting

May 14-16 BSF booth at 2005 Pediatric Academic Societies' Annual Meeting; Washington, DC

May 17

BSF Executive Committee Meeting

May 25

Barth Syndrome Trust Board of Directors' Meeting

## June 2005

June 3-5 Southeastern Regional Outreach; Clearwater Beach, FL

June 11 Western Regional Outreach; Salt Lake City, UT

June 13 BSF of Canada Board Meeting

June 15-18 BSF booth at ASECHO 16th Annual Scientific Session; Boston, MA

June 22 Invited by the American Society of Hematology (ASH) to participate in special meeting between ASH Leadership and Advocacy Groups that represent patients with blood diseases; Washington, DC

## July 2005

July 5 BSF Executive Committee Meeting

July 14 Children's Hospital of Philadelphia Barth Clinic

July 15-16 Mid-Atlantic Outreach; Wynnewood, PA

July BSF Board of Directors' Meeting (date to be determined)

## September 2005

September 8 BSF Executive Committee Meeting

September 11 Barth Syndrome Trust Board of Directors' Meeting

September 28-  
October 1

BSF booth at Child Neurology Society; Los Angeles, CA

## October 2005

October BSF Board of Directors' Meeting

## November 2005

November 13-16 BSF booth at American Heart Association; Dallas, TX

November 15 BSF Executive Committee Meeting

## December 2005

December 3-6 BSF booth at The American Society of Hematology 47th Annual Meeting and Exposition; New Orleans, LA

# FUND RAISING FOR BSF

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

With the help of our dedicated volunteers and family members, BSF set several new records in fund raising in 2004. You raised more money at a grass roots level, almost \$340,000, from more people, businesses and family foundations - more than 740 donations - than ever before. This comparison excludes the sizeable donations we have received in the past from our Anonymous Donor but reflects the growing and much appreciated grass roots effort made by all of BSF's fund raising supporters. The BSF 2004 Financial Report found elsewhere in this newsletter describes the growing effectiveness, and cost, of BSF's programs. None of these programs would be possible without the support of the volunteers who invest their time, creativity and efforts to help BSF raise money.... and have a great time doing it!

I described in some detail the major fund raising efforts of 2004 in our last newsletter – including the Ironman Fund Raiser led by Gary and Colette Rodbell, John Steigerwald and Tim Monetti which raised almost \$150,000, awarding them 2nd place for the Janus Charity Challenge; Jan and Steve Kugelmann's 3<sup>rd</sup> Annual BSF Golf Tournament, which brought in almost \$25,000; Tom and Laurie Monahan and their friend Ed Nottle who raised \$15,000 with a Sports Night in Brockton, Massachusetts; solicitation letters sent to friends and family by the McCurdy, Wilkins and Fairchild families; the Higgins' Bowling Night; business and fraternal sponsorship of our 2004 BSF Conference and a host of other donations which came to BSF by mail and via the internet.

And in 2005, we hope to have an even more successful year in fund raising. The BSF Fund Raising Committee headed by Scott Oldewage and including Leslie Buddemeyer, Jan Kugelmann, Steve McCurdy, and Tom Monahan, has received commitments from past fund raisers for BSF to raise \$200,000 in 2005. The BSF operating budget for 2005 is over \$400,000, so we still have a gap to fill and our friends and family are already stepping up to help!



*Before and after photos of Sarah Bull of Bristol, England, who raised over £5,000 for BSF/BST by shaving her head - true dedication from this Mum! Sarah, you look beautiful and Dave, thank you for your support!*



Perhaps the most dramatic effort is being made by Sarah Bull, Corey, Kai and Ashley's Mum, who shaved off all of her hair on Friday the 13<sup>th</sup> to raise money for BST and BSF! Both Kai and Ashley have Barth syndrome, and Sarah's eldest son Cory has a rare disorder called hypotrichosis - which leaves him without hair or eyebrows. Sarah said: "I wanted to do something to support all of my sons. Cory's hypotrichosis is a totally separate issue from Barth syndrome, but I thought it was a chance to support all of them." Sarah and her husband Dave raised well over £5,000 and received tremen-

dous publicity which increased awareness of Barth syndrome – always a welcome side benefit of fund raising events.

Tom and Laurie Monahan and Ed Nottle continued their efforts on behalf of BSF by raising an additional \$14,000 in a second sports related event in Brockton, Massachusetts.

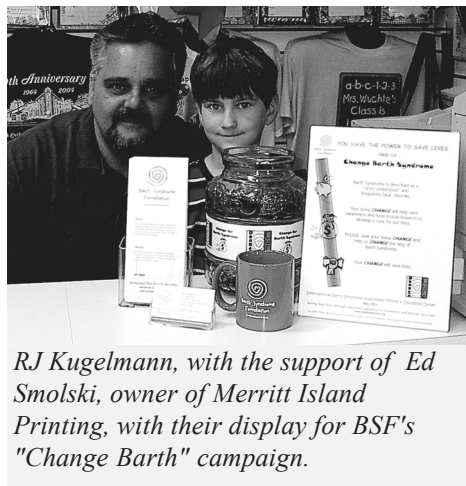
Jan Kugelmann and Leslie Buddemeyer are spearheading the International Barth Syndrome Awareness Month & Donation Drive throughout

*(Continued on page 19)*

# FUND RAISING FOR BSF (Continued from page 18)

May, with families and friends saving coins to increase awareness and benefit BSF.

