Every family with Fabry has a **story to tell**

What role can you play in your family's Fabry story?

Amicus Therapeutics®

The power of your story

As you may have experienced, the journey to a Fabry disease diagnosis can be long and difficult, often involving multiple specialists and potentially misdiagnoses.[1,2]

Your Fabry story has the power to help others avoid this, and may potentially lead them to a healthier future.[3-6]

How?

You may already know that Fabry is a genetic disorder which may be passed down the generations of a family.

But did you know that on average, for every person with Fabry, at least 5 other members of their family can also be diagnosed with the condition?[3]

This means that **you could have children, parents, siblings, aunts, uncles or cousins that also have Fabry but don't yet know**. You could help them.

You may have affected family members that are not experiencing symptoms yet.[7] Others may already be experiencing symptoms but may not realise what the cause is. It is important to know that their experience of symptoms may be different from yours.[7-10]

The variability of Fabry symptoms and how they often overlap with more common conditions contribute to the delays and difficulties in reaching a diagnosis.[1,2,11] Being tested for Fabry or even knowing that Fabry is in the family could help simplify an individual's path to diagnosis. Earlier detection could also mean that those affected can get the support and treatment they need earlier, helping to manage the disease – leading to a potentially healthier future.[4-6]

Knowledge is power

By raising awareness of and educating your family about Fabry, you could potentially help multiple people get the support and treatment they need.

Approaching your family to talk about the realities of Fabry may not be easy for some, but your healthcare team can support you and we hope that this booklet and supporting materials will help. **Remember, there is no one better able to talk about Fabry to your family than you.**

Every family with Fabry has a story to tell. Your Fabry story could help theirs. Start conversations, and make sure everyone in your family knows about Fabry and gets checked.

How we can support you

This booklet is part of a pack provided to you to help you understand the risk of Fabry within your family and encourage you to discuss Fabry disease with your relatives.

The full pack contains:

- This booklet **('Every family with Fabry has a story to tell')** – which aims to help you understand how Fabry is passed on in families, why contacting members of your family is so important and some pointers on what to talk about
- **'The Fabry family tree builder'** booklet – a paper tool to help you draw your family tree and work out which members of your family should be contacted about Fabry. Your doctor can help you complete this or if you prefer, you can complete it alone. An online version is also available here www.fabryfamilytree.com, which may be easier to use as the tool will draw the tree and highlight for you, relatives who may be at risk of Fabry
- A set of **'Our family and Fabry'** leaflets – which you can give to the members of your family who potentially should be tested for Fabry. This leaflet contains information on Fabry disease and a tear-off section that can be taken to their doctor to begin a conversation about checking for Fabry. You can also find a downloadable version here www.fabryfamilytree.com

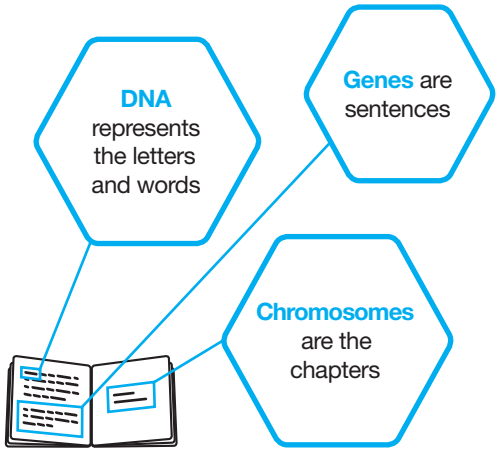
For further support please explore **www.fabryfamilytree.com** or speak to a member of your healthcare team

What causes Fabry?

An easy guide to genetics [12,13]

Every cell of your body is programmed to work in a particular way, for example to help with digestion, keep your heart beating, or fight infections. To do its job properly, every single cell needs a set of instructions. DNA is 'read' by the cell and provides these instructions. A gene is a section of DNA that programmes one specific instruction. The genes themselves are grouped into separate units called chromosomes.

You can think of this like an instruction manual where:



Sometimes there are changes in the DNA – these are called mutations (variants). You can think of these like misspelt words – one wrong letter can completely change the meaning of the word.

CAR
CAT

The genetics of Fabry [1,7]

Fabry is caused by a variety of mutations in a gene called GLA which provides the instructions to make an enzyme (a-galactosidase A). Normally this enzyme helps break down certain sugary-fatty substances (glycosphingolipids) in the cells of our body – but the mutations mean it can't do its job. This leads to a build-up of those substances causing the symptoms of Fabry.

How is Fabry passed down in families?

The GLA gene and Fabry mutations are located on the X chromosome and therefore Fabry is referred to as an "X-linked disorder". [14]

Men and women can both be affected by Fabry but the likelihood of a father or a mother passing down the Fabry mutation is not the same. [7,14]

It depends on the chromosomes they pass onto their children. [14]

Is Fabry always inherited? [7,15]

Fabry and its mutations are most often inherited from a parent. In rare cases it may not be inherited, the Fabry mutations may spontaneously occur and be unique to the individual – these are known as de novo mutations. However, this individual may still be able to pass the disease onto their children.

