

## Lung Cancer and the DDR2 S768R Mutation

This material will help you understand:

- the basics of lung cancer
- the role of the DDR2 gene in lung cancer
- if there are any drugs that might work better if you have certain changes in the DDR2 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 DDR2?

DDR2 is the name of both a gene and a protein. The DDR2 gene contains the instructions for making the DDR2 protein. DDR2 is short for discoidin death receptor 2. 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. Each receptor usually receives one specific signal. These signals are turned on and off as needed.

When the signal binds to DDR2, it tells the cell to move, to grow, or what type of cell to be. When the outside part of DDR2 receives the signal, it activates, or turns on, the inside part.

When the inside part is on, DDR2 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 DDR2 (Figure 1). SRC and STAT are proteins that DDR2 turns on. When the signal stops, the proteins turn off.

## 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 DDR2 mutations in lung cancer?

About 1 in 25 non-small cell lung cancers (NSCLCs) have a change in the DDR2 gene that changes the DDR2 protein. It is most common in squamous cell lung carcinomas, which is a type of NSCLC. Currently, DDR2 mutations are not linked to a person's sex or age. Smoking may increase the risk of DDR2 mutations.

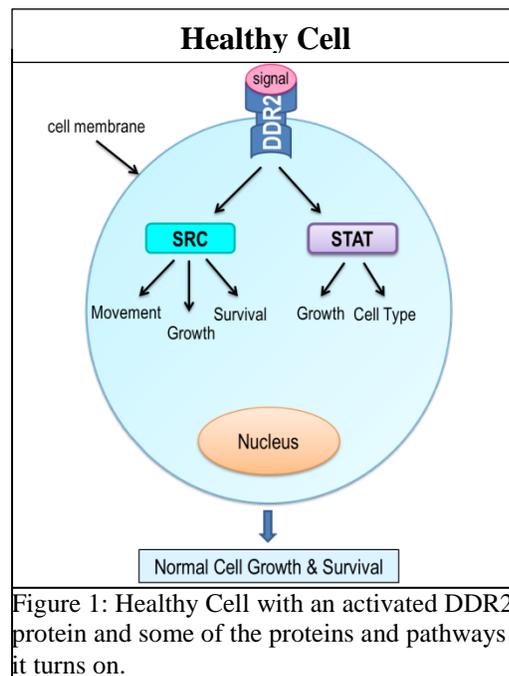
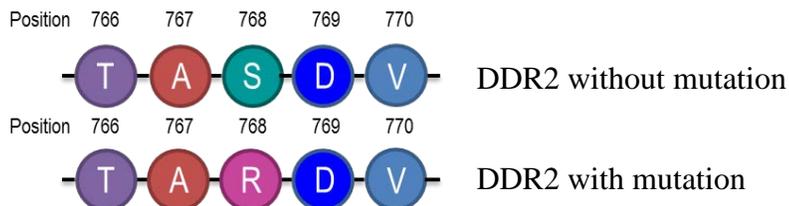


Figure 1: Healthy Cell with an activated DDR2 protein and some of the proteins and pathways it turns on.

### What is the DDR2 S768R mutation?

DDR2 S768R is a specific variation in the part of the DDR2 protein that is inside the cell. Proteins are long chains of amino acids. The DDR2 protein has 855 amino acids. The inside part of the protein starts at amino acid 563 and goes to the end of the protein chain. DDR2 with no mutation at amino acid position 768 has a serine, or S for short. The amino acid at position 768 in DDR2 with the S768R mutation is an arginine, or R for short.



### What is the effect of this mutation?

This mutation is in the part of DDR2 that is inside the cell. Currently, we do not know how this mutation is related to cancer.

### Are there targeted therapies for DDR2 S768R?

At this time, it is unclear if any drugs target DDR2 with this specific mutation. 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 DDR2 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.