Genetic Testing for Familial Chylomicronemia Syndrome (FCS)

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***Yang,** Living with FCS*

Your guide to FCS genetic testing

For patients with symptoms, or a clinical diagnosis, of familial chylomicronemia syndrome (FCS), genetic testing may confirm a diagnosis of FCS. Confirming a diagnosis of FCS can help guide medical management by your healthcare professionals (HCPs).[1]

The FCS Genetic Testing program, sponsored by Ionis Pharmaceuticals, offers confidential genetic testing to eligible patients.

Working in partnership with GeneMatters and their genetic counselors, the FCS Genetic Testing program also provides information, support, and resources during the testing process.

To learn about genetic testing and FCS, read this brochure and visit **KnowYourTGs.com** for more information.

What are genes?

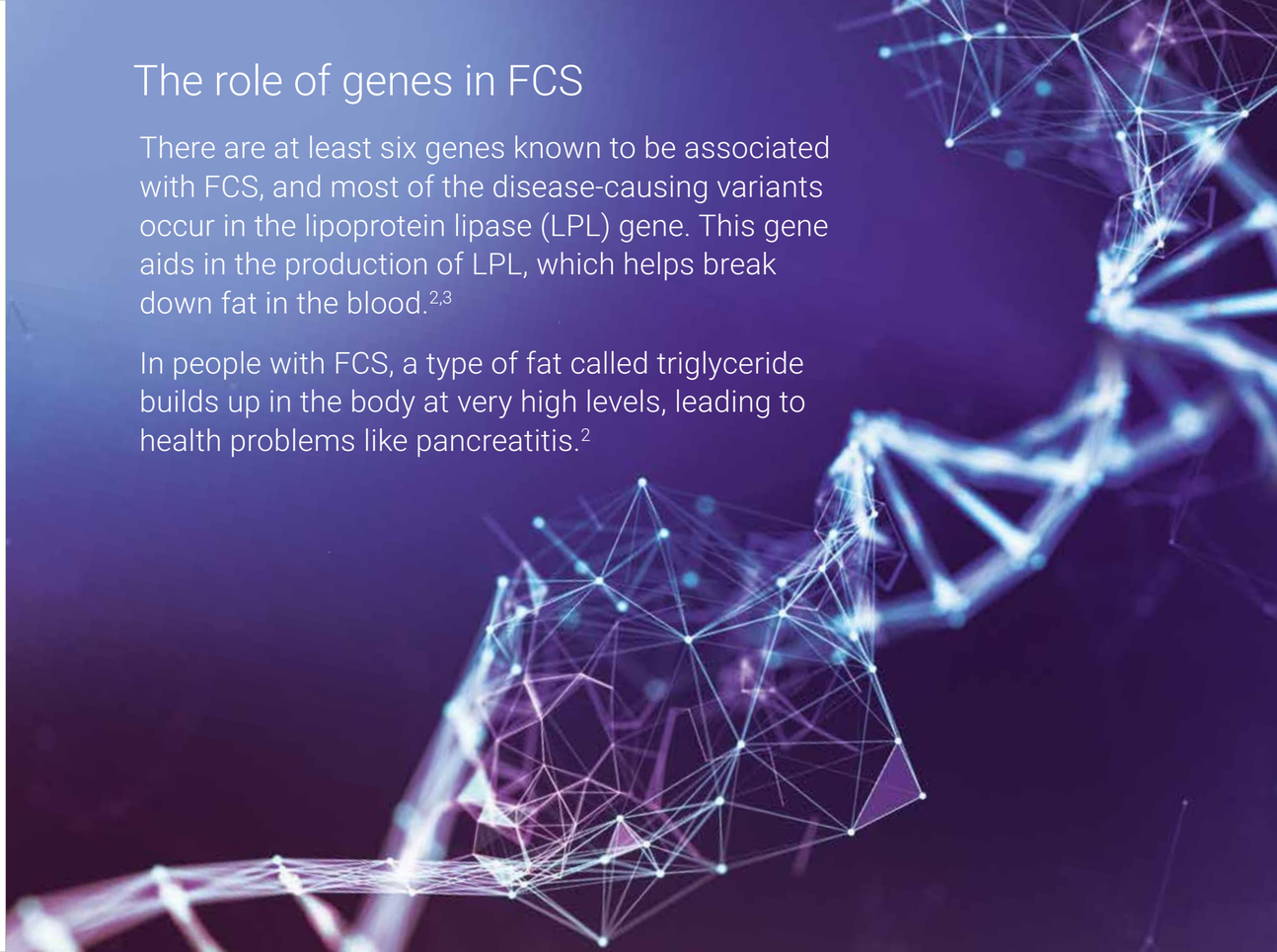
Genes contain DNA and are responsible for making all the different proteins in your body. Each protein has a specific job. Changes to DNA are called *variants*. Some variants may cause disease (also known as *mutations*), whereas other variants may not.

