



Greetings from the Familial Dilated Cardiomyopathy (FDC) Research Group at Oregon Health and Science University. We hope you are well and enjoying the beginnings of Spring 2006. As always, we thank you for your interest and participation in our study.

A NOTE TO FDC FAMILIES SCREENED BY OUR GROUP

Has our research group ever traveled to screen your family members for FDC? If so, we need your help! With our grant cycle ending and the need to obtain further funding from the National Institutes of Health (NIH) to continue our study, having up to date information on our large families is even more important than usual. Such information can be crucial to the study of your family and may impact the progress we are able to report to the NIH as they review our refunding application.

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FDC RESEARCH PARTICIPATION VS CLINICAL GENETIC TESTING

As we reported in our last newsletter (FDC Beat, Volume VI, Issue I, Dec 2005), our lab recently became CLIA-certified. This means that the lab is now able to release genetic testing results. But what does this really mean for FDC genetic testing and study participants? We hope this article will answer some of the questions you may have about these issues.

What is a gene? A **gene** is defined as a unit of heredity that we are born with, which is passed down from generation to generation. Genes code for proteins that perform functions in the body. Changes or alterations within a gene's code can affect the function of the protein. Genetic material (also known as **DNA** and **RNA**), obtained from blood and other tissues such as heart and skin, can be analyzed for such changes. A change in a gene's DNA/RNA that prevents the protein from performing its normal function is called a **mutation**.

What is genetic research? Genetic research involves the study of genetic material for the purpose of better understanding our genes and the role they play in health and disease. Depending on the specifics of the research, one or several genes are analyzed, as determined by the researchers. Genetic research samples are provided voluntarily by willing study participants after signing a research consent form.

Genetic research findings may or may not be available to participants, depending on the specifics of the study and the laboratory doing the testing. Research labs not CLIA-certified are legally not allowed to release results.

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Participation in genetic research is extremely important to scientists' ability to develop clinical genetic tests (further discussed in "What is clinical genetic testing" below), which can be used to help patients and their doctors make health care decisions.

In our FDC research study, the main goal is to identify the genes that cause or predispose individuals and families to dilated cardiomyopathy and heart failure. Better understanding of the genetic causes of FDC will hopefully lead to improved treatment and management of this disease. As with most genetic research, there is no cost to participate in our study.

What does the FDC study's CLIA-certification mean for you? We notify participants if we find a gene associated with FDC in their family. These participants are then given the option of getting their individual genetic test results to find out if they carry the gene mutation associated with FDC in their family. This is known as **CLIA-confirmation testing**. Since we are now CLIA-certified, we can offer research participants this testing in our lab.

If you are notified that we have discovered an FDC disease-causing gene in your family, our genetic counselor will discuss with you the limitations of the testing and the pros and cons of receiving genetic test results. Obtaining genetic test results usually requires submission of a new blood sample. In general, genetic testing performed to confirm research findings (CLIA-confirmation testing) is provided to study participants at no cost. However, because our funding is limited and for research purposes only, genetic testing for additional relatives would be billed to them and/or their insurance.

Why aren't all research participants notified of an FDC gene finding in their family? Why does it take so long? While we would like to identify a genetic cause in all of our participating families, if one exists, there are a number of factors that make it unlikely that we will do so in all cases.

Because there are many genes (greater than 20 currently) that have been suggested to cause FDC and more to be identified, there is no guarantee that we will identify the specific FDC gene(s) in your family. As is common in genetic research, some families have been in our study for a number of years without notification of any findings. This does not mean that there is no genetic cause. Rather, the size of the human genome (humans are thought to have

approximately 30,000 genes), the complexity of the disease, and current limitations in DNA technology affect our ability to identify FDC genes.

These circumstances also affect the length of time it can take to discover the genetic cause in each family. Continuation of research funding is obviously also crucial to our ability to meet the goals of our study.

Another important aspect of FDC research is to understand the incidence of mutations in certain genes, that is, the percentage of families with a specific FDC gene. There is no gene that causes 100% of FDC, so sometimes research focuses on figuring out which gene or genes cause the highest percentage of FDC. This percentage is determined by comparing how many families have a specific FDC gene with how many do not have that same gene as the cause of their FDC. Such research has a broader focus, which means that some genetic research focuses on not finding a gene mutation in a particular family or families.

Thus, even if we don't find the FDC gene in your family, your participation has still contributed and continues to contribute greatly to increasing knowledge about FDC and its causes.

