Centre of Research Excellence in **Pulmonary Fibrosis**

Lung Foundation Australia

Living with Pulmonary Fibrosis

Understanding the Role of Genetics in Pulmonary Fibrosis

Pulmonary fibrosis (PF) is a condition in which the lung tissue becomes thickened and scarred. As with any disease there are many potential causes, including both genetic and environmental factors. Our understanding of the genetic component of PF is developing in line with new information and technologies. Awareness of the role of genetics in your PF might help with your diagnosis and management, and inform other members of your family who may also be at increased chance of developing PF.

What is familial pulmonary fibrosis

1 out of 5 **About 1 in 5 individuals** with idiopathic pulmonary fibrosis have the familial form.

If PF runs in your family, it is called familial pulmonary fibrosis. Familial PF occurs when two or more blood relatives (including yourself) have the condition. In about one-third of families with familial PF, researchers have found variations in specific groups of genes that are believed to be responsible for the condition. The two main types of genes involved are:

- Telomere-related genes (about 30% of familial PF cases)
- Surfactant-related genes (1–3% of familial PF cases).

Even if no one else in your family is affected, these gene variations might still be involved in your PF. For further information on genes and chromosomes, please see the *Centre for Genetics Education fact sheet* at the bottom of this resource.

Find out more about genes involved in PF

Telomeres

Telomeres are protective caps at the ends of your chromosomes (strings of DNA wrapped around proteins), like the plastic tips on shoelaces that prevent fraying. As cells replicate through life, changes in the telomere-related genes can cause the telomeres to become too short too quickly. This affects the body's ability to maintain healthy lung tissue.

Surfactant

Surfactant is a slippery substance in your lungs that helps them to expand when you breathe. Changes in surfactant-related genes can cause abnormal surfactant production, which may lead to increased risk of lung damage and progressive scarring of lung tissue over time.

Genetic testing

Deciding whether to have genetic testing for PF can be a big decision, so it is important you understand what is involved and what you need to consider. Make sure you speak with your healthcare team to get advice that is specific to you. Genetic testing may be worth considering for:

- Individuals with a clinical diagnosis of PF who have a relative who also has PF
- Family members of someone with a known genetic form of PF
- Individuals whose PF began before the age of 50 and is not explained by other conditions (e.g. autoimmune or connective tissue disease)
- Individuals with PF who also have other conditions that might suggest a genetic cause (e.g. blood abnormalities, liver disease, early greying of the hair before the age of 30 years).

What does testing involve?

1 **See your respiratory specialist**

Discuss your options and ask about a referral to a clinical geneticist and/or genetic counsellor.

2 **Visit the clinical geneticist and/or genetic counsellor**

They will talk to you about individual risk, benefits and limitations that may be involved in testing, and whether genetic testing is appropriate for you and your family. Remember that it's your choice to have the test performed or not.

Things you might want to consider include:

- Results may have implications for other family members
- Costs of testing
- Implications for some types of insurance (importantly, health insurance coverage in Australia is not affected by results of genetic testing).

3 **Take the test**

This is usually done through a blood or saliva sample. The sample will be analysed for specific genes associated with PF, and results may take 3-6 months or longer to come back.

4 **Receive your results**

Your genetic counsellor will play an important role in supporting you throughout the testing process. This includes helping you to understand the results and the impact it may have on you and your family members.

If a genetic variant is found

If you have PF, finding a genetic variant can help:

- Explain the cause of your PF
- Influence your treatment decisions
- Identify risks for other related health conditions.

If you don't have PF (for instance you might be the relative of an affected individual), having a genetic variant doesn't necessarily mean that you will develop the disease. Several other factors also play a role:

- **Environmental factors**: Exposure to certain substances like cigarette smoke, dust or pollution can speed up damage to the lungs in individuals with a genetic variant
- **Age**: The risk typically increases with age
- **Other health conditions**: Infections, autoimmune diseases or other medical conditions may interact with genetic factors to determine how PF progresses.

The interaction between genetic and environmental factors is very complex, which is why some individuals with genetic variants never develop symptoms, while others do.

If no genetic variant is found

It is important to know that even if no variant is found, it does not rule out a genetic cause for your PF. This is because there are limitations in the technology used for genetic testing. We are also still learning what many genes do. Therefore, if you have a family history of PF, it is recommended you continue regular monitoring to check if you are developing clinical signs of PF. You may also need to repeat the genetic test in the future as more genes are discovered.

How does finding a genetic variant impact family members?

Your genetic counsellor will discuss the potential impact of finding a variant on you and your family, and you should consider it carefully before deciding if you want to be tested or not. Things you should consider include:

- Other individuals in your family may also carry the genetic variants, and you can pass them down to your children
  - Genetic counselling can help with family planning decisions
- Your treating healthcare team may recommend screening and monitoring for your family to help promote early detection:
  - Early awareness can help with minimising the risk of progression
  - Age of onset and severity can vary and may be earlier in successive generations of a family
  - Certain conditions that are associated with PF genes may also present in other ways, such as liver disease or blood disorders
- It's important to remember that even if a gene is found in a family member who does not have PF, it does not necessarily mean that person will develop the disease.

Does finding a genetic variant change my PF management and treatment?

There are currently no gene-specific treatments for PF, and it is not possible to alter your genes at this time. In some cases, certain treatments such as immunosuppressants may need to be reviewed if a genetic cause of PF is identified.

You may need to have other parts of your body, such as your liver and blood assessed and other specialists may be involved with this (e.g. hepatologists and haematologists).

Your doctor may consider earlier referral for treatment options such as lung transplantation.

Depending on the genetic variant found, you may be eligible for a novel treatment through a clinical trial if this becomes available.

It is important to continue to look after yourself and limit the environmental and lifestyle risk factors that may impact progression. These include:

- Avoid exposure to hazardous agents while you are at work or when taking part in a hobby
- Stop smoking or vaping. It is never too late to stop smoking or vaping, so make sure you speak with your healthcare team about the best way to quit.
- Avoid exposure to second-hand smoke
- Be aware of air quality and avoid exposure to dust, fumes and air pollution, including smoke from bushfires.

Remember, your healthcare team is there to help you. Make sure you speak with them if you would like more information about genetic testing or to find a genetic counsellor in your area. You can also access the *Centre for Genetics Education Service Finder* below for more information, or explore the external links below for further information and support.

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External resources:

- Centre of Research Excellence in Pulmonary Fibrosis: **cre-pf.org.au**
- Centre of Genetics Education – fact sheet: **genetics.edu.au**
- Centre of Genetics Education – service finder: **genetics.edu.au**
- Pulmonary Fibrosis Foundation: **pulmonaryfibrosis.org**
- Team Telomere: **teamtelomere.org**
- National Society of Genetic Counsellors: **nsgc.org**

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