Our genes are inherited from our parents. We receive half of our genes from our mother, and half of our genes from our father.

The role of genes in FCS

There are at least six genes known to be associated with FCS, and most of the disease-causing variants occur in the lipoprotein lipase (LPL) gene. This gene aids in the production of LPL, which helps break down fat in the blood.[2,3]

In people with FCS, a type of fat called triglyceride builds up in the body at very high levels, leading to health problems like pancreatitis.[2]



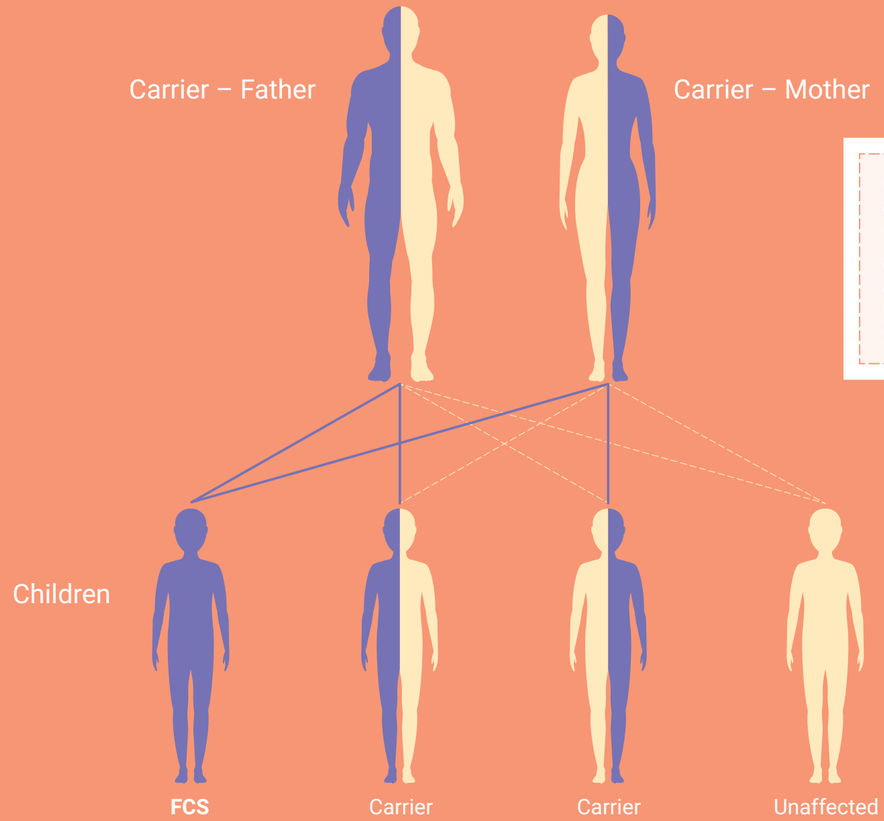
Inheriting FCS

For someone to have FCS, they must inherit two disease-causing genes, one from each parent. This type of inheritance is called autosomal recessive inheritance.

