

Lung Cancer and FGFR1 Amplifications

This material will help you understand:

- the basics of lung cancer
- the role of the FGFR1 gene in lung cancer
- if there are any drugs that might work better if you have certain changes in the FGFR1 gene

What is lung cancer?

Lung cancer is a type of cancer that starts in the lungs. It is the number one cause of cancer deaths in the world. Doctors name lung cancers based on how lung cells look under a microscope. There are two main groups of lung cancer: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). Most people with lung cancer have NSCLC. Adenocarcinoma, squamous cell carcinoma, and large cell carcinoma are types of NSCLC.

What causes lung cancer?

Cancer is a result of changes in our genes. Genes contain the instructions for making proteins. Changes in genes, called mutations, may result in changes in proteins. These changes may cause cells to grow out of control which could lead to cancer.

The biggest risk factor for lung cancer is exposure to cigarette smoke. But, not all lung cancers are due to smoking. Other risk factors include exposure to radon gas, asbestos and pollution.

What are the most common current treatments for lung cancer?

Doctors may treat lung cancer using one or more of these options:

- **Surgery** – operation that removes as much of a cancer tumor as possible.
- **Radiation** – treatment that uses high-energy beams to kill cells in the area where the cancer is growing.
- **Traditional chemotherapy** – drugs that kill growing cells. All cells grow. Cancer cells usually grow faster than most healthy cells. So, these drugs kill more cancer cells. But because these drugs kill healthy cells too, this can cause unwanted side effects.
- **Precision medicine therapy** – treatments that target proteins involved in cancer. These therapies mainly kill cancer cells and not healthy cells. This also means you may have fewer side effects. Two types of precision medicine therapies are:
 - **Small molecule therapy** – mainly acts on cells with specific protein changes. Small molecule therapy uses drugs to target those proteins. Genetic testing can tell if your cancer cells have protein changes that can be targeted. Small molecule therapy is a type of targeted therapy.
 - **Immune-based therapy** – works with your body's defense system to fight cancer. These can mark cancer cells so they are easier for your immune system to find.

Can I pass on mutations found in my cancer cells to my children?

You cannot pass on mutations found only in your cancer cells to your children.

How well does cancer drug treatment work?

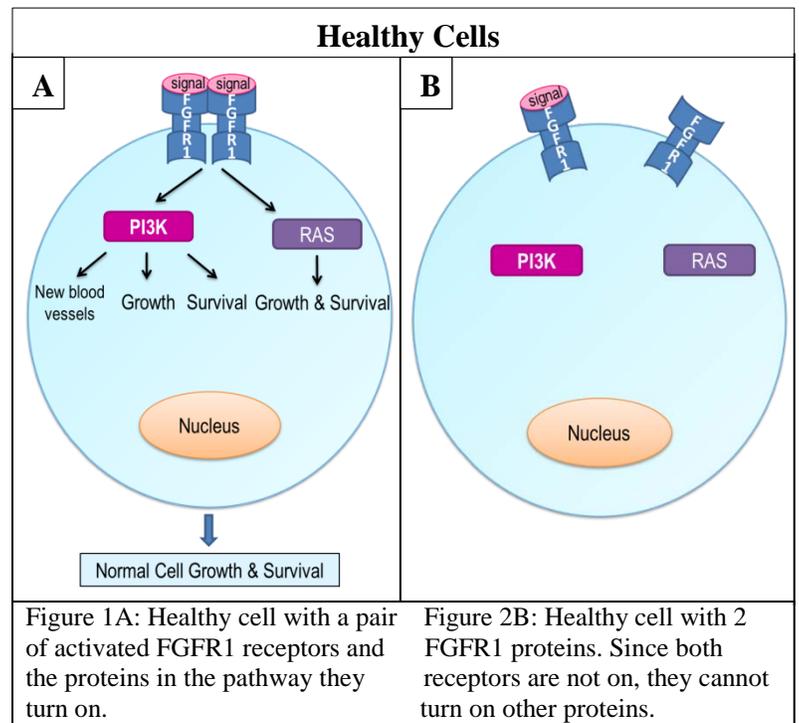
After a while, your cancer cells may stop responding to the drug(s). This means your cancer may start to grow again. Your doctor will do regular checkups to watch for this. If the cancer starts to come back, your doctor can try another drug or treatment.

