

# Heart to Heart

Volume 2, Number 1 • Spring • Summer 2005

## From the PRESIDENT

We are pleased to present our 2004 funded investigators who will pave the way to better understanding of pediatric cardiomyopathy. In this issue, we also cover enrolling in clinical trials and exploring stem cell research. It is only through a combination of these research efforts that we can move closer to finding cures for pediatric cardiomyopathy.

Many thanks to those who gave so generously to our annual appeal this year. We have raised close to \$23,000 and hope to continue receiving donations for our scientific workshop in 2006. I encourage you to contribute, if you have not already done so, to reach our goal of \$75,000 for this important conference.

As many of you know, our Annual Golf Classic is our main income generator and a determining factor in how much research CCF can fund. Preparations for this year's event have started and we are signing up sponsors and procuring items for the event and silent auction. For those of you who contributed or participated in years past, we hope that you will continue to support this event. For those of you new to CCF, we hope that you will get involved as a participant, sponsor, in-kind donor or volunteer. Even if you are out of state, you can still be an event sponsor or make an in-kind donation (CCF will arrange for shipping). Your involvement can make this year's event a great success, enabling us to award more funds to promising investigators.

Have a wonderful summer,

Lisa Yue  
President & Founder

## CCF AWARDS 2004 Research Grants

Since its inception, the mission of the Children's Cardiomyopathy Foundation (CCF) has been to accelerate the search for a cure for pediatric cardiomyopathy by funding basic research. CCF awards grants annually to support research related to all forms of cardiomyopathy affecting children under the age of 18. By awarding small grants, CCF aims to help investigators gather preliminary data and/or obtain sufficient results to apply for more comprehensive support from larger Federal or professional granting institutions. In 2004, CCF awarded two grants for promising research initiatives. This year's awards went to **Ju Chen, PhD**, an Associate Professor of Medicine at **University of California** in San Diego and **Gerald Cox, MD, PhD**, a staff geneticist at **Boston Children's Hospital** and Senior Medical Director at **Genzyme Corporation**.

CCF awarded Dr. Chen \$50,000 to study dilated cardiomyopathy (DCM) at a molecular level. Building on observations

*continued, page 3*



Ju Chen, PhD



Gerald Cox, MD, PhD

## CCF Partner, the Pediatric Cardiomyopathy Registry Awarded \$4.7 million by the NIH

The National Heart Lung and Blood Institute (NHLBI), a division of the National Institute of Health (NIH) has awarded a \$4.7 million five year grant to the **North American Pediatric Cardiomyopathy Registry (PCMR)** to continue and expand the clinical research database of children with cardiomyopathy. This marks the third grant renewal for

this national research resource and an increase in funding from previous years.

The new grant effective from April 2005 to March 2010 will enable the PCMR to: 1) integrate the PCMR and **Pediatric Heart Transplant Study Group** patient data to examine whether and how cardiac transplantation can alter the clinical course of children with cardiomyopathy,

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Children's



Cardiomyopathy  
Foundation

*"A Cause For Today... A Cure For Tomorrow"*

The *Heart to Heart* newsletter is published semi-annually by the Children's Cardiomyopathy Foundation (CCF), a national voluntary health organization dedicated to saving lives and improving the quality of life for those affected by pediatric cardiomyopathy. Pediatric cardiomyopathy is a chronic and life-threatening heart disease that affects roughly 10,000 children in the U.S. CCF's mission is to accelerate the search for a cure by stimulating research, educating physicians, and increasing awareness and advocacy related to the needs of affected children and their families. CCF is a publicly supported tax-exempt organization as described under section 501(c)(3) of the Internal Revenue Service.

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## CCF the Recipient of CIBC WORLD MARKETS and EBAY FOUNDATION Grants

Earlier this year, CCF was awarded two grants from **CIBC World Markets** and **eBay Foundation** in support of CCF's **Parent Empowerment Program**. CIBC World Markets awarded CCF \$30,430 for the development of additional patient education materials and eBay awarded CCF \$2,500 to cover the distribution and fulfillment costs of disseminating the materials to families and physicians nationwide.

Through **Miracle Day**, CIBC World Market's annual fundraising program, all trade generated fees and commissions on a specific day are donated to nominated children's charities. In 2004, CIBC World Markets raised nearly \$11 million in the U.S. to support non-profit organizations that enhance the lives of children who are "in need or at risk". This year, CCF was invited by two of CIBC's largest clients to submit a grant application for this program. This award marks the third year that CCF has been selected for program funding.

CCF was one of several non-profits selected for a **Champion A Charity** grant from eBay Foundation this year. This grant was made possible by **Raymond Yue**, a CCF board member and eBay employee, who nominated CCF for eBay's competitive grant program. Twice a year, eBay Foundation awards approximately \$75,000 through the Champion A Charity program to non-profit organizations that work to improve the quality of life for all.

### Pediatric Cardiomyopathy

#### Registry Awarded, *continued from page 1*

2) compare how children with cardiomyopathy are functioning compared to the population over time and to identify common factors that might predict the clinical course of diagnosed children, and 3) investigate how genetic and viral markers of cardiomyopathy are associated with clinical and functional outcomes in affected children.

Each year the NHLBI receives thousands of research applications from various investigators, which are then scored and ranked based on research significance, approach, innovation, and investigator capability and research environment. CCF's biologic specimen repository, which will provide blood and cardiac tissue for the proposed genetic analysis and viral screening study, was a key component of the grant application. The PCMR grant scored remarkably in the top 2.9% of all submitted grants to the NIH, thereby signifying the importance and strong rationale for this research initiative.