What is clinical genetic testing? Clinical genetic testing examines genetic material for the purpose of diagnosis, prevention, or treatment of a patient. A clinical genetic test is ordered by a health care provider. The sample is tested only for the specific gene or genes requested. Results are reported in writing and generally take about 4-6 weeks. Like other clinical tests (such as when your doctor orders a blood test to check your cholesterol levels), there is a fee for clinical genetic testing which is billed to the patient and/or their insurance. Clinical genetic testing can only be performed by a CLIA-certified laboratory.

Clinical genetic testing for FDC is very limited. There is only one autosomal dominantly inherited (the most common form of inheritance of FDC) FDC gene that is available as a clinical genetic test – the Lamin A/C gene. Lamin A/C is commonly associated with arrhythmias (heart block, atrial fibrillation, pacemakers, etc) as well as dilated cardiomyopathy. The Lamin A/C gene is thought to be the cause of FDC in only about 5-10% of families, meaning the other 90-95% of families have FDC due to some other gene or genes, for which clinical genetic testing is not available.

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It is recommended that anyone considering clinical genetic testing have genetic counseling before the testing to discuss the risks, benefits, and limitations of such testing. Contact the National Society of Genetic Counselors at 312-321-6834 or at <http://www.nsgc.org/resourcelink.asp> for a genetics professional in your area.

FDC families, by participating in various research studies in the U.S. and other countries, have played a key role in the identification of Lamin A/C as an FDC gene and its use as a clinical genetic test. However, while Lamin A/C genetic testing is clinically available, there is still much to be learned about its association with FDC. Thus, it is still important for families with a Lamin A/C mutation (or other gene mutations identified by CLIA-confirmation testing) to participate in FDC research.

FDC Research Participation vs. Clinical Genetic Testing		
	Research Participation	Clinical Genetic Testing
Purpose	To further scientific understanding of FDC	To receive a specific result for a specific patient and a specific gene
Requirements	Signed consent, release for medical records, research blood sample	Test ordered, requisition completed by provider, blood sample from patient
Patient Interaction	Direct contact by study coordinator for consent, family history	No direct patient interaction; all interactions with health care provider
Sample Testing	May be evaluated for none, one, or several genes	Will be tested only for the specific gene requested
Results	No guarantee of a result; participants notified of FDC gene finding can have CLIA-confirmation testing to obtain results	A signed report is issued to provider with gene-specific results
Results to	Results, if reported, are provided directly to patient	Results reported to referring health care provider
Timeline for results	Indefinite, ongoing	Results usually reported within 4-6 weeks
Cost	No cost to participant	Genetic testing charges billed to patient and/or insurance

FDC GROUP MRI STUDY

Our group has recently begun applying a technology known as magnetic resonance imaging (MRI) to the study of FDC. We are trying to understand how well MRI determines heart size, shape, and function, for both people with FDC and their at-risk family members. We hope that MRI may be a more sensitive approach for the early diagnosis of heart muscle disease.

The MRI is a large machine shaped like a small tunnel that uses a powerful magnet to look at the heart tissue. A person lies on a long bed that slides into the MRI tunnel chamber. An IV is inserted in the arm to introduce a contrast material that increases the MRI's ability to look for heart muscle damage. The test takes about 90 minutes. The MRI machine is very noisy, and people that are claustrophobic may need medication to help them relax.

Family members not known to have heart problems (to compare with those diagnosed with FDC) are eligible. People with pacemakers, defibrillators, and any other type of metal implants cannot have MRI.

Heart function results (ejection fraction) derived from the MRI will be provided. If you have never had an echocardiogram and/or EKG, or it has been more than 3 years since these tests were done, these may also be performed and you will be notified of echocardiogram and EKG results. There is no charge for the study MRI or echocardiogram/EKG if performed for research purposes. Our study MRI is only performed at Oregon Health and Science University (OHSU). If you will be in the Portland area and are interested in coming to OHSU for the study MRI, please contact Jessica Kushner at (503) 494-3959, Toll-free 877-800-3430, or by email at kushnerj@ohsu.edu.

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If you have had any of the following since your screening, **PLEASE** contact Jessica Kushner Toll-free at 1-877-800-3430, ext.1, or by email: kushnerj@ohsu.edu. Thanks for your help!

- A change in your health status, such as a diagnosis of cardiomyopathy or other heart problem, irregular heart rhythm, pacemaker, defibrillator, heart transplant, etc.
- An echocardiogram, EKG/ECG, angiogram, or other heart tests/procedures performed (regardless of results)
- A new history of heart problems or sudden death in the family
- Death of a family member previously enrolled in the study
- A family member not previously in the study that has a diagnosis of heart problems or has had heart tests performed that would now like to participate

FDC BEAT Newsletter

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