Why do mutations matter?

Fabry disease is an X-linked disorder. It is caused by a mutation in a gene on the X chromosome and can be passed down by either parent.

Daughter X chromosome. An affected father never passes the disease because daughters inherit their father’s only X chromosome. An affected father never passes the disease to his daughters, but passes his mutation to all of his daughters, who will develop Fabry disease. Since men only have one X chromosome, if they inherit the mutation, Fabry disease will pass to each of his children.

Women have two X chromosomes. A father with Fabry disease passes his mutation to all of his daughters, who will develop Fabry disease. Since men only have one X chromosome, if they inherit the mutation, Fabry disease will pass to each of his children.

ALONG FABRY DISEASE

HOW

A glossary of important terms when discussing Fabry disease.

WHAT PEOPLE LIVING WITH FABRY DISEASE—AND THEIR FAMILIES—NEED TO KNOW

Cell: Basic building block of all living things
Chromosomes: Structures that contain DNA and a person’s genetic code
Mutation: A permanent error in the DNA code
De novo mutation: An alteration in a gene that is not inherited
X-linked disorder: Inherited disorder caused by a mutation in a gene on the X chromosome
Lysosomal storage disorder (LSD): A group of over 50 diseases resulting from the accumulation of waste products in lysosomes
Enzyme: A special type of protein that speeds up a reaction that takes place within a cell
Basic unit that allows for the transmission of genetic information from one generation to the next and contains instructions, or code, for making proteins and enzymes
NP/GAL/01/0007/GLO8-15
Fabry disease is an X-linked disorder. It is caused by a mutation in a gene on the X chromosome and can be passed down by either parent.

**HOW MOTHERS PASS ALONG FABRY DISEASE**

A mother who has the mutation on one of her two X chromosomes has a 50% chance of passing down Fabry disease to each of her children. Since men only have one X chromosome, if they inherit the mutation, they will develop Fabry disease. In affected daughters, the α-Gal A mutation will occur randomly in some cells and not others, so daughters may have less severe or more variable symptoms than sons.

**HOW FATHERS PASS ALONG FABRY DISEASE**

Men have one X chromosome and one Y chromosome. Women have two X chromosomes. A father with Fabry disease passes his mutation to all of his daughters, because daughters inherit their father’s only X chromosome. An affected father never passes the mutation to his sons, because sons inherit a Y chromosome from their fathers.
In Fabry disease, the affected enzyme is α-galactosidase A, or just α-Gal A.

It's a type of disease called a lysosomal storage disorder, or LSD.

People with LSDs have problems making specific lysosomal enzymes.

In Fabry disease, the affected enzyme is α-galactosidase A, or just α-Gal A.

α-Gal A breaks down substances in the cell called globotriaosylceramide (GL-3) and plasma globotriaosylsphingosine (lyso-Gb).

In people with Fabry disease, α-Gal A does not break down GL-3. Instead, GL-3 builds up, particularly in cells lining blood vessels.

This build-up damages tissues and organs, leading to the symptoms of Fabry disease.

Breaking down Fabry: facts about the disease

How does Fabry disease affect the body?

From one person to another, everyone experiences Fabry disease differently.

PSYCHOSOCIAL
- Feelings of guilt, apprehension, depression, isolation, and even fear (may also be experienced by family members)
- Feelings of relief to finally have a diagnosis of Fabry, after years of not knowing

EYES
- A whorled pattern in the cornea
- Fabry cataracts

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

SKIN
- Sweating less than or more than normal
- Small dark red spots called angiokeratomas, particularly between belly button and knees

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

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

PREVENTIVE MEASURES
- A doctor suspects Fabry disease—what happens next?

Breaking down Fabry: facts about the disease

What causes Fabry disease?

Everyone has information coded into their cells called DNA—which is inherited from one’s parents.

Sometimes, mutations occur in the DNA code that makes up a particular gene.

Think of it like spelling. One wrong letter can completely change the meaning of a word!

CAR
CAT

People with some mutations make very little or no α-Gal A.

People with certain types of mutations may make α-Gal A, but it doesn’t function correctly.

What causes Fabry disease?

Breaking down Fabry: facts about the disease

Every patient is unique

Other resources that may be helpful include:

- The Fabry International Network
  fabrynetwork.org
- Fabry Support & Information Group
  fabry.org
- The National Fabry Disease Foundation
  fabrydisease.org
- The Society for Mucopolysaccharide Diseases (UK)
  mpssociety.org.uk
- Canadian Fabry Association
  fabrycanada.com
- Fabry Australia
  fabry.com.au
- National Institutes of Health NINDS Fabry Disease Information Page
  ninds.nih.gov/disorders/fabrys
- The National Organization for Rare Disorders
  rarediseases.org
- EURORDIS – Rare Diseases Europe
  eurordis.org
- National Institutes of Health NINDS Fabry Disease Information Page
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Why do mutations matter?

At least 800 different gene mutations have been identified that can cause Fabry disease.

The type of mutation can affect **when** symptoms appear, **what kind** of symptoms appear, and **how bad** the symptoms are or may become.

It’s important for individuals or families with Fabry to know **which mutation** they have.