Amicus Therapeutics®

The Many Faces of Fabry

Fabry variants, symptoms, and inheritance—how your genetics connect them all.

Knowing more about your Fabry disease can help you better understand the treatment options available to you.

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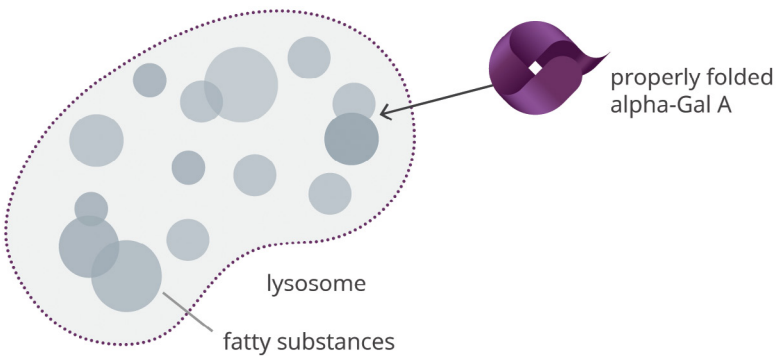
The Many Faces of Fabry

What is Fabry disease?

Fabry is a rare disease that is caused by a change, called a mutation or variant, in the galactosidase alpha (*GLA)* gene.

Normally, the *GLA* gene provides instructions to your body to make an enzyme called alpha-galactosidase A (alpha-Gal A). This enzyme breaks down fatty substances (also called substrates) in the lysosome, a part of the cell that acts like a recycling center.



But in Fabry disease, alpha-Gal A either is absent or doesn't function properly, causing a buildup of fatty substances that leads to cellular damage and Fabry symptoms.

Many genetic variants can cause Fabry disease.

OVER 1,000 genetic variants have been determined to cause Fabry disease.

Part of the reason why Fabry can affect people differently is because the disease is not caused by one single genetic variant. In fact, there are many different changes in the *GLA* gene that can cause Fabry disease.

It is important to note that even if two individuals have the same variant, they may have different symptoms and health issues caused by Fabry disease. Even members of the same family can have the same genetic variant with different effects.

Fabry can affect many parts of the body.

Possible symptoms of Fabry:

HEART
- Irregular heartbeat (fast or slow)
- Heart attack or heart failure
- Enlarged heart

KIDNEYS
- Protein in the urine
- Decreased kidney function
- Kidney failure

NERVOUS SYSTEM
- Nerve pain
- Intolerance to heat, cold, or exercise
- Transient ischemic attack (TIA) and stroke
- Pain or burning in the hands and feet
- Vertigo/feeling dizzy

LUNGS
- Wheezing
- Difficulty breathing, shortness of breath
- Bronchitis
- Chronic cough

PSYCHOLOGICAL
- Feelings of guilt, worry, depression, isolation, and/or fear

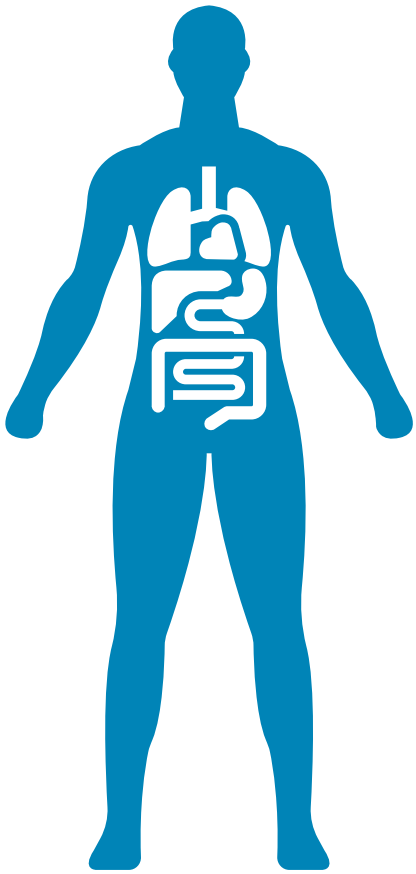
GASTROINTESTINAL
- Nausea, vomiting, cramping, and diarrhea
- Pain/bloating after eating, feeling full after a small amount of food
- Constipation

EARS
- Hearing loss, ringing in the ears (tinnitus)

EYES
- A whorled pattern in the cornea
- Fabry cataracts

SKIN
- Sweating less than normal or not at all
- Small, dark, red spots, mostly appearing between the belly button and upper thighs

OTHER
- Fatigue—A deep feeling of tiredness



Although the symptoms listed above may seem extensive, everyone with Fabry is different. People can experience some, all, or none of these symptoms, and they can get worse at different rates. Take note of how your Fabry affects your body, and talk with your healthcare provider about your symptoms.

