

FDC Research Genetic Testing vs. Clinical Genetic Testing: Understanding the Differences

In our last issue of the FDC Beat (July 2009), we reviewed the new medical guidelines from the Heart Failure Society of America for the evaluation of genetic cardiomyopathy. One section of these guidelines describes the option of clinical genetic testing for people with dilated cardiomyopathy (DCM). In the last few years, and even the last 6 months, several new clinical genetic testing options have become available for DCM, and it can be complex to decide what testing option is right for you.

Through our research study during the last 16 years, we have analyzed the DNA of many families, typically beginning with one person in the family most affected with DCM, for 12 different genes associated with DCM. If we found a change in the DNA in your family that evidence shows is associated with DCM, we have notified you or will be notifying you.

While we continue to do genetic testing as part of our research study, we are providing you with additional information about available clinical genetic tests so that you are aware of all the options available for you and your family. In this issue, we highlight the distinction between clinical genetic testing and research genetic testing (like the genetic testing we do in the FDC Research Project).

Genetic Testing for DCM

Genetic testing is a way of analyzing a person's DNA to determine their specific genetic code. Genetic testing can be used for a number of purposes. For DCM, the goal of genetic testing is to identify mutations, or alterations, in genes associated with increased risk for development of DCM and identify family members that carry these mutations and therefore have an increased risk for developing DCM.

We know that over 30 genes in the human genome have been associated with risk of developing dilated cardiomyopathy. By studying these DCM-associated

genes through various techniques, a DCM-causing misspelling, or mutation, may be identified.

In the early 1990s, genetic testing for DCM used to be a possibility only through research testing laboratories such as ours. Since then, the number of clinical genetic tests (those that can be done through your doctor's office) has increased. The first clinical genetic test available for DCM was for a gene called *LMNA*. As genetic research has continually provided new information, the development of genetic tests for DCM has dramatically increased. Currently, a single test that can target alterations in up to 38 DCM genes can be ordered through a doctor's office. Therefore, today, genetic testing can be done as part of your clinical care through a doctor's office.

Continued on page 2

Dilated Cardiomyopathy During Pregnancy: Is There a Link with FDC?

When we collect family history information from research participants, we routinely ask about heart-related pregnancy complications (such as heart failure). We ask this question to screen for dilated cardiomyopathy (DCM) that occurs during or soon after pregnancy, called peripartum cardiomyopathy (PPCM) or pregnancy associated cardiomyopathy (PACM).

Women with PPCM/PACM have no cardiac problems prior to pregnancy, but then usually present with symptoms of heart failure (for example, fatigue, difficulty breathing, excessive fluid accumulation) during pregnancy or within several months after delivery. The problems with the heart are virtually the same as in DCM: left ventricular enlargement and decreased pumping function, meaning an enlarged heart that is not working efficiently. Some women also have heart rhythm abnormalities or other complications, such as stroke. Although some recover spontaneously, others

Continued on page 3

What is genetic research?

Genetic research, such as ours, involves the study of genetic material, often for the purpose of better understanding our genes and what role they play in human health and disease. Genetic research often looks for links between a specific gene(s) and a specific disease, and can include research on one or many genes. Genetic research can help us to gain a better understanding of the role of genes that have already been discovered or it can identify new genes whose function was previously not understood.

What is research genetic testing?

Research genetic testing means that genes are being analyzed in a research laboratory, as described above. DNA samples are provided voluntarily by willing, consented study participants. Sometimes, genetic research can result in findings that could impact a subject's health or their family member's health. In order to directly release a test result to a person, the laboratory must be legally certified to do so, called CLIA certification, which means the laboratory has met rigorous standards for doing testing for clinical purposes.

Most research laboratories, including ours, are not CLIA-certified. This means that we cannot release the result to you directly; however, through confirmatory testing, you may opt to learn your result. Such testing is conducted by CLIA-certified laboratories that offer this service of confirming results from research laboratories. For their service, these laboratories typically charge a fee, which some individuals can put through their health insurance company while others pay out of pocket (currently costs are approximately \$200-\$400). As with most genetic research, there is no cost to participate in our study.

What can a participant expect from research genetic testing in the FDC Project?

The FDC Research Project studies the genetics of dilated cardiomyopathy, beginning with a person who clearly has DCM of unknown cause. Participation of other family members, whether they have DCM or not, is also very helpful for clarifying the meaning of genetic test results in a family. However, genetic testing does not automatically occur at the time a person is enrolled in the study, and often begins with just one person in the family (a person with DCM). It could be months, years or even decades before any research results are available, and we do not guarantee that we will find significant results.

If we discover a DCM-associated genetic finding in your family, we inform all participating family members that we discovered a significant result. At this time it is the participant's choice to learn their individual result. Then,

we can work with you, your doctor and a CLIA-certified laboratory to have a new blood sample drawn and have your individual research test result confirmed. At that time, the result will be reported to your doctor from the CLIA-certified laboratory and made available to you.

What is the benefit research participation?

In our FDC research study, the main goal is to identify the genes that cause or predispose individuals and families to DCM. Participation in genetic research is extremely important to scientists' ability to develop clinical genetic tests (further discussed below), which can be used to help patients and their doctors make health care decisions. While many genes have already been discovered that are associated with DCM, this still only accounts for approximately 25-30% of cases when a genetic predisposition is suspected, leaving a lot of genetic discovery that still needs to be done. Research like ours plays an important role in trying to identify a cause in the 70-75% of cases remaining for which a genetic cause is suspected, but not identifiable on currently available testing. In addition, the role of known DCM-associated genes is still being studied. Better understanding of the genetic causes of DCM will hopefully lead to improved treatment and management of this disease.