The PCMR was first established in 1995 to track and record the epidemiologic features and clinical outcomes of selected

cardiomyopathies in children up to 18 years old and to promote the development of etiology targeted treatments. Over the years, CCF has worked in partnership with the PCMR, supporting think tank sessions and publication of findings, sending letters of support to the NIH, and establishing a repository linked to PCMR's clinical database. To date, the NHLBI has provided \$10.5 million to develop this registry comprised of clinical data from 3,000 children from 100 medical centers throughout the U.S. and Canada.

### IT'S NOT TOO LATE TO DONATE TO CCF'S ANNUAL RESEARCH FUND

All money reserved for research comes from individual contributions and fundraising events. We do not receive federal or corporate grants in this area.

**Your gift can be the key that  
unlocks the door to a cure!**

Please send your contribution along with your company matching gift form to:

**Children's Cardiomyopathy Foundation**  
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of cypher; a novel protein found in striated muscle cells of the heart and skeleton, Chen is using the CCF seed money to develop mouse models that can be used to mimic the development of DCM in humans. Specific mutations of cypher have recently been found in a certain number of familial and sporadic cases of DCM in

**“CCF awards grants annually to support research related to all forms of cardiomyopathy affecting children under the age of 18. In 2004, CCF awarded two grants for promising research initiatives.”**

children and adults. Two of the mutations are located within the same region (exon 6) of the cypher gene. Chen plans to generate three distinct mouse lines to serve as models for these known human mutations. One mouse line will have a deletion in exon 6 of cypher, and the other two will have specific point mutations within exon 6, mutations already identified in humans. The mouse models will take about a year to establish. Once established, these models will be used to determine how malfunctioning cypher proteins cause certain forms of DCM to develop. Ideally, these mouse models will be used to better understand the biochemical pathways responsible for DCM and ultimately to suggest therapeutic options for cardiomyopathy and consequently heart failure.

Ju Chen, a molecular biologist, has been studying cardiac development and disease since arriving at UCSD as a post-doctoral researcher in 1994. In addition to teaching “Molecular Biology of the Cardiovascular System” in the Department of Medicine, Chen also directs other post-doctoral researchers at his lab, which is devoted to investigating congenital heart disease and cardiomyopathy.

Dr. Gerald Cox, CCF's second award recipient, earned a PhD in the biology of cytoskeletal and contractile proteins and

an MD in pediatrics and genetics. It was through his clinical work, caring for children with genetic disorders that cause cardiomyopathy, that has led him to his current research, which allows him to combine his interests in contractile proteins and genetics.

With \$60,000 from CCF, Cox aims to determine whether sarcomere gene mutations are a common cause of pediatric hypertrophic cardiomyopathy (HCM). Sarcomere proteins form the contractile apparatus present within each muscle cell of the heart. A mutation in one of the proteins can affect how the heart muscle cells contract, causing a maladaptive response, resulting in HCM. Mutations in at least ten different genes encoding sarcomeric proteins have already been identified as causing HCM in adults. In children, however, the causes of HCM are poorly understood and more varied. While some cases of pediatric HCM can be traced to metabolic, familial, syndromic or neuromuscular causes, two-thirds of all cases of pediatric HCM have no known cause and are termed idiopathic. Cox suspects that some proportion of these cases will have sarcomere gene mutations. Moreover, he hypothesizes that children are more likely to carry two mutations, explaining why they may get sick sooner or deteriorate more rapidly than adults.

To test this theory, Dr. Cox has arranged to screen 50 children with HCM enrolled in the Pediatric Cardiomyopathy Registry. Subjects will include equal numbers diagnosed in infancy (under two years old) and later (ages 2-18), and equal numbers with or without a family history of HCM. Eight sarcomeric genes (MHC, MBP, TNNT2, TNNI3, TTN1, alpha-actin, MLC2 and MLC3) will be fully sequenced in all patients to identify possible mutations. Usually, genetic testing is stopped after a single mutation is discovered. Working with the recently established **Laboratory for Molecular Medicine at Harvard-Partners Center for Genetics and Genomics**, full genetic sequencing will be carried out on these genes, potentially revealing multiple mutations.

This study will attempt to answer several critical questions: Is the earlier age of onset of HCM in children compared to adults due to the presence of two mutations, different frequencies of involved

genes, or other mutations in the same genes? Do the mutations correlate with clinical features and echocardiographic findings? Does HCM caused by sarcomeric gene mutations differ from HCM related to other causes? Finally, can these findings help to predict the clinical course of diagnosed children? The results of this study may help decide which children with HCM should undergo testing for sarcomere gene mutations, how the testing should be carried out and the implications of such test results. The testing may also benefit parents of children with HCM as well. Adults of childbearing age may not know that they have a mutation until they bear a child who presents with the disease. Testing can help determine the outcome for future children as well as help anticipate future care and intervention for the parents.

**FUNDING AVAILABLE FOR BIOMEDICAL RESEARCH ON PEDIATRIC CARDIOMYOPATHY**

**(Dilated, Hypertrophic, Restrictive or Arrhythmogenic Right Ventricular Cardiomyopathy)**

**Description of Opportunity:**

The Children's Cardiomyopathy Foundation (CCF) is requesting grant applications for innovative basic, clinical or translational research relevant to the cause or treatment of cardiomyopathy in children under the age of 18 years. CCF's grant program is designed to provide seed funding to investigators for the testing of initial hypotheses and collecting of preliminary data to help secure long-term funding by the NIH and other major granting institutions.

**Application Deadline & Review Process:**

Grant award decisions are made through a careful and detailed peer-review selection process by CCF's Medical Advisors and Board of Directors. Grant guidelines and application are online at [www.childrenscardiomyopathy.org/site/grants.php](http://www.childrenscardiomyopathy.org/site/grants.php). The deadline for grant submission is October 3, 2005 with final award decisions and funding made in December 2005.