And rumor has it that BSF is about to have its own bracelet in BSF blue, modeled after the successful Live Strong bracelet started by the Lance Armstrong Foundation whose mission is to support cancer survivors! (And we even have their blessing to do so.) More on that via the BSF Listserv as details are finalized.



*RJ Kugelmann, with the support of Ed Smolski, owner of Merritt Island Printing, with their display for BSF's "Change Barth" campaign.*

*"If any of you have ever considered raising money and had this 'How on earth am I going to do this...?' feeling straight afterwards... well join the Club!.. Until two years ago raising money for me felt like Mission Impossible.... Yet in 2004, together with a few friends, we managed to raise £8000 for Barth Syndrome Trust in the UK."  
~ Isabelle Lemettre*

There are many, many ways to raise money and awareness for BSF, some of which were described on the BSF Listserv during March. A few comments from these stories are excerpted below:

*"Just before Christmas I approached my CEO and asked how he would feel about creating a charitable donation for the BSF ... he knew nothing about BSF and it was a great time to sit down and create some awareness. ' The more I spoke with my CEO about the disease, the bigger his heart grew.' At the Christmas Party he announced that he would be donating \$500.00 a month as long as the company was profitable that month. At the end of the year, my company will have contributed \$12,000 to \$15,000 for each one of our boys... These people don't know you and many of them don't even know me personally, yet they contribute to our cause."*

*~ Scott Oldewage*

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](http://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.

We all owe a debt of gratitude to these people for recognizing that BSF cannot do what it does for all of us without financial support. Each of our programs takes us closer to our vision. Our progress is accelerating. But we need everyone's help if we hope to achieve our ambitious goals and find an effective treatment and a cure for every boy and man affected by Barth syndrome. We can't live without it!



## SAVE THE DATE FOR BSF's 2006 CONFERENCE

The Barth Syndrome Foundation is pleased to announce that we will be returning to Disney's Coronado Springs Resort in Lake Buena Vista, Florida on **Monday, July 3rd thru Saturday, July 8th, 2006** to host BSF's biennial International Scientific/Medical and Family Conference. Please mark your calendars and start saving for this important conference.

July 3, 2006	Family Reception
July 4-5, 2006	Clinics
July 5, 2006	Scientific/Medical Reception
July 6, 2006	Family & Scientific Sessions
July 7, 2006	Family & Scientific Sessions
July 8, 2006	Family & Scientific Sessions

If you would like further information, please contact:

Shelley Bowen: [sbowen@barthsyndrome.org](mailto:sbowen@barthsyndrome.org)  
Jan Kugelmann: [jkugelmann@barthsyndrome.org](mailto:jkugelmann@barthsyndrome.org)  
Lynda Sedefian: [lsedefian@barthsyndrome.org](mailto:lsedefian@barthsyndrome.org)

# BARTH SYNDROME IN THE

## News



**TIM MONETTI: CONOCO PHILLIPS' IRONMAN**  
~ *ConocoPhillips Trainer Newsletter (Spring 2005)*  
(USA)

**EEN UITERST ZELDZAME AANDOENING (AN EXTREMELY RARE DISORDER)**  
~ *de Stentor (The Netherlands)*  
April 26, 2005

**MOTHER'S SHORT CUT FOR ILL SONS**  
~ *The Evening Post (Bristol, England)*  
March 30, 2005  
Article searchable online at:  
<http://www.epost.co.uk/displayNode.jsp>

**BBC RADIO BRISTOL INTERVIEW**  
~ Bristol, England  
March 30, 2005

**BBC POINTS WEST TV INTERVIEW**  
~ Bristol, England  
March 30, 2005

**JAMES GIVES COMPUTER GAMES A MISS FOR CASH**  
~ *Basingstoke and North Hampshire Gazette*  
(United Kingdom)  
March 4, 2005

**MOTHER CALLS FOR DOCTORS' HELP TO FIGHT RARE DISEASE.**  
~ *The Mercury (South Africa)*  
April 22, 2005  
Article searchable online at:  
[www.themercury.co.za](http://www.themercury.co.za)

**EERSTE SYMPOSIUM BARTH SYNDROOM (FIRST SYMPOSIUM ON BARTH SYNDROME)**  
~ *Dutch Association for Neuromuscular Diseases*  
(The Netherlands)  
April 8, 2005  
Article searchable online at:  
[www.vsn.nl/nieuws/nieuws.php?nieuws\\_id=500](http://www.vsn.nl/nieuws/nieuws.php?nieuws_id=500)

**BARTH SYNDROME: RARE OR RARELY DIAGNOSED**  
~ *Genetic Interest Group Newsletter (Winter 2004/05)*  
(United Kingdom)  
Article searchable online at: [www.gig.org.uk](http://www.gig.org.uk)

