Pulmonary Fibrosis Foundation™

230 East Ohio Street Suite 500 Chicago Illinois 60611 **844.TalkPFF** | **844.825.5733** PHONE

Document Development Group Members

Janet Talbert, MS, CGC,
Medical Genetics and
Genomic Medicine,
Vanderbilt University

Mary Beth Scholand, MD,
Pulmonary, University of Utah

What is Familial Pulmonary Fibrosis?

Pulmonary fibrosis (PF) describes a variety of disorders that may lead to progressive scar accumulation in the lung. This can be the result of occupational, environmental, autoimmune diseases, other specific diseases (such as Sarcoidosis) or rare inherited conditions where pulmonary fibrosis is a feature (for example: Dyskeratosis Congenita or Hermansky Pudlak syndrome). These are known causes of pulmonary fibrosis. Often, the cause of pulmonary fibrosis is unknown: it is then classified as idiopathic.

Pulmonary fibrosis is considered "sporadic" when there are no known relatives with the diagnosis, However, when 2 or more blood relatives have this disease, it is considered familial pulmonary fibrosis (FPF). Currently, it is estimated that one in five people with pulmonary fibrosis have familial pulmonary fibrosis (FPF). In about one-third of families with FPF, variation in a specific gene which is thought to be responsible for the FPF has been discovered.

What is a gene?

Genes are units of genetic information that are passed from parents to children. A gene provides the directions to make the body's proteins, and these proteins carry out certain functions in the body (such as making eye color blue or brown). Each person receives a full set of about 22,000 genes from each of their parents. Therefore, there are two copies of each gene, one from each parent.

What is a variant?

We all have small changes in many of the 22,000 genes. It is these variations that make us different from each other. These changes are called variations (also known as variants or mutations). Variation in genes is common and any two unrelated people have millions of variants between them. Nearly all of these common variants are not harmful: they do not cause or increase the risk of disease. However, in some cases, a specific variant can change or eliminate the function of a gene. Having a damaging variant can increase a person's risk of disease.

To learn more about genetics visit https://medlineplus.gov/genetics/ and https://nigms.nih.gov/education/fact-sheets/Pages/genetics.aspx.

What causes FPF?

We are still learning about all the possible causes of FPF. It is important to know that there is not simply one gene or one variant that causes FPF. Inherited gene variants in two important processes in the body are known to be related to FPF. One pathway is called Telomere and the other is called Surfactant.

The most frequent genetic cause of FPF is harmful variants in genes that are related to telomeres which help to keep chromosomes intact. Chromosomes are physical structures in every cell that contain all genes. These genes involved in FPF help protect the ends of the chromosomes from being damaged. These ends are called telomeres. Telomeres are specialized caps (like the end of shoe lace) that protect our chromosomes throughout our lifetime. It takes a number of genes to keep telomeres working properly. Harmful variants in several of the telomere genes have been discovered and account for about 30% of FPF cases. Genes are given short nicknames or acronyms. The harmful variants in the following telomere genes have been associated with FPF: TERT, TERC, PARN, DKC1, NAF1, RTEL1, NOP10, ZCCHC8, and TINF2.

Harmful variants in genes of another pathway, the surfactant genes (SFTPA1, SFTPA2, SFTPC, and ABCA3), are less common and account for 1-3% of FPF. Surfactant is a slippery substance made inside of lungs so that the lungs can expand and contract easily. A harmful gene variant in one of these genes could cause FPF. The harmful gene variants in the telomere and surfactant pathways are rare in the general population (usually less than 1% of the entire population).

How is FPF inherited?
A harmful variant in only one copy (either mother or father) of the pair of known genes is enough to cause or increase risk for FPF in a person. When a parent has a variant in a gene that can cause FPF, each child has a 50% chance to inherit the harmful variant. A child who inherits the harmful version of the disease variant may not necessarily develop FPF. However, they have increased risk compared to someone with two normal versions of the gene. Different families have different gene variants. Knowing which specific variant is present in a family is critical in helping genetic testing for any other person in that family, because testing one specific gene for a known variant is far easier than testing for all the possible genes.

When should I consider Genetic Testing?
Patients with FPF or likely genetic forms of pulmonary fibrosis should be seen for a genetic evaluation and counseling to determine what, if any, genetic testing is appropriate and to educate the patient about risks and benefits of genetic testing.

What testing is available for people at risk for FPF?
Genetic testing is ordered by a healthcare provider usually from a blood or saliva sample. It searches for a harmful variant in the known genes associated with FPF. The results of genetic testing can help understand the cause of the disease in a family.

How can I get genetic testing for FPF?
Patients interested in genetic testing should first inquire with their care provider. Because there can be unexpected risks associated with genetic testing, counseling by experts such as medical genetic providers (Medical Geneticists, Genetic Counselors) is recommended in order to be fully informed. Genetic specialists can identify which genes should be tested, what tests are available, assist in ordering and teach you about the risks, benefits and limitations of genetic testing. Variations in genes can be confusing and may not provide a simple answer to whether this is the reason a person has FPF. Because not every gene variant that causes FPF is known, even negative results do not rule out an inherited risk.

Costs of genetic tests can be variable and insurance may not always cover these costs. In addition, elective type insurances (such as life, disability) could potentially be impacted based on their genetic test result. This does NOT apply to health insurance per the Genetic Information and Nondiscrimination Act (GINA) and the Affordable Care Act.

Who should be tested for genes in FPF?
In cases where genetic testing is considered, it is currently recommended to test the person with a diagnosis of

FPF instead of an unaffected family member (a relative who doesn't have PF). It is important to remember that currently a harmful gene variant responsible for FPF will only be found in about one-third of patients with FPF. Therefore, up to 70% of patients with FPF will test negative for the current genes known. There are other genes yet to be discovered that run in families. Unaffected family members can base their risk on family history and discuss possible screening with their healthcare professionals. If unaffected relatives strongly desire genetic testing, it is best to work with medical genetics professional to help find available testing options.

Resources

- Genetics Home Reference - Learn about genetics https://medlineplus.gov/genetics/
- National Society of Genetic Counselors (NSGC) (find a counselor): www.nsgc.org
- American Board of Genetic Counselors (ABGC) (find a counselor): www.abgc.net
- Telehealth genetic counselors: www.informeddna.com or other telehealth companies (search "telehealth
- genetics counseling)
- Clinical Trials: www.clinicaltrials.gov
- DNA banking: www.preventiongenetics.com
- National Institute of Health (NIH) Genetics Fact Sheet (NIH https://nigms.nih.gov/education/fact-sheets Pages/genetics.aspx)