What is FGFR1?

FGFR1 is the name of both a gene[🧬] and a protein[🧬]. The FGFR1 gene contains the instructions for making the FGFR1 protein. It is a member of the FGFR family of proteins. FGFR1 is short for fibroblast growth factor receptor type 1. Receptors[🧬] are proteins that are often in cell membranes. The cell membrane is the outside surface of a cell. Receptors have three basic parts. One part is outside the cell, one part crosses the cell membrane, and one part is inside the cell. Receptors receive signals from outside the cell. These signals may tell the cell to grow, divide, or die. These signals are turned on and off as needed.

In healthy cells, a signal binds to FGFR1. When the outside part of FGFR1 receives a signal, it activates, or turns on, the FGFR1 protein. It then pairs with another activated FGFR1. This pairing turns on the part of FGFR1 inside the cell.

When the inside part is on, FGFR1 can turn on other proteins. These other proteins are usually in pathways. Proteins in pathways work together to do specific jobs within the cell. The healthy cell image shows some of the proteins and pathways turned on by FGFR1 (Figure 1A). FGFR1 can turn on at least two different cell growth and survival pathways. PI3K and RAS are proteins FGFR1 turns on. When the signal stops, the FGFR1 proteins turn off and separate (Figure 1B).



How do mutations in proteins affect pathways?

If a mutation[🧬] affects one or more proteins[🧬] in a pathway, the proteins may not be able to be turned on or off as expected. This can cause cells to grow out of control and lead to cancer.

How common are FGFR1 mutations in lung cancer?

About 1 in 5 non-small cell lung cancers (NSCLCs) have a change that alters the amount of FGFR1 protein[🧬] made by a cell. This change is most common in current or former smokers with squamous cell carcinoma, a type of NSCLC. But, FGFR1 mutations[🧬] can happen in all types of NSCLC, regardless of smoking status.

What is an FGFR1 amplification?

An FGFR1 amplification changes how many copies of the FGFR1 gene a cell has. Usually, we have two copies of each gene. We get one copy from our mother and one copy from our father. Cells with a specific gene amplification have extra copies of that gene. Another term for this is copy number variation. This change affects how much FGFR1 protein the cell makes.

What is the effect of these amplifications?

Cells with an FGFR1 amplification make more copies of the FGFR1 protein. With more FGFR1 proteins, cells can grow faster. Cells with these mutations could grow out of control, which can lead to cancer (Figure 2).

Are there targeted therapies for FGFR1 amplifications?

At this time, it is unclear if any drugs target FGFR1 amplifications. But, scientists are working on new potential therapies all the time. So, you should talk to your doctor about your treatment options.

What if I have a different mutation in FGFR1 or “no mutation”?

Your cancer cells might have mutations in this gene or in other genes that were not tested. Your genetic test results will still help your doctor determine the best treatment for you.

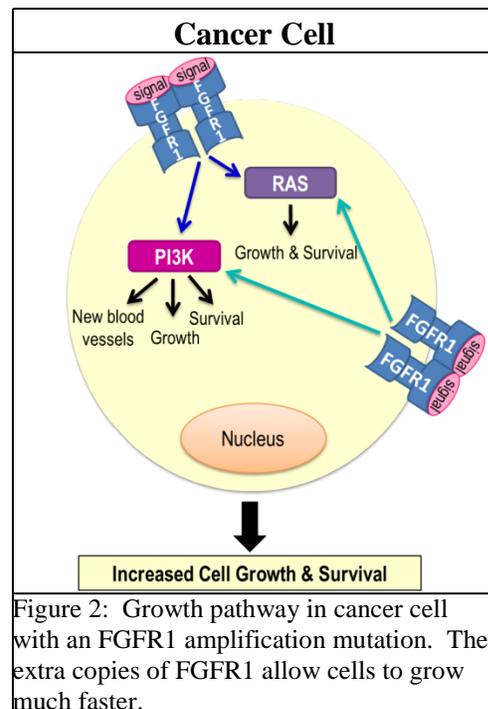


Figure 2: Growth pathway in cancer cell with an FGFR1 amplification mutation. The extra copies of FGFR1 allow cells to grow much faster.