There are different types of Fabry.

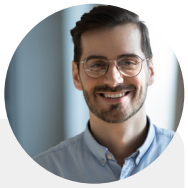
Fabry disease presents along a spectrum:

CLASSIC FABRY IN MALES	This type of Fabry can cause many severe symptoms beginning in early childhood and can lead to serious organ damage.
CLASSIC FABRY IN FEMALES	Symptoms can present during childhood or later in life and range in severity from mild to severe.
LATE-ONSET FABRY	People with this type (both male and female) have some alpha-Gal A enzyme activity and may not experience symptoms until they are adults.
LATE-ONSET, CARDIAC/RENAL	Certain variants may lead to late-onset Fabry affecting primarily the heart (cardiac) or the kidneys (renal).
UNCERTAIN SIGNIFICANCE	Variants of uncertain significance either lack enough evidence or have conflicting evidence of their ability to cause Fabry disease. A person with a variant of uncertain significance may or may not experience Fabry disease symptoms.

Although Fabry presentation is highly variable, it is often progressive, meaning that the disease tends to get worse over time. Your healthcare provider may want to pay close attention to specific parts of your body that your Fabry disease is affecting the most, and order necessary tests. Make sure to monitor your symptoms and routinely talk to your healthcare team.

There's no one journey to diagnosis.

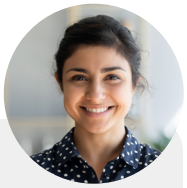
Fabry disease patient profiles*:



CLASSIC FABRY IN MALES

Connor, 37 years old

- Connor first started experiencing symptoms as a child. His gastrointestinal issues were thought to be related to lactose intolerance. He also had unexplained feelings of fatigue and lack of sweating, which resulted in exercise tolerance issues.
- Following a misdiagnosis of polycystic kidney disease, Connor was properly diagnosed with Fabry disease after opting for genetic testing.
- He was finally diagnosed with classic Fabry disease in his late 30s.



CLASSIC FABRY IN FEMALES

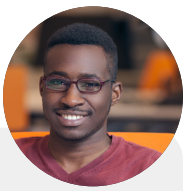
Natalie, 20 years old

- Her mother first noticed Natalie's symptoms when she was 6 years old. She experienced the same intense pain in her hands and feet, fatigue, and gastrointestinal issues as her mother and siblings had experienced.
- After genetic testing confirmed that her mother and siblings had Fabry, the disease was traced back in Natalie's family tree, which led to her own genetic testing and confirmation of Fabry.
- Natalie was diagnosed at 6 years old.

LATE-ONSET, CARDIAC FABRY

José, 61 years old

- At the age of 40, José was treated for elevated blood pressure and abnormal heart rhythm.
- At the age of 60, his heart conditions worsened, and he found a new cardiologist who recommended genetic testing.
- It was discovered that Fabry disease was causing José's heart issues all along.



UNCERTAIN SIGNIFICANCE

Darryl, 29 years old

- Darryl struggled with fatigue, heat intolerance, and burning in his hands and feet for years without a known cause.
- He underwent extensive testing, including a genetic test, which identified Fabry disease of uncertain significance.
- Darryl's diagnosis also led to the Fabry diagnosis of a parent who had passed away after being misdiagnosed with another condition.

*Images do not depict real patients. Names and other identifying information have been changed to protect patient privacy.

Why men and women inherit Fabry differently.

Chromosomes carry genetic information and vary by sex. You may already know that males have one X and one Y chromosome, while females have two X chromosomes. You may also know that Fabry disease is caused by a variant in the *GLA* gene located on the X chromosome.

100% of the time, fathers pass Fabry to their daughters.

FATHERS

A male with Fabry disease passes it only to his daughters, never to his sons, because daughters always get their father's X chromosome carrying the variant that causes Fabry disease.

50% of the time, mothers pass Fabry to their children, male or female.

MOTHERS

Because only one X chromosome is needed in each cell, and females carry two X chromosomes, one of the two X chromosomes in each cell inactivates, or turns off. This means that those genes on the inactive chromosome are not expressed.

Understand Fabry genetics, by looking at calico cats.

Calico cats have multiple colors in their fur and are almost always female. Why? Calico cats' fur color is determined by genes on the X chromosome. Because female cats inherit both their father's and mother's X chromosome, they can have both their mother's and father's fur colors shown in different parts of their coat.