**Eligibility Requirements:**

Principal investigator must hold an MD, PhD or equivalent degree and reside in the United States. The investigator must have a faculty appointment at an accredited U.S. institution and have the proven ability to pursue independent research as evidenced by original research in peer-reviewed journals.

**Available Funding & Award Duration:**

Funding is available in the range of US\$25,000 to US\$50,000 for one year of total direct costs. For grant renewals, CCF funding is limited to two years (consecutive or otherwise) of support.

**Contact Details:**

Lisa Yue, President

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# PARENT EMPOWERMENT PROGRAM

## Progresses to Next Step

Following a grant from the **Medtronic Foundation** to develop patient education materials, CCF has been working with the **Healthcare Branding Group (HBG)**, a Chicago based strategic marketing firm, to do a needs assessment study for our **Parent Empowerment Program**. To date, HBG has received 50 online surveys from parents with children with cardiomyopathy and has conducted 25 interviews with pediatric cardiologists, cardiac nurses and geneticists at top children's hospitals. The following key findings have emerged from the 25 question parent survey posted online from December 2004 to March 2005:

- Most people initially turn to their physician/nurse for information and support upon diagnosis. They prefer to receive printed information from their physicians.
- Most respondents use the internet as an additional resource for independent research to answer their questions.
- The leading cause of dissatisfaction with available information (excluding CCF's information) is insufficient attention paid to pediatric cardiomyopathy. Many found that the complexity of the disease and the small number of those afflicted hinders the physician from providing appropriate information.
- The type of information that most respondents would like to see available are: infant-oriented information, information on research and treatment specific to pediatric cardiomyopathy, genetic research and testing, and how to talk with kids/siblings about the disease. Similar to responses from their physician, parents would like to see the following topics covered: lifestyle issues, nutrition, medical management and coping with a chronic disease.
- A large percentage ranked their greatest fear as losing their child. The fear of the unknown and the challenges of managing the disease, often while feeling alone, are of utmost concern to parents.

However, knowledge and information was the greatest factor in reducing this fear.

- As for daily challenges, the limitation of the condition is at the forefront of their minds. Concern range from the emotional impact of having their child sit out activities to the possibility that the child is not telling them about their symptoms.
- For the majority, family/friends and faith are the two most important means of support and coping. Results were mixed from those devout in their faith to those who are more interested in scientific advances.

Based on HBG's physician interviews, the consensus was that a comprehensive document written in lay language was definitely needed but that the challenge would be to communicate a complex and variable disease with many causes in a concise and understandable manner. The preference was for the information to be separated by disease types, be in printed format with links to various sites for more detailed information and for the material to be bilingual (Spanish, English). Some physicians also expressed interest in a video component with short vignettes explaining the different forms of the disease and showing family/patient interviews on living and coping with the disease.

Moving forward, CCF will work with HBG to develop an easy to understand booklet that answers general questions about pediatric cardiomyopathy. There will also be fact sheets on three of the most common forms of cardiomyopathy (HCM, DCM, RCM), which could be inserted into the basic booklet. These new materials will be available through physicians and online through CCF's website the later part of 2005. Once CCF receives additional grant funding, CCF will explore developing a complimentary DVD/CD-rom and adding webcasts or video footage to our website.

# National



## Working with the NHLBI...

CCF was invited in February to the **Fourth Annual National Heart Lung and Blood Institute (NHLBI) Public Interest Organization Meeting**. The meeting was a wonderful opportunity to meet with NHLBI staff, network with other patient organizations and attend scientific sessions on cell based and gene therapy, advances in imaging, tissue reengineering, and new developments in genetics, genomics and proteomics. This year, CCF was asked to facilitate the "Funding Research" roundtable discussion.

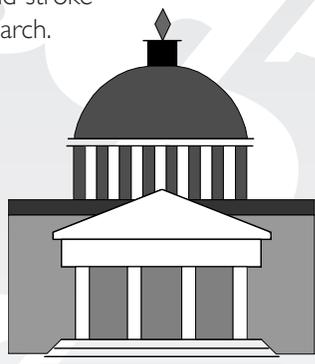
On a related note, CCF is pleased that the NHLBI and the **Office of Rare Diseases** convened a **Working Group on Cardiomyopathies in Children with Rare Diseases** on March 14 in Bethesda, Maryland. A working group brings together a small group of biomedical investigators to advise the NHLBI on areas of research that are not currently being adequately investigated. This meeting was initiated after the appeals of several lay advocacy organizations, including CCF, to request better understanding of the causes and treatment strategies of cardiomyopathies in children. Two of CCF's medical advisors, **Dr. Jeff Towbin** and **Dr. Steve Lipshultz** spoke about the latest findings on

children with cardiomyopathy, the research voids and the need for better standards of care. A formal meeting report will be posted on the NHLBI website ([www.nhlbi.nih.gov](http://www.nhlbi.nih.gov)) and published in a major medical journal in 2006.

## Budget Updates from Capital Hill

For fiscal year 2005 the **National Institute of Health (NIH)** budget increased 2 percent to \$28.4 billion. Of this amount, \$2.9 billion was allocated to the **National Heart Lung and Blood Institute**, the 3rd largest budget within the NIH.

CCF is a member of the **American Heart Association National Coalition for Heart and Stroke Research** and for fiscal year 2006, the group is recommending a 6% increase to \$30 billion for the NIH budget. This would roughly translate to an appropriation of \$3.1 billion for the NHLBI including \$1.9 billion for heart and stroke-related research.