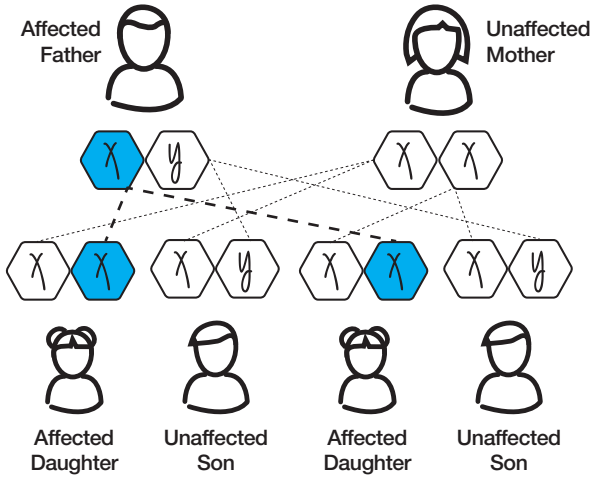
The X and Y chromosomes determine the sex of a person: [14]

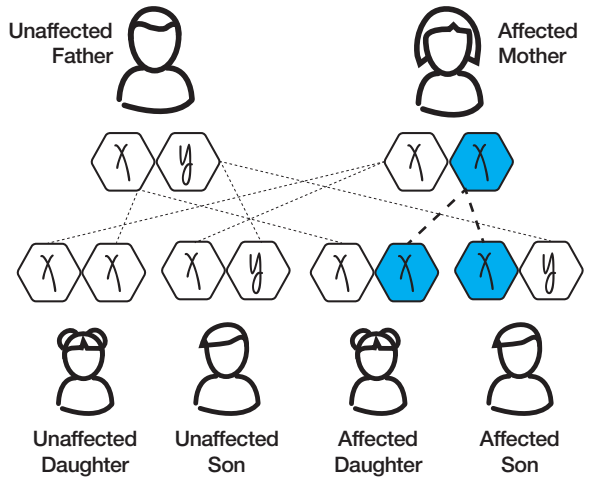
Women have **two X chromosomes** – sons and daughters will randomly receive one of these X chromosomes

Men have **one X and one Y chromosome** – sons will receive the Y chromosome and daughters the X chromosome

A father affected by Fabry disease will pass the Fabry mutation on to all of his daughters but none of his sons: [14]

This is because the father only has one X chromosome that must contain the Fabry mutation – his daughters will inherit this, but his sons won't (they will inherit his Y chromosome)



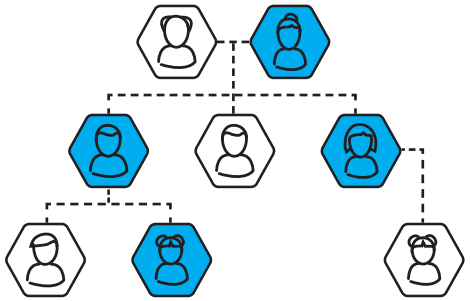


A mother affected by Fabry disease has a 50:50 chance of passing the Fabry mutation onto any of her daughters or sons: [14]

This is because the mother has two X chromosomes, and either the X chromosome with the Fabry mutation or the X chromosome without the Fabry mutation could be passed randomly onto her children

What role can you play in your family's Fabry story?

The genetics and inheritance of Fabry means that **it is possible you have family members that have the Fabry mutation**.



You could help them.

Fabry symptoms can be hard to recognise and so some people with the disease are never diagnosed, while others experience long delays (the average is 15 years).[1,2,11] By sharing your Fabry story you could help your family members avoid this.[3]

But it's not just about diagnosis. Because Fabry is a progressive disease, it gets worse over time.[1] You can help create an opportunity for those with a mutation to benefit from early detection and treatment which could mean a potentially healthier future.[4-6]

The first step to helping them is finding out who **might** have a Fabry mutation – these are your at-risk relatives that should be contacted. You can do this with the assistance of someone from your healthcare team, but we have also tried to equip you to be able to do it alone. 'The Fabry family tree builder' paper tool can help you work out who is important to speak to. Alternatively, the online tool can do the work for you, automatically highlighting the at-risk relatives in your family tree.

The next step is to speak to them.

Fabry could be in your family. Work-out who is at risk and make sure they know

Starting conversations

There's no such thing as an 'average' family

Everyone has their own way of communicating with their family and talking about Fabry is no different. Some people might do it face-to-face or over the phone, while others would prefer to do it online or via a letter – it's completely your choice. If you are unsure, a member of your healthcare team can advise you on how to approach the situation. If you are finding it difficult to find the right words, you can download a pre-written letter to help get you started here www.fabryfamilytree.com.

