FDC BEAT

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Newsletter of the Familial Dilated Cardiomyopathy Project at Oregon Health & Science University
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The Familial Dilated Cardiomyopathy Research Project - 2006

Greetings from the Familial Dilated Cardiomyopathy (FDC) Research Group at Oregon Health and Science University. It has been another busy year here. Our program has continued to enroll new participants and families from all over the U.S. and Canada, and maintained contact with those previously enrolled. We've made new contributions to the FDC medical literature and presented valuable information about FDC to colleagues. And of course, we continue the work toward our main goal - identifying genes associated with FDC.

This issue of our newsletter reviews some of the accomplishments and progress in FDC research this past year. It also includes some suggestions on how you can continue to play an important role in furthering understanding of FDC, to improve treatment and prevention of this condition.

We wish you and yours a healthy and happy holiday season, with best wishes for the New Year.

INSIDE THIS ISSUE

FDC STUDY 2006

STUDY ENROLLMENT. Some families have been involved in our study since its beginning in the early 1990s. Others have come on board sometime throughout the years or even in the past few months. Families find us in a variety of ways; many local families receive their clinical care at OHSU, while other local and non-local families are referred by a health care provider or find our website while searching for information about FDC. We currently have over 300 families involved in our study (see category breakdown below), with over 1600 blood samples from individual family members submitted. We regularly receive inquiries about our study, and have been in contact with over 100 additional families that have shown interest and are in the process of enrollment.

As of December 2006, we have 135 FDC families enrolled in our study. These are families in which we have confirmed FDC (dilated cardiomyopathy of unexplained cause, i.e. "idiopathic dilated cardiomyopathy" or "IDC") with medical records in at least 2 family members, and have received a blood sample from at least one of these relatives. While this is the minimum needed to be enrolled as a "confirmed" FDC family, medical records or death certificates of any family members with a history of heart problems or heart tests performed, and blood samples from any interested relatives (including those without heart problems) are extremely helpful to the study.

Families with no additional evidence or family history of heart problems are called "IDC families;" there are currently 58 in our study. We also have 135 families enrolled which are categorized as probable or possible FDC. These are families in which we haven't confirmed FDC, however in many cases FDC could be confirmed if we receive additional medical records and/or blood samples from family members.

Accurate family categorization is important to our understanding of FDC and any gene findings. Please check in with us if there have been any changes in your family history, and to see how your family is currently categorized and what may be needed to more accurately categorize your family for our study.

STUDY ACTIVITIES.

MRI Study. Thanks to those of you who participated in our MRI screening. As noted in our last newsletter (FDC Beat,Vol. VI, Iss. I, May 2006), we began study of magnetic resonance imaging (MRI) technology as a potential tool in the diagnosis of FDC, particularly early diagnosis of at-risk family members. Preliminary findings are being submitted for publication, with hope of additional study in the future.

Family screening. We have recommended that children, siblings, and parents of a person with IDC/FDC have an echocardiogram and EKG, to look for early signs of the condition that may benefit from early treatment, and that this screening be performed about every 3-5 years if the baseline tests are normal. Our group has screened over 800 family members since the study's inception. Over 40 individuals were screened by us this past year, mostly at the OHSU campus, but including one screening trip to the Midwest late in 2005. Funding limits the amount of screening our group can perform, so we encourage you to discuss the screening recommendations with your health care provider. Many health care providers may be unaware of these recommendations, so if you bring them to attention you may be able to have the test performed clinically with coverage through your health insurance company.

Because we cannot screen all participants ourselves, we do rely heavily on your medical records to know your heart's health status. Again, please keep us updated on any heart tests you have had done and contact us for a medical record release form so we can request copies of results.

FDC Gene Sequencing. While a number of genes have been reported to cause FDC (see "FDC Gene Update" section), it is still largely unknown how commonly each of these genes may be responsible for FDC. In other words, what is the chance that a certain gene causes disease in an FDC or IDC family? Early in 2006, we started a project looking at 6 particular genes that have been associated with FDC, to see how frequently alterations in these genes are found in our study families. One challenge to this type of gene study is to determine whether alterations found are actually harmful to the gene's function vs. a simple variation that is not disease causing. The best way to attempt to figure out such a dilemma is to see how an alteration tracks in a family – is it found in all family members with heart problems? Are family members without known heart problems free of the alteration? So once again, updated medical records and blood samples from any willing family members can help answer these questions. We may contact your family to discuss such issues, but please don't hesitate to contact us for updates and additional blood kits for your family as well.

Linkage studies. Linkage is a laboratory technique used to find additional genes that may be associated with FDC. Linkage requires very large families with 8-10 living family members diagnosed with FDC. Most of our travel in the past has involved screening families in which linkage can be used to try and identify FDC gene(s). The laboratory side of this work continues. As with gene sequencing, linkage studies can be complicated by lack of data and new development of heart problems in family members previously thought to be unaffected. With continued funding, we plan to rescreen our large participating families. Until such time, updated medical records will be most helpful to this aspect of our research.