# Understanding **CLINICAL TRIALS**

**Before any new therapy can be ruled safe** for widespread use, clinical trials are a necessary step in evaluating the effectiveness and possible risks with new treatment procedures. In the next few sections, we will cover the basics of clinical trials, participation considerations, updates on trials for pediatric cardiomyopathy and various resources for identifying appropriate clinical trials to enroll in.

### What is a Clinical Trial

A clinical trial or clinical research is a scientific study that helps to answer specific health questions by studying how a new medicine or treatment works in people. Through carefully conducted clinical studies, doctors can more rapidly and safely find new and better ways to prevent, detect, diagnose, control, and treat illnesses.

Many new medicines and treatments are first found to be helpful in test tubes and in animals. Before a new drug, surgical procedure, or therapy can be routinely prescribed by doctors, it must go through a rigorous testing process in humans to make sure it is safe and effective compared to the current treatment. Usually, many study volunteers are required because people are highly variable in how they respond to treatments. This testing in humans is permitted only if a person volunteers for participation and understands the risks and benefits of taking part in a study. This involves a patient informed consent to participate and the volunteer's understanding of what is involved in the study, including potential risks and benefits. All studies associated with a medical institution are reviewed by their Internal Review Board (IRB) to ensure it is scientific and ethically sound before enrolling patients.

There are two types of research studies to consider: 1) single institution and 2) national or multi-center studies. Institutional supported studies are usually led by a primary investigator at a medical institution or a group of doctors from the same institution. Often their studies draw from their existing base of patients and

they are located at university teaching hospitals that see a large number of patients. National or multi-center studies are usually federally funded and involve several centers with co-investigators contributing data.

### Why Participate?

Getting more families to enroll in clinical trials on cardiomyopathy is important for accelerating research on the disease but there are many more benefits to the participant. Parents can play a more active role in their child's healthcare, gain access to new research treatments before they are widely available and obtain expert medical care at leading healthcare facilities during the trial. Families who enroll will also have the personal satisfaction of knowing that their participation will help to advance patient care. Through the publication of research findings, physicians will become better educated about the disease leading to improved diagnosis and treatment for others.

### How to Select and Participate in a Study

There are a number of resources available to help people find and interpret research on their disease. Physicians commonly use the **National Library of Medicine's** resource **PubMed** ([www.pubmed.gov](http://www.pubmed.gov)) for a comprehensive listing of medical abstracts and publications. They may also use the **Computer Retrieval of Information on Scientific Projects** ([www.crisp.cit.nih.gov/](http://www.crisp.cit.nih.gov/)) to search for federally funded biomedical research projects conducted at universities,

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## Understanding Clinical Trials

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hospitals, and other research institutions. PubMed's counterpart, **Medline Plus** ([www.medlineplus.gov](http://www.medlineplus.gov)) is the consumer site for published medical studies.

It is important to note that there may be research studies that have been conducted or are underway that have not lead to published papers. In a 1990 study, it was found that only 20% of unpublished investigators had submitted manuscripts to a scientific journal. Some studies never make it to print because of negative findings or the investigator simply decided to not issue a manuscript based on his/her findings. Due to the stringent peer review process of top medical journals, there maybe a delay of one year before findings make their way to a published article.

For information on studies that are currently recruiting patients, the most popular is the **National Institute of**

**Health (NIH) site, ClinicalTrials.gov**, which lists more than 10,000 federally and privately supported trials worldwide with links to completed studies and resulting publications. This site provides regularly updated details about a trial's purpose, procedure, research phase, eligibility and contact information. Parents can search the database by a number of criteria such as condition (cardiomyopathy, heart failure), sponsor or recruitment status (recruiting, completed etc). Other useful information at [clinicaltrials.gov](http://clinicaltrials.gov) include: *Understanding Clinical Trials, What's New and Genetics Home Reference*.

For NIH studies conducted on site at their clinical center in Bethesda, Maryland, the **Warren Grant Magnuson Clinical Center** site maintains their own listings of clinical trials at <http://clinicalstudies.info.nih.gov>. Other sites that provide information on clinical trials are:

**centerwatch.com** - lists over 41,000 active IRB approved studies, along with

summaries of completed trials and updates on new therapies approved by the Food and Drug Administration.

**trialscentral.org** - provides trial listings and review summaries from the Center for Clinical Trials and is affiliated with the UK based Cochrane Collaboration, a pioneer in the development of "evidence-based" medical guidelines.

While access to current and comprehensive clinical trials information can help to support informed health care decision-making, it is advisable to consult with a doctor before relying on the results of a particular study. A cardiologist or geneticist can help to recommend appropriate research studies for each family or child.

*Excerpts from the Children's Cardiomyopathy Foundation website, **Pediatric Cardiology Today**, Vol 2, Issue 3 March 2004, and **Wall Street Journal**, June 17, 2004.*

# What to Expect From **CLINICAL TRIALS**

When a person considers participating in a clinical trial, there are several things he or she should be aware of, in order to have realistic expectations and adequate knowledge of possible risks and benefits:

