

## GLA

The *GLA* gene is one of many genes that helps cells to break down substances they no longer need. The *GLA* gene makes a protein which breaks down a fatty substance in the cell called globotriaosylceramide. When this protein doesn't work properly, this fatty substance can build up in the cell, which can affect organs such as the heart, kidneys, and skin.

### Impact of *GLA* mutations

Individuals with a mutation in the *GLA* gene are at increased risk of developing a disorder called Fabry disease. Fabry disease typically only affects males, however females may also develop symptoms. Having Fabry disease can cause problems throughout the body, including the heart, kidney, and nervous system.

### Disorders associated with the *GLA* gene

Mutations in the *GLA* gene have been associated with the following disorders:

#### Fabry Disease

Individuals with Fabry disease are unable to break down a type of fat called globotriaosylceramide (GL-3) in the body. Beginning in childhood, GL-3 builds up and accumulates throughout the body, which can cause problems in the heart, skin, eye, kidneys, brain and nervous system. While Fabry disease typically only affects males, females may develop symptoms ranging from mild to severe.

Common symptoms in childhood or adolescence include dark red or blue patches on the skin (angiokeratomas), abdominal pain, and visual impairment caused by clouding of the eye (corneal whorling and opacity). Other common symptoms of Fabry disease include episodes of severe, burning pain in the hands and feet (acroparesthesias), and reduced sweating (hypohidrosis). In adulthood, individuals with Fabry disease may also experience life-threatening complications such as kidney damage, heart attack, and stroke. The lifespan of an individual with Fabry disease is variable and primarily depends on the severity of heart and kidney problems.

Many individuals with Fabry disease develop a cardiac condition called left ventricular hypertrophy, caused by heart muscle cells that become filled with GL-3, that has symptoms that resemble hypertrophic cardiomyopathy (HCM). HCM is associated with an abnormal thickening (hypertrophy) of the heart muscle in the major pumping chamber of the heart, called the left ventricle. This means blood is pumped out of the heart less efficiently and blood flow may even be blocked in some individuals. Symptoms of HCM may include fatigue, shortness of breath with exertion, pounding sensations in the heart (palpitations), light-headedness, dizziness or fainting. When untreated, HCM can lead to heart failure, sudden cardiac arrest, or sudden cardiac death. Individuals may experience other problems with the heart, such as problems with

the valves that allow blood to flow through the heart, chest pain, irregular heartbeat, and others.

Diagnosing Fabry disease typically involves a blood test that measures the breakdown of GL-3 in white blood cells, as well as evaluation of an individual's medical and family histories, physical exam, hearing assessment, and examination of the skin, eyes, brain, heart, and kidneys. These evaluations may be combined with genetic testing to diagnose Fabry disease.

Treatment for individuals with Fabry disease may include enzyme replacement therapy, which helps breakdown GL-3. Pain medications may be used to help reduce the frequency and severity of pain episodes. Other medications, hemodialysis, or kidney transplant may be required by individuals with renal involvement. Ongoing evaluation of the brain, eyes, heart, and hearing may be recommended.

### Interesting information about the *GLA* gene

Fabry disease is an X-linked disorder. This means that having a mutation in a single copy of the *GLA* gene causes Fabry disease in males and does not typically cause Fabry disease in females. This is because the *GLA* gene is located on the X chromosome, and males only have one copy of the X chromosome, while females have two copies. Even if a female has one mutation, the extra copy can usually make up for the impact of the mutation on the other.

Certain mutations in the *GLA* gene have a milder impact than others. Some specific mutations are known to cause symptoms that only affect the heart or kidneys and appear later in life.

### Useful resources

#### **Fabry International Network**

Promotes collaboration between organizations to support those affected by Fabry disease by enabling communication and advocating for good practices.

<http://www.fabrynetwork.org>

#### **Fabry Support and Information Group**

Raises awareness of Fabry disease and its symptoms by connecting patients, family members, and caregivers.

<http://www.fabry.org/>

#### **National Fabry Disease Foundation**

Supports the Fabry disease community by promoting education, awareness, advocacy and research dedicated to Fabry disease.

<http://www.fabrydisease.org>

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