**MEMBER SUCCESS SPOTLIGHT: BARTH SYNDROME FOUNDATION**  
~ *G. Advocacy Newsletter (Winter 2004) (USA)*  
Article searchable online at: [www.geneticalliance.org](http://www.geneticalliance.org)

## FAMILY SERVICES ~

By Shelia Mann, Chair, Family Services

## STRIDES TO FOSTERING EMPOWERMENT



Recently, after taking part in the Volunteer Enrichment Workshop in Steinhatchee, Florida, I have had the pleasure of taking on the role of BSF Family Services Chair, along with Chris Hope, who has taken on the role as Co-Chair. Along with our wonderful team of volunteers, our goal is to

ensure that all BSF members receive the support and educational materials needed to properly care for their Barth individual, in an accurate and timely manner. We are also here to provide guidance and emotional support.

In order to do this, we had to map out a plan, creating goals & objectives for upcoming projects

in 2005. Many have stated that printed materials with specific facts and information pertaining to Barth syndrome are greatly needed. Well, we have great news; we are now creating these documents!

Once completed, we will incorporate these Fact Sheets, along with the updated edition of BSF Practical TIPS, to create a BSF Resource Guide. This Resource Guide will be bound and printed for each affected Barth Family to have. They will also be included in the New Family Packets that are sent out to new families who join. Family Services is currently working on the following Fact Sheets: Heart Failure; Neutropenia; Genetics; Medications; and Metabolics.

As you can see, Family Services has been very busy! Chris and I are very excited with what our team of volunteers has accomplished in six short months.

(Continued on page 28)

# BSF AWARENESS IN THE PUBLIC EYE

By *Stephen Kugelmann, VP, Awareness*

Physician awareness is a difficult thing to measure. After several years of attending conferences, sending direct mail, and phone campaigns, it is very difficult to quantify the number of physicians that we are reaching. So one could ask; why are we spending money on physician awareness? What is the return on our investment?

I think the best reason is that we should not assume that physicians will know all of the different issues associated with each rare disorder. They need the support of the patient advocacy organization to compile the information and distribute it. Likewise, we cannot assume that the pharmaceutical companies will push the information out, nor the publishers of medical literature. Therefore, the burden at this time rests on our shoulders.

With that in mind, one would ask "How can we improve our effort to raise awareness?" We have two battles to fight in this arena. One is expanding the knowledge base of the physicians about Barth syndrome. Secondly, having the physician convey the information to the patient they are treating. Physicians may learn about Barth syndrome through the published literature and correctly diagnose their patient, but never communicate the fact that there is an international

organization that can benefit the patient. Over the past six months we have succeeded in reaching hundreds of physicians. Several of which have clearly stated that they are caring for a Barth child. However, direct contact with the family has not occurred. This is of great concern given the fact that the Barth Syndrome Foundation and its international affiliates can support the family beyond the physician's capability. I understand the diagnosing physician's rationale behind not promoting a lay advocacy organization. But, I also feel that we need to be more in the public eye so we don't rely on the physician to communicate the information.

Our methods to date have been successful, but we know that there is much more work to be done. We need a broader approach yielding a larger audience, both in the lay community and the scientific/medical community. Although we do find value in the more in-depth contacts that we make with physicians at medical conferences, the Awareness team continues to develop other initiatives that will reach the broader audience. With that said, here is a brief summary of our latest endeavors.

We've made a key contact in a medical trade magazine distributed in Canada called *The Medical Post*, which is distributed to 50,000 doctors in Canada.



*Michael and Michelle Telles, along with Steve Kugelmann, VP of Awareness, set-up shop at the 2005 American College of Human Genetics Annual Clinical Genetics Meeting in Dallas, Texas.*

They offered us advertising space and we jumped at the opportunity, supplying an ad that ran in the most recent issue. We have also been able to secure advertising space at the Dallas-Fort Worth, Texas airport. Clear Channel Airports has agreed to post our ads in their concourse billboards during the American Heart Association conference this November. We are also pursuing an opportunity for a documentary that will run on mainstream television. With millions in viewership, this may prove to be our best tool for reaching the lay community. In the very near future the success of our work in this area will be determined. We will keep you posted with an update on the Listserv.

So, what is the return on our investment? Simply stated it is knowing that we were a participant in the proper diagnosis of another child with Barth syndrome. As our numbers grow, so does the strength of the organization and all of us benefit from this strength.



# BARTH SYNDROME TRUST

## SUMMARY OF SUCCESS IN 2004



By Michaela Damin, Chair, Barth Syndrome Trust



*"The White Rabbit put on his spectacles. 'Where shall I begin, please your Majesty?' he asked. 'Begin at the beginning,' the King said gravely, 'and go on till you come to the end: then stop.'" (Lewis Carroll, Alice in Wonderland)*

*A team of committed volunteers brainstorm with Michaela Damin, Chair of Barth Syndrome Trust, during the workshop held from April 30 thru May 1, 2005.*

**T**he end of 2004 marked the first financial year-end of the Barth Syndrome Trust (BST). We began at the beginning and now we go on...