The 'Our family and Fabry' leaflets may be a good resource to help you explain Fabry to your family. It may also help your family members understand why they need to be aware of Fabry and what to do next.

Some important points to cover when talking to at-risk relatives (All of these are covered in the 'Our family and Fabry' leaflet):

- Fabry is a condition that can be associated with a wide variety of symptoms, even members of the same family can have very different experiences of symptoms (The 'Our family and Fabry' leaflet has a helpful diagram)[1,2,7-10]
- Based on how Fabry is passed down in families and your family tree, it is possible that they could be at risk of Fabry[14]
- A genetic test, usually on a cheek swab, blood or other tissue sample, should be able to tell them if they carry a Fabry mutation[7,16]
- There are treatment options available for Fabry disease and as Fabry can get worse over time, treatment at an early stage may have health benefits[4-6]

For further support please explore **www.fabryfamilytree.com**
or speak to a member of your healthcare team

What are the next steps for my relatives?

If your family members would like to find out more about Fabry, or be tested, the next step for them is to go and see a healthcare professional. Depending on the individual situation this might be:

- Your doctor, a genetic counsellor or a member of your healthcare team
- Someone your doctor refers them to
- Taking the tear-off section in the 'Our family and Fabry' leaflet to their own doctor, who may refer them on

They can have a discussion with a healthcare professional, who will likely assess their potential risk of having Fabry, explain the nature of the genetic tests including potential advantages and disadvantages, and arrange for a test if it is appropriate and should they wish it.

Genetic tests are usually performed on a cheek swab, blood or other tissue sample.[16] Tests will be performed to look for mutations associated with Fabry.[7]

If a Fabry mutation is found, their medical team will discuss more about the disease, how to manage it and any potential implications.

Fabry may affect your relatives

Make sure they know and get checked

Fabry is generally passed down in families – some of your relatives could have Fabry and not know yet. You could help them in just two steps – supported by your healthcare team and/or this pack and 'The Fabry family tree builder' online tool.

Your relatives can then choose to begin the process of checking if they do or do not have Fabry. If they do, you may have helped them avoid a long path to diagnosis.[1,3]

You may have also helped them to start managing their disease at an earlier stage and potentially improve their future health.[4-6]

Even those who choose not to be tested for Fabry could be better equipped if Fabry symptoms develop. Sharing that Fabry disease is in the family with a medical team could help prompt a diagnosis.

Every family with Fabry has a story to tell. Your Fabry story could help theirs.

Every family with Fabry has a **story to tell**

Once my brother understood that Fabry could be passed down in families he made sure everyone was aware and got tested. He was strong for us, and those of us that have Fabry don't have to have such a difficult time trying to get a diagnosis like he did.

What role can you play in your family's Fabry story?

For more information and access to tools that can help your family, visit:

www.fabryfamilytree.com

Disclaimer: This pack and supporting materials are designed to help you find family members who might have Fabry. They do not in any way suggest a diagnosis of Fabry disease. Any concerned individual should speak to a healthcare professional.

The photograph and story are for illustrative purposes only; the individual depicted is not a family member of someone with Fabry.

References:

1. Germain D. Orphanet. J Rare Dis. 2010;5:30 **2.** Hilz MJ et al. Dig Liver Dis. 2018:50(5):429-437 **3.** Laney DA & Fernhoff PM. J Genet Counsel. 2008:17:79-83 **4.** Oritz A, et al. Mol Genet Metab. 2018;123(4):416-427 **5.** Mehta A & Hughes DA. Fabry disease. GeneReviews®. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1292/ [Last accessed August 2019] **6.** Germain DP et al. Clin Genet. 2019;96(2):107-117 **7.** Laney DA, et al. J Genet Couns. 2013;22(5):555-564 **8.** Cammarata G, et al. Biomed Res Int. 2015;504784 **9.** Yamamoto S et al. Intern Med. 2019;58(4):603-607 **10.** Laney DA. Mol Genet Metab. 2019:126(2):S90-91 **11.** Hoffmann B & Mayatepek E. Dtsch Arztebl Int. 2009;106(26):440-447 **12.** DNA, genes, chromosomes and mutations. Genetic Alliance UK. Available at: https://www.geneticalliance.org.uk/information/learn-about-genetics/ dna-genes-chromosomes-and-mutations/ [Last accessed August 2019] **13.** What is a gene? Genetic Home Reference. Available at: https://ghr.nlm.nih.gov/primer/basics/gene [Last accessed August 2019] **14.** How is Fabry Disease Inherited. National Fabry Disease Foundation. Available at: https://www.fabrydisease.org/index.php/about-fabry-disease/fabry-disease-inheritance [Last accessed August 2019] **15.** Desnick RJ et al. Ann Intern Med. 2003;138(4):338-46. **16.** How is genetic testing done? Genetics Home Reference. Available at: https://ghr.nlm.nih.gov/primer/ testing/procedure [Last accessed August 2019]

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