FDC GENE UPDATE

To date, 29 different genes have been reported as potential causes for FDC. Five additional locations within our genetic material (DNA) have been linked with FDC; however the specific genes in these locations have not yet been identified. Again, the frequency with which each gene is responsible for causing FDC is unknown, although none are thought to cause the majority of FDC.

24 of the 29 reported FDC genes are inherited in an autosomal dominant pattern, meaning each child of a parent carrying a disease-causing alteration (mutation) in such a gene has a 50% of also carrying the mutation, putting them at risk to develop FDC and pass along the mutation to their children.

With the exception of the Lamin A/C gene, clinical genetic testing for other autosomal dominant FDC genes is not yet available in the U.S. Continued identification of FDC genes, and the study of the frequency of FDC gene alterations will help increase the availability of genetic testing for the genes that most commonly cause FDC.

FDC GROUP PUBLICATIONS AND PRESENTATIONS

Below are references to two articles published in the medical literature by our group in the past year. Such publications are an important way to show progress in our research.

Familial dilated cardiomyopathy. RE Hershberger. *Progress in Pediatric Cardiology* 2005; 20:161-168.

Clinical characteristics of 304 kindreds evaluated for familial dilated cardiomyopathy. JD Kushner, D Nauman, D Burgess, S Ludwigsen, SB Parks, G Pantely, EL Burkett, RE Hershberger. *Journal of Cardiac Failure* 2006; 12:422-429.

In addition to medical journal publications, various members of our clinical and laboratory personnel presented information about FDC and our research to colleagues at annual cardiology and genetics conferences, and lectures on the OHSU campus. These presentations always spark interest from colleagues, often leading to referrals of additional families to our study.

HAVE YOU CHECKED YOUR FAMILY HISTORY LATELY???

Family medical history is one of the most important parts of understanding FDC. What is known about the family history can impact one's diagnosis, treatment, and management of heart problems. Knowing who in the family has a history of heart problems influences who else in the family is considered "at-risk," as well as the subsequent recommendations given to at-risk relatives to address early diagnosis and possible prevention of serious heart problems. Family history information is also crucial to understanding research findings as new genes are being evaluated for the roles they may play in causing FDC. Family history changes over time, so collecting family history is an ongoing process. In general, the more family history information you have, the more accurately you can be given information about the presence and/or risk of FDC in you and your relatives.

Family history suspicious for FDC:

- **Heart failure**, sometimes referred to as "congestive heart failure" or "dropsy" or in infants "blue baby"
- **Cardiomyopathy** heart muscle disease of any cause
- **Heart transplant**
- **Heart attack**, especially if sudden and no history or
- coronary artery disease/stents/bypass surgery
- **Arrhythmias/irregular heart beat**
- **Pacemakers, defibrillators**
- **Fainting spells**, sometimes thought to be a seizure disorder
- **Sudden or unexplained death**, especially at a young age
- **Stroke**

Holidays, reunions, and other family celebrations can be a good time to check in with your family members about their health. Often one or two relatives keep up with other family members and may be a good source of family health history information. Perhaps you or another relative is willing to compile the family tree and update it 1-2 times a year if other family members will provide information as needed. When collecting family history information regarding FDC, make note of the existence of the problems listed above or any other type of heart problems. Collect information about date of birth or current age, how many brothers/sisters/children each person had, and cause/age of death. Collect information for at least 3 generations on both sides of the family (even if FDC seems obvious on one side of the family, heart problems can be present on both sides). If a relative has a history of or suspicion of heart problems, ask about that person's parents, siblings, and children, too.

There are a number of resources available to those interested in collecting family medical history information. One new tool, available online from the U.S. Surgeon General, allows you to create a personalized family health history report, and will draw you a pedigree (family tree) based on the information you provide. This tool can be found at: https://familyhistory.hhs.gov/

So if you haven't asked about Aunt Rose and her kids in a while, consider doing so at the family get together you may be having this holiday season. And don't forget to contact us with any information so we can update our files to better study your family!

FDC BULLETIN BOARD

CALL US AT OUR TOLL FREE NUMBER: 877-800-3430

MEDICAL FOLLOW-UP

If anyone in your family is newly diagnosed with heart problems, please let us know. Also, if you or anyone in your family has heart tests performed, either for follow-up or for the first time, regardless of results, we would be interested in receiving copies. Please contact us and we will send you a medical record release form. If we have sent you medical record release forms, please send us the completed forms as soon as possible.

EMAIL US THROUGH THE "Contact Us" PAGE ON OUR WEBSITE: WWW.FDC.TO

BLOOD KIT REMINDER

Our current consent forms expire 12/15/2006. If we have sent you a blood kit and you did not sign the form prior to this date, please contact us for an updated consent form prior to sending in your blood.

CONTACT INFORMATION UPDATES

If you have moved and/or have an email address we can contact you at, please call or email us so we can get in touch with you for any follow-up and continue to send you our newsletter.

FDC BEAT Newsletter

FDC BEAT is a triannual publication of the Familial Dilated Cardiomyopathy Project in the Division of Cardiology at Oregon Health and Science University in Portland, Oregon. The newsletter is not copyrighted and readers are welcome to photocopy its content to share with family members and health care professionals. We welcome your feedback.

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