At the end of this report you will find a summary Statement of Assets and Liabilities for the year ending December 31, 2004. An independent examination was conducted by the firm of Keens, Shay & Keens.

### **THE UK VOLUNTEER WORKSHOP**

BST held its first Volunteer Workshop in Romsey, Hampshire this year. We felt that we needed to:

- provide more information about BST/BSF to our volunteers
- agree on the basic direction of the group and lay down the basis for the development of a formalised strategic plan
- ensure that all volunteers' skills and interests were well matched with their roles in the group

What will follow is a summary of the main goals of each of our programs, as discussed and agreed during the workshop. For each goal stated, there are a number of detailed objectives and action steps, which state exactly how we plan to go about achieving our objectives. As this is still being finalized after the workshop, I will just mention the main headings herein:

### **AWARENESS COMMITTEE**

**(Helen Coleman, Lisa Gilmour, Michaela Damin)**

**Goal: To ensure that all appropriate medical professionals are aware of Barth syndrome and have ready access to the latest tools to:**

- make a timely and accurate diagnosis
- know about advances in treatment for those who have Barth syndrome

### **PUBLICATIONS COMMITTEE**

**(Lorna Moore, Rob Manton, Greg Manton, Michaela Damin)**

**Goal 1: To ensure quality control of all documents generated by organisation for accuracy and target specificity.**

**Goal 2: To partner with appropriate medical journals to promote information about BST and Barth syndrome.**

### **FAMILY SERVICES**

**(Annick Manton, Helen Coleman, Sarah Bull, Eva Antomarchi, Joke van Loo)**

**Goal: To create a caring community that will offer each Barth family information, guidance and emotional support.**

**FUND RAISING COMMITTEE (Terri Allison, Dave Bull, Greg Manton, Majella Brehaut)**

**Goal: To build and sustain a broad base of committed contributors and fund-raisers who will provide the financial resources required to achieve our vision.**

*(Continued on page 23)*

## **SCIENCE AND MEDICINE**

(Michaela Damin)

**Goal 1:** *To stimulate the development of successful treatments for Barth syndrome (a multi-system disorder) and enable their delivery.*

**Goal 2:** *To encourage UK representation in the Scientific and Medical initiatives in the:*

- decision-making process of the scientific and medical decisions through the SMAB
- effort to develop regional leadership for the UK

## **ADMINISTRATION**

(Jerome Doherty-Bigara, Lorna Moore, Michaela Damin, Greg Manton, Majella Brehaut)

**Goal:** *To inspire and make effective and efficient use of resources through our dedication to seeing the organisation's collective vision to fruition.*

## **TECHNOLOGY** (Marco Damin)

**Goal:** *To optimize use of technology in an organisation dependent on ready access to information.*

So as you can see, we accomplished quite a bit in two days. These are some of the views of those who attended..

"We learned a lot about how the Trust and Foundation work. It wasn't until this weekend that we realised how vital our contribution as a volunteer really is. We always



*Lisa Gilmour, a member of BST's Awareness Committee, gives a 'press preparation' course during the BST Workshop.*

thought that everything was under control and working just fine with the help of the Founder Members. We now understand that they cannot possibly do everything. We are not a very big group with less than 100 boys affected worldwide, therefore, we all need to work as a team to make progress." ~ *Dave Bull*

"I found the workshop both very hard work and yet very rewarding. It was good to meet up with people from the Trust that I had previously met, but better yet to meet new friends, all with a common goal of bringing Barth syndrome to the knowledge of 'Joe Public'. We all have our part to play, ...and I feel happy with my newly found role in Family Services. The workshop also brought home to me how important our fund raising has to be in order to fund the research that is so clearly needed if we are to be able to firstly treat this disorder, then in time to find a cure. Equally, we must get the Registry up and running, so that our scientists have a point of reference." ~ *Helen Coleman*

## ***Other news...***

### **Families**

**Membership:** We currently have 28 member families in the UK and Europe (23 individuals with BTHS). This represents an increase of 12% in the past six months. We welcome Annick Manton, Sarah Bull and Helen Coleman as new committee members in the Family Services Team in the UK. In The Netherlands, Jo van Loo continues in her devoted service to our Dutch and German speaking families. In France, we welcome Eva Antomarchi who will forge links with French speaking families in Europe.

### **Awareness**

Have you heard of "Jeans for Genes" (J4G) ([www.jeansforgenes.org.uk](http://www.jeansforgenes.org.uk))?

Jeans for Genes is a national charity raising funds for children with genetic disorders. On October 7th, everyone in the UK will be asked to jump into his or her jeans and make a donation to the charity. A percentage of the donations will be given to the Genetic Interest Group (GIG) this year. GIG in turn has nominated BST (along with five other charities) to participate in the development of a Patient Charter for Barth syndrome.

A Patient Charter is a kind of road map. When parents and health professionals first come across Barth syndrome, it will tell them where to go and what to do to ensure that the child is receiving the best possible care.