Fabry disease works the same way. Because the *GLA* gene is located on the X chromosome, a woman with Fabry can have one X chromosome with a variant that causes Fabry and one X chromosome without a Fabry variant. Throughout the body, only one of the two X chromosomes may be expressed, meaning its effects will be felt. This random expression varies from cell to cell, which can lead to variable symptom presentation and severity in women with Fabry.

Debunking past myths about women with Fabry.

Women with Fabry disease may experience all, or just some, of its effects to different extents, or they might never experience any of them. But if you are a woman who is experiencing symptoms of Fabry, you are in the majority.

Because women have two X chromosomes, the *GLA* gene that causes Fabry may work normally in some cells but not others. This is believed to be one reason why women have more variable symptoms than men.

Genetic testing is required to diagnose Fabry in women. Genetic testing will also provide important information on your *GLA* variant, which can help determine your potential treatment options.

"Taking the time to find a doctor who is willing to hear you, and searching out the best treatment options for you, is so important."

—Veronica, a woman with Fabry, on choosing supportive healthcare providers

WOMEN WITH FABRY

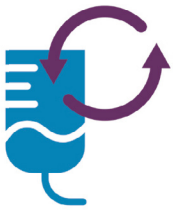
It was once incorrectly thought that women were most often only carriers of Fabry disease, meaning that they could pass it on to their children but not experience the effects of the disease. Despite past misconceptions, we now know that most women who have a variant in the *GLA* gene that causes Fabry do experience its effects, often as severely as men.

Genetic testing helps inform treatment options.

There are several tests to diagnose Fabry disease. A blood test can determine alpha-Gal A enzyme activity. However, the level of enzyme activity measured while you are untreated does not determine your treatment options. A genetic test is more precise and may help determine your treatment options.

Oral therapy may be an option for adults with a *GLA* gene variant that is amenable (responsive) to Galafold® (migalastat). Your healthcare provider can help you identify if your *GLA* variant is amenable.

Galafold
An oral option for adults with confirmed Fabry disease and an amenable *GLA* gene variant.



Enzyme replacement therapy (ERT)
Administered intravenously (IV) for patients with Fabry disease.

Galafold is designed to work with your own enzyme. Ask your healthcare provider if Galafold is right for you.

Indication and Select Important Safety Information

What is Galafold?

Galafold® (migalastat) is a prescription medicine used to treat adults with Fabry disease who have a certain genetic change (variant) in the galactosidase alpha gene *(GLA)* that is responsive (amenable) to Galafold.

It is not known if Galafold is safe and effective in children.

Please see full Important Safety Information on the last page and click here for Full Prescribing Information, including Patient Information and Instructions for Use, also available at Galafold.com.

What it means to have an amenable *GLA* gene variant.

Galafold® (migalastat) 123 mg capsule

Certain *GLA* gene variants lead to a deficient, misfolded alpha-Gal A enzyme that may be stabilized by Galafold. These variants are considered to be amenable. Even if you've had a test in the past that determined you had little or no enzyme activity, your variant may still be amenable to Galafold.

The type of Fabry you have does not determine the type of treatment you may receive. Only a genetic test can determine if your variant is amenable to Galafold. Individual response to Galafold may vary.

"Once I found out I had Fabry disease, I discovered Galafold. Having it as an option totally changed the game for me." —Rebecca, an actual Galafold patient, on her treatment plan

Select Important Safety Information

Before taking Galafold, tell your healthcare provider about all of your medical conditions, including if you:

- have kidney problems.
- are pregnant or plan to become pregnant. It is not known if Galafold will harm your unborn baby.
- are breastfeeding or plan to breastfeed. Galafold may pass into breast milk. Talk to your healthcare provider about the best way to feed your baby if you take Galafold.

Please see full Important Safety Information on the last page and click here for Full Prescribing Information, including Patient Information and Instructions for Use, also available at Galafold.com.

"Getting a diagnosis of Fabry was one of the best things, if not the best thing, because for the first time I finally had a diagnosis." —Alex, an actual Galafold® (migalastat) patient

Important Safety Information

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Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Especially tell your healthcare provider if you take medicines or supplements containing caffeine as these medicines or supplements may affect how Galafold works.

How should I take Galafold?

Do not eat food, or take or drink any product that contains caffeine at least 2 hours before **and** 2 hours after taking Galafold to give a minimum 4 hour fast.

What are the possible side effects of Galafold?

The most common side effects of Galafold include headache, stuffy or runny nose and sore throat, urinary tract infection, nausea, and fever.

These are not all the possible side effects of Galafold. Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Amicus Therapeutics at 1-877-4AMICUS.

Please click here for Full Prescribing Information, including Patient Information and Instructions for Use, also available at Galafold.com.

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