Clinical Genetic Testing

What is clinical genetic testing?

Clinical genetic testing examines genetic material for the purpose of diagnosis, prevention, or treatment of a particular disease. Thus, it can only be performed by a CLIA-certified laboratory and must be ordered by a health care provider. The sample is tested only for the specific gene or genes requested, which should be genes that are known to be associated with a disease. Results are reported in writing to the health care provider, who in turn can release the results directly to a patient. In general, it currently takes about 4-8 weeks to receive results.

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 can range from several hundred to several thousand dollars. This can be billed to the patient and/or their health insurance plan. Health insurance coverage can be variable; however, many insurance plans do cover at least a portion of the genetic testing cost in people with DCM of unknown cause.

What is the benefit of clinical genetic testing?

One major benefit of clinical testing is that results are available within a set time frame. If a mutation is identified through clinical genetic testing for DCM, this information may immediately be used in the clinical care

Research V. Clinical Genetic Testing: In Summary

	Research	Clinical
Is there a charge for testing?	No	Yes
What genes can be tested?	Already discovered genes and new genes	Genes already discovered
Can I receive results?	By confirming them with a clinical test	Yes – through a health care provider
Time frame for results?	No time frame; not guaranteed	4-8 weeks
Is it a part of my Medical Record?	No	Yes

of the person with DCM. In addition, once a DCM-causing mutation has been identified in a family, relatives without DCM can be tested to determine whether they carry this mutation or not. Based on these results, a health care provider may choose to be more or less aggressive about cardiac screening for DCM.

What DCM clinical genetic testing is available?

In the last few years several new testing options have become available for DCM, some as recently available as

November 2009. There are only a few laboratories in the country (less than 10) offering clinical genetic testing for DCM. Of the approximately 30 known genes associated with DCM, labs currently offer testing for just a few to up to 38 genes. Although more than 30 genes have been identified as associated with DCM, a disease causing mutation is still only identified approximately 25-30% of the time.

Where can I go for DCM clinical genetic testing?

Clinical genetic testing for DCM needs to be ordered by a health care provider. This is a complex, rapidly developing field, and therefore it is advisable to seek a consult with health care professionals who specialize in cardiac genetic medicine. This consult should include genetic counseling to be sure you understand the risks, benefits, and limitations of genetic testing. Genetic counseling can be provided by various health care providers, although ideally by a certified genetic counselor or a geneticist (a doctor who specializes in genetics).

To find a genetic counselor near you, you can contact the National Society of Genetic Counselors at <http://www.nsgc.org/resourcelink.cfm> or at 312-321-6834. To find a geneticist near you, you can go to www.acmg.net and then click the link for “find a geneticist.” You could also ask your physician for a referral in your local area.

DCM during pregnancy...

Continued from page 1

eventually develop advanced DCM later in life and may require significant intervention such as heart transplantation. Others, unfortunately, do not survive. PPCM and PACM are serious medical problems, and the presenting symptoms may be overlooked as normal pregnancy findings.

PPCM and PACM are thought to be rare conditions, historically believed to result from a different cause than FDC. Inflammation, antibody abnormalities and environmental causes such as high salt intake have been proposed as possible causes for PPCM/PACM. However, we have observed that PPCM/PACM is significantly more common among our FDC study families. With this in mind, we believe that PPCM/PACM can result (at least in some cases) from alterations in the same genes that cause FDC. If so, this would mean that the daughter of a male with DCM can develop PPCM/PACM if they both carry a DCM-causing gene. Such women can benefit from cardiovascular screening before and during her pregnancy. Conversely, a woman with a diagnosis of PPCM/PACM should be also asked about her family history of heart problems, and echocardiogram and EKG screening of first-degree relatives (parents/siblings/children) should be considered because of the possibility of FDC in the family. It is also possible that different genes, perhaps those relevant in heart function during pregnancy (and not implicated in FDC as of today) may play a role in PPCM/PACM.

We are working to discover these possible - yet to be identified - genes. We would also like to understand why PPCM/PACM occurs and to predict who in the family will benefit from personalized follow-up. For this reason, part of our research has focused on PPCM/PACM. You can help us reach our goals. If you were diagnosed with PPCM/PACM, we may currently be exploring your case and in need of additional information or records.

You can help us understand the cause of DCM during pregnancy:

- ♥ Contact us if either you or a family member has or had DCM that occurred during or soon after pregnancy or if in your family, the only affected people are women with PPCM/PACM.
- ♥ Talk with your doctor, family and friends about PPCM/PACM and have them contact us to participate in our research. We can supply additional information.

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 had 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 form(s), please send us the completed form(s) as soon as possible.

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

ADD ME TO THE MAILING LIST

If you are not currently a participant in our study, but would like to receive our newsletter, please contact us with your name and address, and we will be pleased to add you to our mailing list.

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 publication of the Familial Dilated Cardiomyopathy Project in the Cardiovascular Division at the University of Miami, Miller School of Medicine in Miami, FL. The newsletter is not copyrighted and readers may photocopy its content to share with family members and health care professionals. We welcome your feedback.

**The FDC Project Group
Cardiovascular Division
P.O. Box 019132, C-205
Miami, FL, 33101**

66495H

ADDRESS SERVICE REQUESTED

TO: