Frequently asked questions

WHAT IS MYFSHD?

MyFSHD is a source dedicated to educating those seeking information about all aspects of facioscapulohumeral muscular dystrophy (FSHD), and connecting people around the globe with the Peter and Takako Jones Lab at the University of Nevada, Reno, USA, where they can take part in the saliva-based FSHD research level diagnostic testing, at no cost to individuals, to learn about their own potential FSHD disease status.

WHAT IS FSHD?

FSHD refers to facioscapulohumeral muscular dystrophy. It is a genetic muscle disease that affects males and females of all ages and ethnicities worldwide. It is one of the nine categories of muscular dystrophies that includes Becker muscular dystrophy (BMD), Duchenne muscular dystrophy (DMD), Congenital muscular dystrophy (CMD), FSHD, Limb-girdle muscular dystrophy (LGMD), Oculopharyngeal muscular dystrophy (OPMD), Myotonic dystrophy (DM), Emery-Dreifuss muscular dystrophy (EDMD), and Distal muscular dystrophy. For more information, see “About FSHD” on this website.

WHAT ARE THE PHYSICAL SIGNS OF FSHD?

Briefly, clinical symptoms of FSHD include weakness in the face, shoulder girdle, upper arms, abdomen and legs. Noticeable symptoms typically appear in the second decade of life for males and third decade of life for females; however, symptoms may appear much earlier or later in life, and clinical presentation is highly variable among individuals even within families.

Progression of pathology is generally slow and can appear asymmetric for a long time.

In addition, individuals may be genetically FSHD yet never exhibit any clinical symptoms of the disease throughout their lives.

WHAT CAUSES FSHD?

Ultimately, FSHD is caused by genetic mutations that result in expression of the pathogenic *DUX4* gene in skeletal muscles.

Genetically, FSHD1 is caused by mutations in one’s DNA that reduce the size of the chromosome 4q35 D4Z4 array resulting aberrant expression in skeletal muscle of the *DUX4* gene from within the D4Z4 array. FSHD2 is caused by genetic mutations that affect the proteins that keep the *DUX4* gene OFF, similarly resulting in the *DUX4* gene being expressed in skeletal muscles.

Epigenetically, the genetic mutations that cause both FSHD1 and FSHD2 result in the loss of a repressive chromatin structure (an epigenetic change) that normally silences gene expression from the chromosome 4q35 D4Z4 array and instead results in a chromatin structure that allows aberrant *DUX4* gene expression in skeletal muscle from within the array.

Ultimately, it is the aberrant increase in *DUX4* gene expression in skeletal muscle that leads to FSHD pathology.

NO ONE IN MY FAMILY HAS FSHD. HOW DID I GET FSHD?

FSHD spontaneously affects ~1:20,000 individuals. In de novo (new) cases, it is caused by spontaneous random mutations in the chromosome 4q D4Z4 array for FSHD1 or in the *SMCHD1*, *DNMT3B*, or *LRIF1* genes for FSHD2.

In addition, many genetic FSHD individuals are asymptomatic or very mildly affected, so family members may in fact be FSHD and not realize it.

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FSHD IS IN MY FAMILY BUT I FEEL FINE. COULD I OR MY KIDS STILL BE AT RISK FOR FSHD?

Yes. Being affected with FSHD is a combination of clinical presentation and genetics. However, one can be genetically FSHD and not show clinical symptoms until much later in life, if ever. If a blood relative has been genetically diagnosed with FSHD, you may want to be tested regardless of having no symptoms.

I HAVE ALREADY HAD CHILDREN. DID I PASS MY FSHD ON TO MY KIDS?

The best way to know if you passed on your FSHD genetics to your kids is through clinically approved genetic testing. Alternatively, our FSHD research testing can provide a strong indication of FSHD genetic inheritance while keeping the results off of your child's medical record.

FSHD is a dominant genetic disease meaning only one genetic mutation is required to pass on the disease genetics. In general, if you are FSHD1, there is a 50% chance to pass the FSHD1 genetics to each child. If you are FSHD2, the statistical chances are more complicated to calculate and are between 25-50% to pass on to one's child and depend on certain genetic criteria in the other parent.

DOES MYFSHD PERFORM FSHD DIAGNOSTIC TESTING?

No. MyFSHD does not perform any testing. MyFSHD connects interested individuals with the laboratory that does the testing, the Peter and Takako Jones Lab at University of Nevada, Reno, USA.

MyFSHD does not learn of your results, distribute your results, or keep your information.

WHAT IS THIS FSHD RESEARCH TEST?

This test is a saliva-based test that identifies specific genetic sequences and epigenetic signatures (i.e., DNA methylation) in your DNA that together strongly correlate with FSHD type 1 or FSHD type 2 and distinguish these cases from healthy or non-FSHD individuals. It does not directly detect an FSHD1 D4Z4 deletion or an FSHD2 mutation. Thus, your report will state if your methylation status correlates with what is known for FSHD1, FSHD2, or does not correlate with FSHD.

WHAT DOES IT MEAN TO BE A "RESEARCH TEST?"

A research test is performed in a research lab as opposed to a USA government CLIA-certified (Clinical Laboratory Improvement Amendments) laboratory. In the USA, all laboratory testing performed on people in which the results of the testing are for clinical purposes (including family planning) must be performed in a CLIA-certified facility.

This research testing is performed in the Peter and Takako Jones Lab located at the University of Nevada, Reno, USA, which is not CLIA-certified. Therefore, the results are not considered an official genetic diagnosis for FSHD, and the results do not become part of your official medical record or your insurance record. In addition, this research testing will not meet clinical trial inclusion criteria.

You may show your research testing results to your medical doctor; however, the results are not supposed to be used to make medical decisions or to be used for family planning, and your medical doctor may ignore the results. However, these results could be helpful for deciding on whether you would like to further pursue CLIA-approved genetic testing.

WHO IS THIS RESEARCH TESTING FOR?

- Individuals who would like to help advance FSHD research. You can opt not to have results returned to you if you don't want to know about your FSHD status.
- Individuals with confirmed FSHD who want more information about their disease status.
- Individuals with a clinical diagnosis of FSHD but no genetic confirmation of FSHD1 or 2.
- Individuals diagnosed clinically as FSHD but with a negative FSHD1 genetic test that is interpreted as FSHD2, yet

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without confirmation of FSHD2.
- Individuals with FSHD in their family who want information about their own FSHD status.
- Individuals who want information on their children's FSHD status without having clinically relevant results documented in their medical record.
- Adults who want information on their own potential to have FSHD without having clinically relevant results documented in their medical record.

WILL RESEARCH TESTING RESULTS GET ME INTO A CLINICAL TRIAL?

No. While each clinical trial will determine its own inclusion criteria, you will undoubtedly need to undergo CLIA-approved genetic testing to be eligible for FSHD clinical trials. At this time, epigenetic testing of any sort does not meet FSHD clinical trial inclusion criteria.

HOW MUCH WILL THE RESEARCH TEST COST ME?

The test itself will cost you nothing. The actual test costs will be covered through research grants and donations made to the Peter and Takako Jones Lab at University of Nevada, Reno, USA, from foundations and generous individuals interested in making FSHD research testing available at no cost to those in need in the USA and around the world.

For international participants, it is helpful if you can pay for the return shipping of the saliva sample as it is often much less expensive for you to pay shipping through your local postal office than for the laboratory to arrange for FedEx or DHL courier service; however, we understand that international shipping can still be expensive and, if necessary, the research lab will cover the costs for the return shipping.

WHY IS THIS RESEARCH TEST FREE FOR ME?

Traditional FSHD diagnostic testing is expensive, often not covered by insurance, and not widely available. Thus, many individuals with clinical symptoms of FSHD or at genetic risk for FSHD go untested. The development of epigenetic testing has greatly reduced the cost of testing. In addition, since this test can be performed on a saliva sample instead of a blood sample, and can be collected in your home and then sent through the mail, the testing can be performed on anyone in the world, regardless of one's income or location.

This is currently a research test and part of a research project. The testing laboratory, the Peter and Takako Jones Lab located at University of Nevada, Reno, USA, analyzes the results to learn more about the factors that contribute to variability of FSHD severity in families. By participating, you are helping the research community better understand FSHD.

Testing costs are covered by research grants and donations made to the Peter and Takako Jones Lab from foundations and generous individuals who want to help people who otherwise could not access or afford FSHD testing.

Even though the results are not considered clinically relevant, they are highly accurate and can provide some insight to one's potential to be affected by FSHD. In addition, they may help individuals make decisions about future clinically relevant testing.

AFTER I MAIL BACK MY KIT, HOW LONG UNTIL I GET MY RESULTS?

Once your saliva kit is received by the lab (which can take a week in the USA and much longer internationally), it typically takes about three to six weeks to get your results. However, sometimes there are difficulties with a particular sample or the sequencing facility has delay. If you have not received your results and you had requested them, please reach out to peterjones@med.unr.edu.

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WHAT DO I HAVE TO DO FOR THE TEST? DO I HAVE TO GIVE BLOOD?

You do not need to give blood. You only need to provide some of your saliva for this test to be performed. This can be provided from the privacy of your own home.

BESIDES ME, WILL ANYONE ELSE SEE MY RESULTS?

Your results are returned only to you or a family member if you request that your results be returned to them. If under 18, your results are returned to your parent or guardian who signed the consent form. We do not share your identifiable results with anyone.

IS MY INFORMATION SECURE?

Yes. Your identifiable information is kept separately in a HIPAA secure database at University of Nevada, Reno, USA, accessible only to the principle investigators of the study and the institutional review board. In addition, we do not provide your information or your results to anyone, and we do not reveal your participation to anyone. You may choose to reveal your results to family members, friends, or your physician, but that is entirely up to you.

In the lab, your DNA and test results are de-identified and no one other than the principle investigators (Drs. Peter and Takako Jones) is able to match the results to an individual.

HOW LONG WILL THE LAB KEEP MY RESULTS?

Your de-identified results will become part of a research project and will be kept indefinitely. Your results are de-identified in the lab and the identification key is kept separately in a HIPAA secure file.

HOW LONG WILL THE LAB KEEP MY DNA SAMPLE?

This depends upon your answer on the consent form when you fill it out. You can choose to: 1) have your sample destroyed after the Peter and Takako Jones Lab uses it, 2) have your sample stored but be asked before it is used again, or 3) allow the Peter and Takako Jones Lab to use it for additional research studies relating to FSHD. Regardless, your sample is de-identified in the lab and the identification key is kept separately in a HIPAA secure file.

HOW ACCURATE ARE THE TEST RESULTS?

In addition to the research testing, the procedure is constantly being validated against samples with a confirmed genetic diagnosis of FSHD1, FSHD2, or healthy/not FSHD. To date, a result consistent with FSHD is >99% accurate, and a result consistent with not FSHD/healthy is >97% accurate.

WHAT WILL THE TEST REVEAL?

This research test will determine if: 1) you have FSHD-permissive or nonpermissive genetics, and 2) your epigenetic status correlates with FSHD or does not correlate with FSHD. In addition, for most FSHD cases the test can distinguish between FSHD1 and FSHD2.

IF THE TEST REVEALS I DON'T HAVE FSHD, WILL IT INDICATE WHAT I MIGHT HAVE?

No. This test only reveals your likelihood for FSHD compared with not FSHD. It does not identify any other diseases regardless of your clinical symptoms. We do not sequence your genome, which means that your genomic data remains with you and cannot be obtained from us, used by us, or stolen.

DOES A POSITIVE TEST MEAN THAT I HAVE FSHD?

A determination of FSHD means you very likely have the genetic components of FSHD; however, being genetically FSHD does not mean you are clinically FSHD. A true diagnosis of FSHD is a combination of genetics and clinical presentation and should only be made by a qualified neurologist.