A person who inherits only one disease-causing gene is called a carrier.[2]

The diagram on the right shows how FCS is inherited. When two parents are carriers, each child they have together has a:

- **1 in 4 (or 25%) chance to have FCS.** This means the child has two *mutations*, one passed down from each parent.
- **1 in 2 (or 50%) chance to be a carrier of FCS.** This means the child has one *mutation* and the child will not have FCS. They are more likely to have higher triglyceride levels.[2]
- **1 in 4 (or 25%) chance to be unaffected.** This means the child does not have FCS and is not a carrier.



Unaffected – a person who does not have FCS and is not a carrier.

Carrier – a person who does not have FCS, but may have hypertriglyceridemia (high triglyceride levels)

Benefit of genetic testing for FCS

Genetic testing looks for variants in a person's genes that may cause FCS. Healthcare professionals may use genetic tests for two main reasons:

1. **Confirming an FCS diagnosis**
Genetic testing can help people suspected of having or clinically diagnosed with FCS see if they have disease-causing variants in FCS-related genes. In this case, the test may confirm their disease.[1]

2. **Guide treatment and management**
Finding out that FCS is the right diagnosis is important because it may help healthcare professionals make lifestyle recommendations and referrals to specialists, such as a lipidologist.[4]

***Fred,** Living with FCS*
(with his wife and caregiver Lynne)

Eligibility for testing

The FCS Genetic Testing program is sponsored by Ionis Pharmaceuticals and available to certain qualifying patients. Talk with your healthcare professional to see if you qualify for the program. You qualify if you have:

- Extremely high (severe) triglyceride levels (more than 880 mg/dL or 10 mmol/L), on two fasting blood tests in a row.
- No other known causes of high TG levels.

Get your questions answered

The FCS Genetic Testing program has partnered with GeneMatters to provide information on FCS, as well as support surrounding the genetic testing process.

The FCS Genetic Testing program offers genetic counseling through GeneMatters, an independent genetic counseling service.

Call +1 888.478.1494 to learn more.

How to get genetic testing for FCS

- Make an appointment with a healthcare professional (HCP) to discuss genetic testing.
- Share the **KnowYourTGs.com/genetic-testing** webpage with your HCP. Your HCP will check if you qualify for the confidential FCS Genetic Testing program.
- If you qualify, your HCP can order a genetic test at: **https://www.preventiongenetics.com/sponsoredTesting/Ionis_FCS**. Testing involves either a saliva sample, an oral swab or a blood draw.
- All tests can be done at your doctor's office, or a saliva kit or oral swab kit can be mailed directly to your home.
- If a saliva kit or oral swab kit is sent to your home, the kit will arrive a few days after ordering. Follow instructions for collection and how to mail the kit to the lab.
- Testing takes about 3-4 weeks. When results are available, talk with your HCP. You may be scheduled to talk with a genetic counselor about your results and what they mean.
- To learn more about FCS genetic testing, visit **KnowYourTGs.com/genetic-testing** or call the GeneMatters hotline **+1 888.478.1494**.

** Doctors, nurses, physicians' assistants, and genetic counselors are examples of healthcare professionals who may be able to order genetic tests in your state.*

What to expect on your results report

Genetic testing usually shows one of three results:

1 **POSITIVE**

A positive can occur in two ways:

A. **Expected to have FCS.** The test found two disease-causing variants in one of the genes that cause FCS. These variants are likely an explanation for some of your health problems.

B. **Carrier of FCS.** The test found one disease-causing variant in one of the genes that cause FCS.

2 **NEGATIVE**

The test did not find a *variant* in any of the genes known to cause FCS.

3 **VARIANT OF UNCERTAIN SIGNIFICANCE**

One or more variants were found in the genes tested, but the lab does not have enough information to determine if the variant(s) causes FCS or not.

Note: If you are not found to have a disease-causing variant but you have a diagnosis of FCS by your doctor, this result does not change your diagnosis.