(Continued on page 25)

# BSF OF CANADA RECEIVES REGISTRATION AS A CHARITY



Barth Syndrome  
Foundation of Canada

By Lynn Elwood, President



From left to right: BSF of Canada's Board of Directors include Cathy Ritter, Lynn Elwood, Karen Gordon, and Chris Hope. Lois Galbraith (front), is their Executive Assistant.

It's been a busy few months at the Barth Syndrome Foundation of Canada (BSFCA). Here are some highlights:

We held our first Annual General

Meeting of members via teleconference. The meeting was very well attended and we used it to give an update on all the program areas we've been orchestrating. Also at this meeting we elected our first official board of directors. We've been working for a few years as an acting board and it was time to make things official. The Canadian Board of Directors include: Lynn Elwood, *President*; Cathy Ritter, *Vice President*; Karen Gordon, *Secretary*; and Chris Hope, *Treasurer*. We have also appointed an Executive Assistant, Lois Galbraith, who takes notes at our meetings and helps us to stay organized.

We have been successful in our bid to become an officially registered charity. This means we are able to provide official tax receipts for donations from Canadians in the year 2005 and onwards. It also means we are tax exempt for a number of things and have an official way to show our legitimacy to investors, donators and other charities we work with. This is a very key step in our growth and thanks go out to the Canadian Board and our auditors who have worked hard to make this a reality.

We've been very lucky to have expanded the group of volunteers that are working with us, as well as people and firms who are donating. We won't name them all here but we're keeping a list and expect to publish that later in the year. It's very gratifying to

see such a long list of people who are helping our boys and there are many wonderful stories of their generosity. Thanks to all of you.

This year we've gone from getting our feet wet with fund raising (our poinsettia program) to being involved in several large fund raising efforts. In June, there will be a musical variety show in Markham, Ontario, which is being organized by producers Tony Murphy and Audrey Hintze. In September, we have our first annual Barth Syndrome Foundation of Canada Golf Classic. This is a large undertaking and it is keeping Cathy Ritter and Lois Galbraith quite busy. We're very excited about the sponsorship we've received so far from our primary sponsors Hope Aero and The Buss Megg Society, plus all the other hole sponsors and prize donators. There is great interest and we'll soon be signing up golfers to participate. There is another September fund raising plan by a volunteer in the investigation stages. We'll share information on that when it is official.

We've been quite active in program areas as well. All of us work as part of the BSF on the Scientific and Medical, Family Services, Awareness and Technology committees. Since most of those updates are covered in other articles we'll just mention a few Canadian specific highlights here:

- Resource Centres across the country are displaying our material for doctors and patients to reference.
- We have found several interested physicians, including two doctors treating Barth syndrome patients.
- We have a regular program of contacting Canadian families with updates from the BSF. All Canadian families have been contacted and their registry information updated.
- Our first of several ads has been published in a physician magazine distributed to 50,000 physicians across Canada.

(Continued on page 25)



**BSF OF CANADA** (Cont'd from page 24)

- We are planning for a Canadian clinic and Outreach session, hopefully in 2005.

This is a small sample of some of the great work that is going on within the BSFCa. With the help of our volunteers we have come a long way, and we are looking forward to all that we can achieve in the coming months. Below is a summary of BSFCa's Statement of Financial Position for 2004.



Barth Syndrome Foundation of Canada Statement of Financial Position at December 31, 2004	
<b>Assets</b>	<b>\$ 900</b>
<b>Excess of Revenue over Expenses</b>	<b>\$ 6,909</b>
<b>Net Assets - End of Period</b>	<b>\$ 7,809</b>

**BARTH TRUST  
OF SOUTH AFRICA  
OFFICIALLY FORMED**

*By Jeannette Thorpe, General*

BSF's affiliate in South Africa has officially been formed. It is called The Barth Trust of South Africa. The trustees include: Colyn Townsend (Attorney); Peter Duncan (Accountant); Nigel Thorpe (General); Jeannette Thorpe (General). We are in the process of applying for our Non-Profit status. I will keep you posted as this new affiliate unfolds!

On Saturday, June 4, 2005, Jeannette is hosting a "Mini Horseracing" fund raiser where Shetland ponies will be ridden by jockeys from the jockey academy. There will be four races run on a floodlit field. She is hoping to raise extra funds through auctioning off the horses of each race. This is a formal, black tie event, with a 3-course meal being provided. 220 guests have already committed to attend!

**BARTH SYNDROME TRUST  
SUMMARY OF SUCCESS IN 2004**

*(Continued from page 23)*

The members of BST will work actively with GIG and J4G this year to raise awareness of Barth syndrome in the media. Our members will also participate in the interview process to describe their experiences with the syndrome and to help draft the Patient Charter.

**Fund Raising**

Our ever-grateful thanks go to all our members and friends who have either made a personal donation to the Trust or who have run fund raising events for us over the past few months. A special note of thanks must also go to all those who have donated their time and expertise or who have made an in-kind donation to the Trust. Your names are inscribed on the back of this newsletter and on our hearts.