- **What is the purpose of the trial?** Is the intent to find a cure, or simply a treatment, or perhaps preventive measures or a diagnostic test? Don't sign up for a clinical trial unless your expectations are in line with the study's objective.
- **Is an experimental clinical trial appropriate for you?** Have you tried the standard treatments and failed to benefit from them? Are you willing to try a treatment for which little is known, rather than try a treatment that has risks and possible benefits that are well understood?
- **What are the known risks and benefits of the experimental treatment?** How many people have been in the experiment before you? Did they experience any harm?
- **Is the experimental product only slightly different from other available treatments** (e.g., a slightly revised version of an existing drug), or is it a completely new approach to treatment?
- **Who is paying for the study?** Is it supported by government funds or a commercial firm? Does your doctor have a commercial interest in the therapy (e.g., a patent, royalties, etc.)? Some universities have "Conflict of Interest" committees who review these factors and decide whether a commercial conflict may influence the outcome of a study.
- **Is this a "placebo controlled" trial or will the experimental treatment be compared to the standard treatment for your disease?** Is there a chance that you will receive the placebo and if so, how much risk does this represent? Will you have the option to receive the treatment after the trial?
- **If you are harmed by the experimental treatment, who will pay for your medical care?**
- **What will happen when the study is finished?** Will you be able to continue using the treatment or will it be stopped even though you feel you are benefiting from the products? Will the manufacturer promise you can have continued access?
- **While the vast majority of experimental treatments are free**, will you or your insurance be liable for any costs related to your medical care while you are participating in the clinical trial?

*Reprinted with permission from the Winter 2003/2004 edition of the National Organization for Rare Disorders newsletter, **Orphan Disease Update**.*

**Dr. Seema Mital** is the Assistant Professor of Pediatrics at **Columbia University** and the Director of Molecular Cardiology Research at the **Children's Hospital of New York**. The focus of Dr. Mital's research is understanding the genetic factors that determine the severity and outcome of cardiomyopathy in children. We caught up with Dr. Mital to ask her a few basic questions about the status and challenges of doing research on pediatric cardiomyopathy.

**1) Can you give us a brief overview of the current multinational clinical trials on cardiomyopathy in children? Why haven't there been more national studies conducted on this disease?**

There are a few ongoing multicenter clinical trials in pediatric cardiomyopathy:

- Safety and efficacy study of carvedilol to treat children with congestive heart failure.
- Phase IB clinical trial to establish the safety and tolerability of a multiple-dose regimen of idebenone administered to patients with Friedreich's ataxia.
- Trial of Myozyme recombinant human acid alpha glucosidase enzyme as a potential treatment for Pompe disease
- Trial of a special diet for patients with fatty acid oxidation disorders (Dr. Charles Roe, Baylor)

There are several obstacles in doing research in children with any form of heart disease including cardiomyopathy:

- Relatively small population of children with cardiomyopathy per center makes it difficult to get adequate numbers of patients to power a clinical trial.
- Based on positive results of trials in adult heart failure, use of newer drugs often becomes standard therapy for children with cardiomyopathy in community practice. This makes it increasingly difficult to enroll patients subsequently in randomized controlled trials.
- Lack of research infrastructure to design and conduct clinical trials in pediatric centers.
- Relative lack of research funding and physicians trained in clinical research.

Since 2001, there has been an initiative at the **National Institute of Health** to support and fund a collaborative research

infrastructure, the **Pediatric Heart Network**, amongst pediatric cardiology centers to develop and implement studies and trials in children with heart disease. An upcoming study will involve an echocardiographic assessment of the progression of dilated cardiomyopathy in children. Also, since 1997, pharmaceutical companies are required and encouraged by the Food and Drug Administration to conduct drug trials in children through various incentives. Hopefully, some of these efforts will translate into additional trials in pediatric cardiomyopathy.

**2) How far are we from actually pinpointing genetic mutations that cause cardiomyopathy in children? What are the obstacles in doing research in this area?**

Currently we are able to identify several genetic mutations that cause cardiomyopathy in children. At least 50% of hypertrophic cardiomyopathy cases and 30-40% of dilated cardiomyopathy cases can be familial or inherited. For children with inherited or familial hypertrophic cardiomyopathy, 11 genes have been identified containing almost 150 mutations (alterations), most of which are related to mutations in genes that regulate contractile proteins in heart muscle. For children with inherited dilated cardiomyopathy, mutations in at least 13 genes have been identified, most of which are in the cytoskeletal components or genes that encode the structural proteins of heart muscle. In addition, a few of the metabolic/mitochondrial cardiomyopathies are being studied

for gene defects that can cause enzyme deficiencies. Most genetic testing is currently only available through research labs at various institutions. It is anticipated that there will be more clinically certified (CLIA) labs that will be able to perform genetic testing on a commercial basis.

Some of the obstacles to research in this area include:

- Candidate genes can have mutations at many different sites in different patients making it technically challenging to pinpoint the site of the defect if there are only a few affected family members.
- The likelihood of identifying genetic mutations in patients that present for the first time without a family history of the disease is low.
- The effect of a particular gene mutation on a patient's outcome or clinical course is difficult to predict. This is because genetic defects may affect some individuals more than others depending on the penetrance of the gene, the modifying influence of other genes or the environment.
- Large-scale population studies are needed to correlate the effect of genotype on clinical disease. This is difficult given that children with inherited cardiomyopathies constitute a relatively small population.

There are attempts to expand the existing registries and create DNA banks across institutions that will permit testing for many of the known mutations as well as identify new mutations in children with cardiomyopathy on a larger scale.

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# *the promise of* **CELL THERAPY**

**Much medical hope** has been pinned on stem cells to replace or repair damaged or dead cells in diseased organs, including the heart. Earlier this year, a clinical study conducted in South America by University of Pittsburgh physicians found that injections of adult stem cells in 30 patients with heart failure resulted in better pumping action than with patients who underwent surgery but received a placebo. This particular study marked a milestone in stem cell research because it was the first randomized, controlled study of this kind. Experts realize that more research needs to be done to determine the safety and efficacy of using cell based therapies to treat heart disease. Scientists are, however, optimistic about the potential of this novel treatment and believe that it is just a matter of time before it can lead to cures for heart disease as well as a host of other incurable diseases.