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Many people who fit the genetic criteria for FSHD are clinically asymptomatic and may remain so for much or all of their lives. However, be aware that although you may feel fine now, you may show symptoms 5, 10 or 20+ years down the line. Being aware of your genetic risk may make you more aware of physical changes over time and help you better understand the possible underlying cause of any physical decline. In addition, it allows you to make long-term plans for the potential to be affected and to consider getting official FSHD testing at the appropriate time for you.

HOW WILL KNOWING THE RESULTS HELP ME?

There are several ways participating in this research testing may help you. You may learn that you or your children have genetic and epigenetic signatures consistent with FSHD. Alternatively, you may learn that you or your children have genetic and epigenetic signatures indicating that it is highly unlikely or impossible to have FSHD. Either result may help you decide if you want to pursue clinically relevant, approved diagnostic testing in the future. A full explanation of potential benefits will be explained on the research consent form that will be sent to you if you choose to participate in the study.

ARE THERE ANY RISKS INVOLVED WITH HAVING THIS RESEARCH TEST PERFORMED?

Yes. Your (or your children's) results from this research testing may reveal that you (or your child) are consistent with being positive for FSHD. If you have a family history of FSHD, you may learn that you did in fact inherit the familial pathogenic FSHD chromosome. If you are having your child or children tested, you may find out that they inherited the familial FSHD genetics. Take some time to consider if you really want to know this information, understanding that the results could reveal either situation, FSHD or not FSHD.

In addition, no testing is perfect. Despite the best efforts for accuracy, there is a small chance that the research testing will not give a correct result.

While your identifiable information is kept in a HIPAA secure database and the de-identified results are kept separate, there is always a small potential for data breach resulting in your participation and/or results being revealed.

A full explanation of risks will be explained on the research consent form that will be sent to you if you choose to participate in the study.

I HAVE ALREADY HAD GENETIC TESTING. COULD MY GENETIC TEST RESULTS BE WRONG?

Yes. Some current CLIA-approved clinically utilized genetic testing often does not determine if an FSHD1-sized chromosome 4 deletion is on a required FSHD-permissive chromosome 4A. The Peter and Takako Jones Lab has found several instances of genetically confirmed FSHD1 where the deletion was actually on a nonpermissive chromosome 4B, which cannot result in FSHD. Thus, incomplete genetic testing prevented an accurate genetic diagnosis of not being FSHD1.

It should be noted that FSHD1 optical mapping (Bionano) and molecular combing (Genomic Vision) do provide the necessary A/B haplotyping. Also, A/B haplotyping from PGFE/Southern blotting for FSHD1 can be requested at the University of Iowa Diagnostic Laboratory.

HOW DO I GET A CLINICALLY RELEVANT CONFIRMATION OF MY RESEARCH TEST RESULT?

In the USA, clinically relevant diagnostic testing that will go on your medical record and make you eligible for clinical trials and workers' compensation can be obtained through several sites, including Athena Diagnostics, Quest Diagnostics, PerkinElmer Genomics, and the University of Iowa Diagnostic Laboratory. You may need a recommendation from a physician, and insurance may or may not cover this testing.

In Canada, testing is available at the Children's Hospital of Eastern Ontario Molecular Genetics Diagnostic Laboratory.

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In Europe, testing is available at the University of Leiden Medical Center in The Netherlands and Hopitaux Universitaires de Marseille-Hopital de la Timone.

CAN I USE THESE RESULTS FOR FAMILY PLANNING?

While these results are informative as to your FSHD status, only clinically relevant testing performed in a CLIA-approved laboratory should be used for family planning. Consultation with a genetic counselor is highly recommended as well.

IS PRENATAL TESTING AVAILABLE FOR FSHD?

Yes. When combined with IVF, there is a preimplantation screening that can be performed to identify embryos that likely do and do not have the familial FSHD1 chromosome. Please see this video for more information. If considering this approach, it is advisable to discuss this and other aspects of family planning with your medical doctor and/or a genetic counselor.