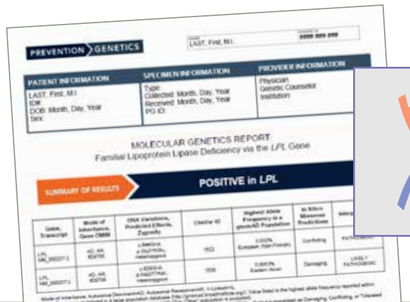
Speak to a genetic counselor

Genetic counselors are specially-trained healthcare professionals. They can:

- Support you in making choices while going through the testing process
- Prepare you before your test by explaining what to expect
- Go over test results to help you understand your report and what it means

Talk to a genetic counselor for more information and consider including the test results in your FCS CareBook for future reference and discussion with your HCP. Visit **KnowYourTGs.com/get-tools** for your free copy of the CareBook.

> “Genetic Counselors provide education on a rare disease and help individuals understand what this condition means for them, their future, and their families.”
>
> – Kiley Johnson, Genetic Counselor, GeneMatters


PREVENTION > GENETICS

PATIENT INFORMATION

SPECIMEN INFORMATION

PROVIDER INFORMATION

MOLECULAR GENETICS REPORT
Familial Lipoprotein Lipase Deficiency via the *LPL* Gene

SUMMARY OF RESULTS

POSITIVE in *LPL*

FCS Genetic Testing Program offers education on disease and genetic testing. **Please call GeneMatters with any questions at +1 888.478.1494.**

FCS Genetic Testing has partnered with GeneMatters to offer genetic test counseling services. Each counseling session is unique to the individual patient and may discuss the points below.

BEFORE YOUR TEST, A GENETIC COUNSELOR MAY DISCUSS:

- Why your HCP referred you for testing
- Your medical and family history
- Information about FCS
- The risks, benefits, and limitations of genetic testing
- The possible test results from genetic testing
- A plan for how to get a genetic test and discuss the results
- Concerns you may have about genetic testing

AFTER YOUR TEST, A GENETIC COUNSELOR MAY DISCUSS:

- The results of the genetic test & what they mean for you
- Some of the same information reviewed before the test
- Your concerns and feelings you may have about your results
- Any impact the test results have for you and your family
- Resources, if you need more information
- A plan based on your test results
- How to talk about the test results with your family
- Who else in your family may benefit from genetic testing

What to do next

1. Talk to your healthcare professional (HCP) about getting a genetic test for FCS.
2. Call GeneMatters at **+1 888.478.1494** to learn more about the testing process.
3. Visit **KnowYourTGs.com** for FCS-related information, tools, and support.
4. Get a free copy of the FCS CareBook at **KnowYourTGs.com/get-tools**. Include genetic test results in your FCS CareBook for future reference and discussions with your healthcare team.

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1. Laufs U, Parhofer KG, Ginsberg HN, Hegele RA. Clinical review on triglycerides. *Eur Heart J.* 2020;41(1):99-109c.
2. Carrasquilla GD, Christiansen MR, Kilpeläinen TO. The genetic basis of hypertriglyceridemia. *Curr Atheroscler Rep.* 2021;23(8):39.
3. Dron JS, Dilliott AA, Lawson A, McIntyre AD, Davis BD, Wang J, et al. Loss-of-function CREB3L3 variants in patients with severe hypertriglyceridemia. *Arterioscler Thromb Vasc Biol.* 2020;40(8):1935-41.
4. Moulin P, Dufour R, Averna M, Arca M, Cefalù AB, Noto D, et al. Identification and diagnosis of patients with familial chylomicronaemia syndrome (FCS): Expert panel recommendations and proposal of an "FCS score". *Atherosclerosis.* 2018;275:265-72.