A while back my son Nicholas, who has Barth syndrome, said to me "Wow Mummy, I'm really lucky that I have so many people all working for me." I admit that I do suspect that the power might be going to his head somewhat! However, it is deeply gratifying to know that there are so many people all working together for my boy and yours.

With grateful thanks always,

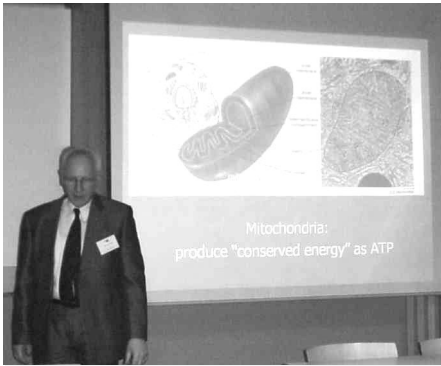
Michaela Damin  
Chairperson



Barth Syndrome Trust Statement of Financial Position as of December 31, 2004	
<b>Assets</b>	
Donations & Fundraising Activities	£ 16,956.00
<b>Expenses</b>	
Family Services and Education	£ 2,964.00
Physician and Public Awareness	£ 400.00
Administration	£ 187.00
<b>Total Expenses</b>	<b>£ 3,551.00</b>
<b>Net Assets - End of Period</b>	<b>£ 13,405.00</b>

# MAINLAND OF EUROPE HOSTS FIRST CONFERENCE FOR FAMILIES WITH BARTH SYNDROME

By Joke van Loo, The Netherlands



*Prof. Peter Barth lectures about the diagnosis, metabolic and neurologic findings of Barth syndrome.*

Children's Hospital, Academic Medical Center in Amsterdam.

The families were welcomed by Prof. Bwee Tien Poll-The, Chair of Pediatric Neurology at Emma Children's Hospital and Jo van Loo, European representative for the Barth Syndrome Trust. After lunch the families received information from a team of specialists from the Emma Children's Hospital, Academic Medical Center in Amsterdam.

Peter G. Barth, M.D., Ph.D., Emeritus Professor of Pediatric Neurology at Emma Children's Hospital, gave a lecture about diagnosis, metabolic findings and neurology.

Jan Lam, M.D., Pediatric Cardiologist, Department of Pediatric Cardiology at Emma Children's Hospital, gave a lecture about cardiomyopathy.



Taco W. Kuijpers, M.D., Ph.D. (left), Chair of Pediatric Immunology at Emma Children's Hospital, informed all families about the lack of neutrophil leucocytes (neutropenia) in Barth syndrome.

**O**n Friday April 15, 2005 the first conference for families with Barth syndrome on the mainland of Europe was held, organized by the Barth Syndrome Trust in togetherness with Emma



Frédéric M. Vaz, Ph.D. (left), of the Laboratory of Genetic Metabolic Disease at the Academic Medical Center, gave a presentation about some perspectives from research. Then a panel discussion followed where families asked questions and received answers from the speakers.

Finally, Shelley Bowen, President of the Barth Syndrome Foundation, Michaela Damin, Chairperson of the Barth Syndrome Trust, together with Jo van Loo, European representative for the Barth Syndrome Trust, presented information to the families about the ongoing operational programs of the foundation. In the meantime, two enthusiastic volunteers took care of the children and they had a very good time together.

Seven families with Barth syndrome were present: four families from the Netherlands and three from Belgium, including eight persons with Barth syndrome, ages 2 - 39 years. All families appreciated this wonderful meeting very much. The feedback I received from the families was very positive.

"I enjoyed the meeting in Amsterdam very much and so did my 36 year old brother (who also has Barth syndrome), and my parents who now were able to meet the famous Shelley Bowen and Michaela from the UK!" ~ *Veerle Swennen*

They told me it felt so good to have met everyone and to have been able to talk about all those Barth syndrome aspects with the families and with the doctors.

"This day felt so good, so warm [not in temperature], so real, so special. I have learned a lot. Thank you all for this very special day! It was also an honor to meet The Professor Barth.

~ *Tanja Kuipers*



# TO BARTH AND BEYOND

By Helen Coleman, Hampshire, UK

William was born on September 27, 1989, a much wanted first baby after three unexplained miscarriages. His birth was induced at 40 weeks when it was found that he was in the breech position after a normal pregnancy. He was slow to feed and my midwife began to have some concerns about his slow weight gain, and that he seemed to sweat more than most babies. I wasn't too worried, I was just glad to finally have my baby!

At 16 weeks, it was clear that he was having some problems, so we were sent to our local paediatric hospital, who were puzzled at what was wrong with him, until a routine chest X-Ray revealed an enormous heart trying to beat in William's tiny chest! After that, all hell broke loose and we were 'blue-lighted' to the nearest cardiothoracic unit. There began a long round of ECGs, cardiac catheters and echoes. He was diagnosed with dilated cardiomyopathy and started on masses of medication to support his heart function. Subsequently, we were referred to Great Ormond Street in London, who broke the news to us that our six month old baby's only hope of survival was a transplant, and that they were prepared to have his name added to the urgent list right there and then!