## • **What are stem cells?**

Each adult body has hundreds, perhaps thousands, of different cell types. These tiny structures serve both a structural and a functional role in the body, performing a variety of specific actions to sustain the body's tissues and organs. Stem cells are "blank" cells that have the potential to develop into any kind of body tissue, such as skin cells or heart cells. There are different types of stem cells with different degrees of versatility. Some (pluripotent cells) can give rise to every cell type in the body. Others (multipotent cells) give rise to a more limited number of cell types usually found in the tissue from which they are derived from (i.e. skin stem cells that give rise to only various types of skin cells).

## • **Where do stem cells come from?**

Stem cells can be obtained from muscle, bone marrow or embryonic tissues. The cells that have the greatest developmental capability are those that are extracted from unused frozen embryos or from donated fetal material after the termina-

tion of a pregnancy. Stem cells from embryos and fetuses have a much greater potential because embryonic stem cells have the greatest ability to multiply and can develop into virtually any type of cell in the human body. Nuclear transplantation is another way to obtain cells. In this procedure, an individual's DNA is inserted into an egg and the egg is activated to divide. After only a few cell divisions, scientists extract the stem cells. The advantage of this technique is that these stem cells are genetically matched to the recipient, reducing the risk of rejection.

An alternative to embryonic stem cells are adult stem cells harvested from a patient's bone marrow, muscle, or umbilical cord blood which can be stored after the birth of a baby. However these types of cells are not as versatile as embryonic cells and so are less capable of growing into as many different kinds of tissue. Some studies have challenged this belief showing that adult stem cells from bone marrow or blood do have the ability to develop into completely different cell types if they receive the right biochemical signals. Stem cells derived from bone marrow include several different types of cells including those that differentiate into myocytes or heart muscle cells as well as those that stimulate the formation of new blood vessels in the heart. The latter may be particularly useful in heart failure secondary to coronary artery disease.

## • **What is stem cell therapy?**

Cell therapy relates to replacing diseased or dysfunctional cells with healthy, functioning ones. The therapy is similar to the process of organ transplantation except the treatment consists of the transplantation of cells rather than organs. The goal is for the healthy cells to become integrated into the body and begin functioning like the patient's own cells. These new procedures could potentially be used on the area of damaged heart muscle to replace lost or dead muscle cells.

In a 2002 study, it was found that stem

cells could exist in the heart atrium (pumping chamber). This opens up the possibility that these specialized cells can be isolated and used to repair damage to the heart. The hope is that stem cells can be isolated from a tissue specimen taken from a child undergoing biopsy or surgery, then amplified and differentiated in the laboratory and returned to the child to help grow healthy cardiac tissue.

## • **What is the progress on stem cell therapy?**

Research is now being conducted on both adult and embryonic stem cells to determine the characteristics and potential of both to cure disease. Most of the ongoing clinical trials (single and multi-center) on stem cell transplantation are on adults with coronary artery disease that have had heart attacks or those with heart failure. This includes a ten-site US clinical trial involving transplantation of myoblasts (muscle cells from the patient's own muscle biopsy) that are grown and injected into the damaged heart muscle during coronary bypass surgery. Three years ago, a team of researchers found that bone marrow cells could also replace heart muscle damaged after a heart attack. Studies are also being carried out in Europe involving cells taken from the thigh of patients with heart failure, cultured in the laboratory and then injected into the patient's damaged heart muscle. This appears to have helped the heart muscle recover and pump more efficiently.

In 2003, doctors at **Beaumont Hospital** in Michigan treated a 16-year-old boy who had suffered a massive heart attack as a result of being shot in the heart with a nail gun. In this experiment, doctors harvested the blood stem cells from his own body and inserted them through a catheter into his heart. The result was a dramatic restoration of damaged heart tissue, and the boy did not require a heart transplant.

In the more recent **University of Pittsburgh** randomized controlled study, bone marrow cells harvested from

patients with congestive heart failure were injected into various damaged spots in the heart. Six months later, patients that received the stem cell therapy showed a 35% increase in blood pumping efficiency compared to a 5% improvement in those who received the “dummy” injections of saline solution. Doctors in Germany have had great success with a similar process.

In 2004 there was some basic research using mouse embryonic stem cells to correct a specific syndrome of congenital heart defects that develop in fetal mice. This experiment showed that introducing embryonic stem cells directly into the embryo helped the mother mouse produce hormones that could protect tissues from the disease or repair the damage when it occurred. This presents some interesting therapeutic possibilities for genetic based cardiomyopathies. Even with these advances, it is important to note that studies have only been carried out on a small number of patients.

#### • **What are the challenges and risk with stem cell therapy?**

There are still many scientific challenges that must be overcome before the possibility of cardiac cell transplantation can be a realistic treatment for cardiomyopathy. First, most experimental studies are short-term studies. The concern remains whether the so-called benefits can be sustained for longer periods of time such that the transplanted stem cells grow, survive and replace the dead cells without tissue overgrowth or tumor formation. Clinical trials in humans evaluating the effect of myoblast (heart muscle cells) transplantation have demonstrated a significant risk of arrhythmias due to failure of the injected cells to form gap junctions with the surrounding cells to allow normal conduction of electrical impulses. If the transplanted cells fail to survive, the benefits could be transient and the risk of arrhythmias and scar formation could be evident during longer follow-up.

There have not been any large trials performed on adults or children with non-ischemic heart disease yet. The

difficulty is that the area of scar tissue and muscle damage in non-ischemic cardiomyopathy is not localized like patients with myocardial infarction that have discrete areas of injury. If the entire area of the heart is affected, this makes it more difficult to target the stem cells to the site of injury. As a result, the ideal approach for delivery of stem cells is still unclear (i.e. intracoronary via a catheter, inside the left ventricle or directly into heart muscle from the surface of the heart, etc).