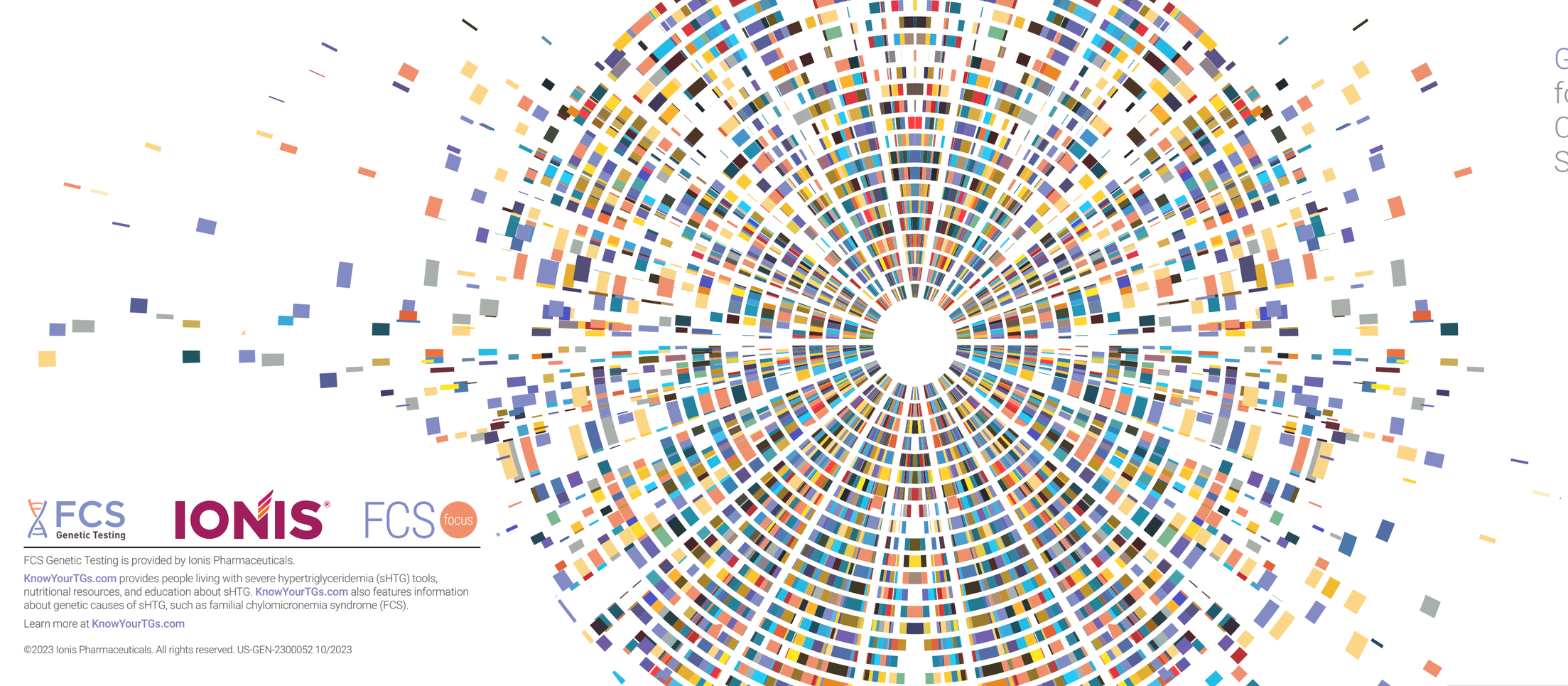
"Having this conclusive diagnosis meant I didn't have to self-investigate my own symptoms and my own debilitating chronic condition."

– Charles, Living with FCS

Notes

Use this page to jot down any additional items you would like to discuss with your healthcare professional.

Genetic Testing for Familial Chylomicronemia Syndrome (FCS)



FCS Genetic Testing

IONIS®

FCS focus

FCS Genetic Testing is provided by Ionis Pharmaceuticals.

KnowYourTGs.com provides people living with severe hypertriglyceridemia (sHTG) tools, nutritional resources, and education about sHTG. KnowYourTGs.com also features information about genetic causes of sHTG, such as familial chylomicronemia syndrome (FCS).

Learn more at KnowYourTGs.com