We came home to wait for the call and tried to live as normal a life as possible, and William's heart function actually improved enough in the next few months, that they were able to take his name off the urgent list. Things changed when William was nearly 2, when he became very sick, very quickly, He clearly needed a transplant pretty quickly then, and he had the best 2nd

birthday present when a heart became available for him.

He recovered well from the surgery, and we returned home again three weeks later with a new lease of life for us all. He was still very small and underweight for his age, but we hoped that he would pick up, now that he had his new heart. Over the next five years or so, he managed nursery school but was still a lot smaller than all the other children.

In the autumn of 1993, I discovered I was pregnant again, and then went down with flu the next day! William had it too, and we were both in bed together, feeling like death, when the phone rang. It was William's transplant physician from GOS to tell me that he had just read an article in one of his medical journals, describing this new genetic disorder that had just been discovered called Barth syndrome. He said it was as though he had just read about William; it fitted all the symptoms that he was experiencing, his unexplained dilated cardiomyopathy, small and weak stature and the horrendous mouth ulcers that he was now beginning to suffer with. At last we felt that we had some explanation for William, but it also raised a question over my pregnancy. If it was another boy, could we go through another heart transplant and all that involved? We decided we had to find out what sex the baby was in order to make the right decision, and were very relieved to find that I was carrying a girl (although we now know she could still be a carrier of the faulty gene).

Now that we knew what it was, we tried to find out all we could about it, but all there was then were a few articles in medical text books and journals. All too complicated to

understand fully, and all very bleak in their prognosis for boys with Barth.

About five years later, we met Dr. Colin Steward at the Bristol Children's Hospital. We were amazed

then to find out how rare the disorder was and at that time, he only knew of five other families in the UK. Last year, we had the first UK clinic in Bristol, and we met Michaela Damin and her family, and a few more families who had affected boys. It was clear by then that more boys are being diagnosed.

Until the clinic, I hadn't heard about the BSF and Trust, but since then we have joined the Listserv and learned so much from other families' experiences. I hope I may have been able to add my voice and helped by our experiences.

It is clear that raising the awareness of the syndrome is paramount, particularly amongst the medical profession. So many of William's doctors are still unaware of its existence. The more they know about it, the better chance new families will have of an early diagnosis and treatment for the symptoms. I am sure that none of us would wish any other family the long struggle that many of us have had over the years before we got a diagnosis. If I can 'do my bit' in raising awareness and supporting the new families, then I know that the knowledge I have had to gain over the last (nearly) 16 years will not be wasted.



*Helen, who recently attended the workshop held in the UK.*



# FAMILY SERVICES...

## FOSTERING EMPOWERMENT

(Continued from page 20)

In an effort to build and maintain an accurate, up-to-date Family Membership List, our team has spent many volunteer hours calling families and updating their membership data. We want to ensure that no family falls through the crack. We need every family and their information in order to learn more about this disorder. Currently, we have completed all the updates for North American families. If your family has not been contacted and is from the North American region, we need to update your family membership data! Please contact me at: [smann@barthsyndrome.org](mailto:smann@barthsyndrome.org) or Chris Hope at: [chope@barthsyndrome.org](mailto:chope@barthsyndrome.org) so that we may do so.

We have just begun to update the Australian and European (UK) families membership data. So please anticipate a call soon from US Family Services or Annick Manton, our UK Family Services Chair, [amanton@barthsyndrome.org](mailto:amanton@barthsyndrome.org).

BSF is here to support you and we will help in any way possible! Please continue to take advantage of the Family Listserv, and contact Chris Hope or myself with any questions or concerns you may have relating to Family Services.



# A TEEN'S PERSPECTIVE

By Kevin Baffa, Pennsylvania



Hello. My name is Kevin Baffa. I am now 16 years old and was officially diagnosed with Barth syndrome when I was in 1<sup>st</sup> grade.

Barth syndrome affects me in most of the ways it does other "Barth Boys." I have trouble doing a lot of physical activity at any given time. Another way that Barth affects me is that I can't go to school everyday of the week due to fatigue and hospital visits. Fatigue also affects my social life. Even if I would like to go out with my friends, I will choose to stay home just so I can conserve some energy for my school schedule.

My life has changed a lot since the conference. I now attend high school part-time, as opposed to home schooling, which I did last year. Meeting other "Barth Boys" has been a good experience. Now, when I have the opportunity, I can talk on the phone, e-mail, or sometimes even visit with them, as opposed to just seeing everyone every two years.

The BSF has also done a lot to help me, especially the conferences. Although I have had a lot of needles poked in me for BSF, I know it's all for a good cause ... research for a treatment/cure. I guess all I can really do for BSF is help them with whatever tests/studies they need me to be a part of, and continue to be supportive with our family's fund raising efforts.



# SIBLING SPOTLIGHT

By Jess Wiederspan, Nebraska

This section provides an opportunity to learn more about our wonderful BSF brothers and sisters. The featured siblings for this issue are Lee Kugelmann and Corey Bull. If you have comments or suggestions for future editions of the Sibling Spotlight, Please e-mail Jess Wiederspan at [onionhater1979@yahoo.com](mailto:onionhater1979@yahoo.com).