There are ethical concerns as well with cell therapy. While use of stem cells from skeletal muscle and bone marrow is permitted, federal regulations limit the use of embryonic stem cell lines in the US. Currently all embryonic stem cell research in the US is privately funded, and the lack of federal funding has limited research in this area.

#### • **What about the future?**

Even though most of the work done in this field has been experimental and no cures have been developed, most scientists say that the field is extremely promising. All the studies conducted thus far pave the way for larger clinical trials for heart attack and heart failure patients. Most likely, research will continue in larger adult populations until a therapy is proven safe and effective before clinical trials for children can be considered.

US institutions that are strong in stem cell research include **Harvard University, Johns Hopkins University, University of Wisconsin, Duke University, University of Minnesota, Northwestern University, Stanford, University of California at San Francisco, University of California at San Diego and University of Toronto** amongst others. The passage of bills in states like California and Massachusetts, to provide state funding for stem cell research, will undoubtedly help to expand research in this field.

*More information can be found at the **International Society of Stem Cell Research** ([www.isscr.org](http://www.isscr.org)) or the **Stem Cell Research Foundation** ([www.stemcellresearchfoundation.org](http://www.stemcellresearchfoundation.org)).*

## **Q&A with Dr. Seema Mital**

*continued from page 7*

### **3) If I want to enroll in research, how do I find the right study and what are the steps involved in participating?**

Research in this area can be found at specialized Pediatric Cardiomyopathy Centers, which your cardiologist can refer you to. Research is currently being performed in many areas important to all types of cardiomyopathy, including identification of gene mutations that can cause the disease, determining other genetic factors that can affect how the heart responds to having the gene defect, and why some patients respond better to medicines compared to others.

Steps involved in participating in research include:

- Referral by your private cardiologist to the research center.
- Evaluation by the research investigator to determine if your child is eligible for participating in the study.
- Discussion of the risks and benefits of the study with the investigator to enable you to give informed consent for participation.
- Baseline testing and serial evaluation as determined by the research protocol.

It is important to recognize that participating in a research study may not always provide immediate benefits to the patient.

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*“The focus of Dr. Mital’s research is understanding the genetic factors that determine the severity and outcome of cardiomyopathy in children.”*

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However, research studies permit physicians to evaluate the benefits of a new drug or identify a new cause of cardiomyopathy through the study of large numbers of patients. Results of such research are expected to yield important diagnostic and treatment information that can improve management and outcome of cardiomyopathy for the future.

# CCF “Curebands” Now Available!

## CCF’s “A CURE FOR TOMORROW”

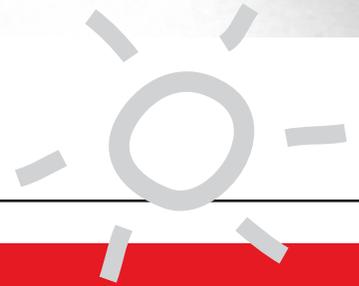
**awareness wristbands are now available!** These bright red wristbands were inspired by similar cause related wristbands which have proved to be extremely popular with the children/youth, celebrity and sports crowd. Made of heavy gauge rubber with our tagline; “A CURE FOR TOMORROW” engraved on the front and our website address featured on the back, these wristbands provide an inspirational message of hope, as well a link to further information about pediatric cardiomyopathy.

CCF’s Curebands are a fun way to tell the world that a cure is possible and to spread awareness of cardiomyopathy to family members, friends, co-workers and neighbors. The money from the sale of these wristbands will support CCF’s mission of research, education and support.

Curebands can be promoted year round in a variety of ways in your school, workplace and community:

- ✓ **Encourage family and friends** to initiate a chain e-mail letter with a link to CCF’s website to help promote the Cureband program.
- ✓ **Consider Curebands as fun merchandise** to sell at fairs and events, as well as the perfect giveaway at school functions and birthday parties.
- ✓ **Forward a Cureband** to your local television, radio, and newspaper outlets, along with a personal note explaining the need for increased awareness of pediatric cardiomyopathy. Let them know about CCF’s mission and ask them to do a story on the disease and the Foundation.
- ✓ **Send a Cureband** to a celebrity or “person of influence” and invite them to get involved in our grass roots awareness campaign.
- ✓ **Approach local retailers**, malls, business contacts and social organizations to promote Curebands in their stores or at their office/member meetings. Let others in your line of work know how important their help is.

The wristbands are available in adult/teen size (8 inches in circumference). Wristbands retail for \$5 each or \$20 for 5 bands. To place your order, please download the order form from [www.childrenscardiomyopathy.org/site/merchandise.php](http://www.childrenscardiomyopathy.org/site/merchandise.php) and mail in your payment to CCF.

