[sender's address]

[Date]

Dear Family Member,

I have been diagnosed with familial hypercholesterolemia (FH). FH is caused by a change in a gene responsible for removing the bad, LDL (low-density lipoprotein), cholesterol from our bodies, thus causing very high cholesterol levels at a young age. This can lead to early heart disease such as heart attacks, strokes and narrowing of the heart valves at a young age. The good news is that heart damage due to FH can be prevented if diagnosed early and treated. My gene test shows that I have a specific change [*insert cDNA change and protein change*] in the [*insert gene identifier*] gene.

Since FH is passed down through families you might also have it. One way to find out if you have it is to get the FH gene test. If you have the gene test and it is positive then your doctor can start a medication to prevent the heart damage.
I found out about my FH through a study being done at Duke and the Medical College of Wisconsin called 'Implementing familial hypercholesterolemia cascade screening'. Because my test was positive, as part of this study they are offering testing for this specific gene change to my family members at no charge. The researchers are offering this testing because it is recommended by the National Lipid Association as part of normal medical care (https://www.lipid.org/sites/default/files/articles/familial_hypercholesterolemia_1.pdf) and they are interested in learning how many relatives decide to have this test done. You do not have to be in the research study to have the gene test. Your own primary care provider can use the specific gene information in this letter to order the test, but if it is not done as part of the research study you or your insurance will be billed for the test.

If you are interest in being tested as part of the study, the lab at the Medical College of Wisconsin is willing to perform the testing for you and you will not be charged for the test as long as your sample is returned to the laboratory by [*insert date, 30 days from when the letter is sent*]. If you are interested in having the testing done there through a mail-in kit, please contact the Medical College of Wisconsin's clinical laboratory at 414-955-2550 to get more information. My study ID is [proband's study ID]. Below is more information about the study and what is involved.

What is involved?

The FH test involves you collecting and sending a saliva sample to the lab which will analyze the DNA in the sample for genetic testing. Saliva sample collection requires you to spit plastic tube until the collected saliva reaches the fill line. There are no physical risks associated with providing saliva sample, however you may experience a dry mouth. If you have difficulty producing enough saliva, please ask for an oral swab kit.

The purpose of the research is to find out how often people would want to be tested for FH. If you send a sample for FH testing as part of this study, the lab will send information to the researchers on the number of sample collection kits sent out (total across all families), number of sample collection kits returned (total across all families), number of positive and negative results (total across all families), gender, and age. Your individual, personal information will not be sent to the researchers.

What is being tested?

The lab will only test you for the specific gene change that was found in in my test and no other genes associated with FH or other health conditions will be analyzed or interpreted.

The results of this DNA test could be:

1. Positive, in which case it means that:
    a. you have a risk for health complications related to FH
    b. you should talk with your primary care provider about this finding
    b. other family members might also have a risk for FH
2. Negative, in which case it will:
    a. Reduce, but not eliminate the possibility that you could have FH

Results Reporting

This genetic testing is a clinical test done in a CLIA (Clinical Laboratory Improvement Amendments)/CAP (College of American Pathologists) approved clinical laboratory. A genetic counselor or a research nurse will contact you to explain the test results. A clinical report with results will be provided to you and the primary care provider you designate. If you have not provided any information about your primary care provider, test results will be sent to the clinical lab director at MCW. We expect results to be available within 2 months, possibly sooner.

Confidentiality

A clinical report with results will only be released to you and the referring certified healthcare professional(s) listed on the test requisition form. You will be provided with a copy of your genetic test results. All laboratory data (clinical and genetic information) obtained through this clinical testing will remain confidential. Your personal information will be kept confidential by the lab and will not be shared with the study team. The only information the study team will receive is the number of tests that the lab runs and the number of those that are tested positive for FH.

The Genetic Information Nondiscrimination Act (GINA), a federal law, provides some protections against genetic discrimination. Here is some information about the Genetic Information Nondiscrimination Act (GINA):

- GINA is a Federal law that protects your genetic and family history information from health insurance companies and employers.
- Health insurance companies and group plans may not request genetic information from this study;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Limitations of testing

Some types of DNA changes that could cause a specific genetic disorder may not be detected by this test. As with most molecular genetics tests, this test has technical limitations that may prevent detection of specific rare variants due to poor DNA quality, inherent DNA sequence properties, or other types of limitations. In this testing, you will only be tested for the gene change previously identified. There are many genes that can cause FH, and as part of the research study only specific genes and gene changes were tested. If the test is negative you should talk with your primary care provider about additional testing if you have a high cholesterol that is concerning for a hereditary cholesterol disorder.

Possible sources of error

There may be possible sources of error including, but not limited to, trace contamination, rare technical errors in the laboratory, rare DNA variants that compromise data analysis, inconsistent scientific classification systems, and inaccurate reporting of family relationships or clinical diagnosis information (e.g., sample tubes getting mixed up). If the testing laboratory suspects any of these errors in your sample, you may be asked to provide a new sample for testing.

Risks versus Benefits

It is your responsibility to consider the possible impact of your test results as they relate to insurance rates, obtaining disability or life insurance and employment. The benefit of being tested is that it could lead to early diagnosis and treatment of the FH.

Alternatives to this genetic testing

You are under no obligation to participate in this genetic testing. Remember you can choose to get the testing done anywhere and you do not have to have it done at Medical College of Wisconsin. You can also choose not to get genetic testing for FH.

Who can I talk to if I have questions?

If you do choose to have the test done through this study, you will be offered genetic counseling with a geneticist, genetic counselor or other qualified healthcare professional who can answer questions, provide information and advice about alternatives before having this test. Further testing or additional physician consults may be warranted. If you have any questions about the testing, please contact a genetics provider in the Medical College of Wisconsin's clinical laboratory at 414-955-2550.

If you have questions about FH or this letter, you can take it to your health care provider or you can contact a genetic counselor who can help you understand FH and what it may mean for you and your family. Thank you.

Sincerely,

[study participant's name]