## LEE KUGELMANN



**Name:** Elizabeth Lee Kugelmann

**Age:** 12

**Grade:** 7th (only for a little while-school is almost over)

**Sibling with Barth syndrome:** R.J.

**Location:** Merritt Island, Florida

**Hobbies:** Dance (Ballet and Jazz), Reading, Shopping

**Place I Hope to Visit:** Paris, France

**Favorite Movie:** 13 Going On 30

**Special Talent or Skill:** I have been dancing since I was 18 months old; now I am in a dance company.

**Unique thing about me:** I don't want school to end! If I could get rid of science, exams, and getting up early, school would be great!

**Favorite Color:** Blue

## COREY BULL



**Name:** Corey Michael Alan Bull

**Age:** 7

**Grade:** Year 2 at school

**Sibling with Barth syndrome:** Both of my brothers have

## Sibling Spotlight

(cont'd from page 28)

Barth syndrome. They are Kai who is 3 (and a half), and Ashley who is 1 (and a half)

**Location:** Bristol, England

**When I grow up I want to:** be a famous football player and teach kids how to play football

**Place I Hope to Visit:** Where Santa lives

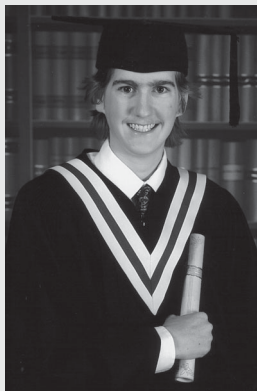
**Favorite Movie:** I don't know which is my favorite film, but I love The Simpsons

**Unique thing about me:** I can eat much more food than most of my family, but then I need to eat a lot because I do a lot of running, and I am very fast!



## CLASS OF 2005

On behalf of BSF, we would like to congratulate our high school graduates, Robert Hope of Ontario, Canada (picture featured below) and Jason Warstler of Kansas.



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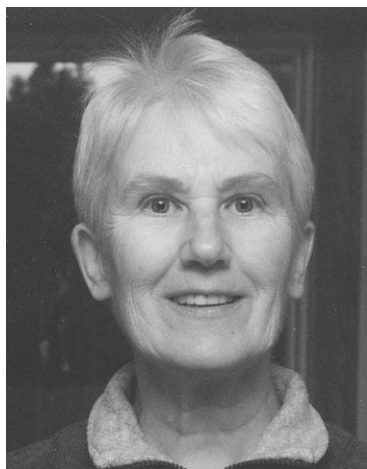
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# IN HONOR OF HER YEARS OF DEVOTION TO BSF



**O**n behalf of BSF and all of our families, we would publicly like to thank Iris Gonzalez, Ph.D., for her years of service and devotion to our families, on the occasion of her retirement from the Molecular Diagnostics Laboratory, Alfred I. DuPont Hospital for Children in Wilmington, DE. Iris, you have been an invaluable asset to all of us. Within our community one need only to say your name and the term 'friend' comes to mind. We at BSF are very happy we won't have to say goodbye to you—that would be way too hard. You have been such a champion for all of our boys, and for that we are grateful. And, thank you for being so interested, so kind, so compassionate, so concerned about our sons, our questions, our worries. Thank you for being so willing and prompt in answering any and all questions we have asked over the last several years in a way that we can understand. We all appreciate the exquisite expertise, care and, yes, even love that you have put into your work with all of us. Your involvement with so many families tends to be early on in our respective journeys, when we are frightened and overwhelmed. Your personal touch, in addition to your knowledge and willingness to explain in ways that even confused laymen can comprehend, is a true gift. As a scientist and a human being, you have left your mark on all of us involved with Barth syndrome; we will be forever grateful. ~ *The Barth Syndrome Board of Directors and Barth Community*

"Most BSF families know you because your work represents one of the pillars, in fact the most crucial one, in diagnosis of Barth syndrome: mutation analyses. You have assembled such a large database that any geneticist in the world can draw from it and compare a mutation or possible mutation with that database. Let me also emphasize to all participants in the listserv that you did a very special job with the BSF grant in sorting out the problem of the transcription of the *TAZ* gene (the gene associated with Barth syndrome). While the *TAZ* gene is present throughout nature, and even present, for example, in yeasts, one exon (coding part of the gene), exon 5, has not been found until recently in other animals than the human. Moreover, until recently no pathogenic mutations had been found in exon 5. This made the significance of exon 5 incomprehensible. By studying monkeys and human-like apes for the first time you solved this problem in an elegant way. You found that exon five became functional as a separate exon, such as in the human, after the so-called hominoid apes, like Orang Utan and Chimpanzee split off from the more old and new world monkeys. This means nothing less than that in the early evolution of man the development of the *TAZ* gene has a story of its own. I admire your great modesty, so allow me to briefly mention this absolutely fascinating discovery which is a tribute to both basic thinking and well-designed experiments. Let me wish you all the best, and thank you for all your great contributions." ~ *Peter Barth, M.D., Ph.D.*

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



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