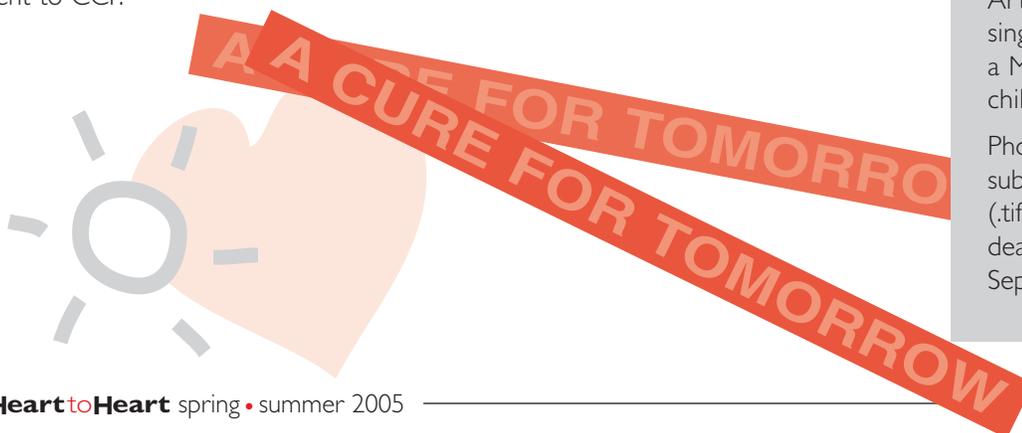


To subscribe to **Heart to Heart**, the newsletter of the Children’s Cardiomyopathy Foundation, please email name and mailing address to [newsletter@childrenscardiomyopathy.org](mailto:newsletter@childrenscardiomyopathy.org) with the title “Subscribe” in the header.

## We Want to Hear from You!

Please tell us what you would like covered in future *Heart to Heart* issues. Families affected by cardiomyopathy as well as physicians and nurses are encouraged to submit articles, news updates and/or personal stories for the newsletter. Articles can be up to two pages single space in length and sent as a MS Word file to [newsletter@childrenscardiomyopathy.org](mailto:newsletter@childrenscardiomyopathy.org)

Photographs and artwork can be submitted as standard image files (.tif, .gif, .jpeg). The submission deadline for our Fall/Winter issue is September 1, 2005.



# Use eBay to Donate to CCF

Instead of arranging a garage sale, you can now sell your vintage or unused items through **eBay Giving Works**, a program that allows anyone to raise money safely and efficiently for CCF. Simply, select CCF from the list of pre-approved non-profit organizations and designate the percentage of proceeds you would like to donate for each listing. Ebay is collaborating with **Mission Fish**, a nonprofit organization, to manage the listing, processing and tracking of eBay charity sales.



To list something on eBay, just go directly to [www.missionfish.org](http://www.missionfish.org) and click on "Sell Your Item". You will then be asked to select your charity (Children's Cardiomyopathy Foundation). After registering with Mission Fish (you will need to

first register for an eBay account), designate the percent of the final sale price you wish to donate (10-100%) and input your listing information according to the prompts. Mission Fish will then notify you when your listing has been approved by CCF and submitted to eBay.



## Family Gives Back in Daughter's Memory

The Amanda McPhearson Foundation selected CCF as a beneficiary in their yearend donations. The California based foundation was started by Mary McPhearson in memory of her daughter Amanda who had dilated cardiomyopathy. Amanda was only 8 years old when the disease, contracted through a virus (viral myocarditis), claimed her life. The Foundation has been a strong supporter of medical research and community projects.

*CCF would like to thank the Amanda McPhearson Foundation and all our other tribute donors who have donated in memory of or in honor of a child with cardiomyopathy.*



## MORE PATIENT INFORMATION Resources...

The Health Resource contacted CCF earlier this year about their medical information service. The Health Resource has been in existence for 20 years and provides individualized, comprehensive research report on specific medical conditions. Customized bound reports contain information on mainstream, experimental and alternative treatment options in the form of articles, summaries from medical and lay publications, self-help tips, information on specialists, internet resources, support groups and a medical glossary. Each tailored report is developed with a family's questions, concerns and informational needs in mind. The reports are \$295 plus shipping. For those with limited financial resources, the Health Resource can lower the cost to \$75 or less. CCF will receive a donation of \$50 for every full price report purchased when CCF is mentioned. For more information, please contact Jan Guthrie, Director at 800-949-0090 or visit their website at [www.thehealthresource.com](http://www.thehealthresource.com)



Address Service Requested



Tel: 201.227.8852  
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www.childrenscardiomyopathy.org

The Children's Cardiomyopathy Foundation (CCF) is a non-profit, voluntary health organization focused on pediatric cardiomyopathy - a chronic and life-threatening heart disease that affects children. CCF is dedicated to improving treatments and finding cures through the support of medical research, education, and increased awareness and advocacy.

P.O. Box 547, Tenafly, NJ 07670

The Newsletter of the Children's  
Cardiomyopathy Foundation

Volume 2, Number 1 • Spring • Summer 2005

# Heart to Heart

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# Welcome to Heart to Heart

The Newsletter of the  
Children's Cardiomyopathy Foundation  
Volume 2, Number 1 • Spring • Summer 2005

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### • Foundation News

**Cover:** CCF announces 2004 research grant recipients.

**Pg 1, 4 & 5:** NHLBI awards research funding and conducts workshop on pediatric cardiomyopathy.

### • Fundraising Update

**Pg 2:** CCF awarded grants from CIBC World Markets & eBay Foundation

### • Family Information

**Pg 4:** Parent Empowerment Program moves forward with survey results.

**Pg 5:** Learn about researching and participating in clinical trials.

### • Medical Information

**Pg 8:** Cell therapy holds promise for future cures.

## 3RD ANNUAL Children's Cardiomyopathy Foundation

# Golf Classic

Thursday, September 15, 2005

11:00am - 7:30pm at the  
New York Country Club, New Hempstead, NY

**Don't miss this fun-filled day on the course!**

Player Fee: \$400/person Reception Guest: \$100/person

Includes BBQ lunch, greens and cart fees, cocktails, silent auction and light supper.

We offer a range of sponsorship and in-kind donation options with prominent recognition at the event and on all publicity and marketing materials. Please call 201-227-8852 for more information.



**NOW AVAILABLE - CCF's "Cure for Tomorrow" red wristbands!** A great way to spread awareness of cardiomyopathy in your school, workplace and community.

See page 10 for all the latest information.