

## Lung Cancer and the MAP2K1 K57N Mutation

This material will help you understand:

- the basics of lung cancer
- the role of the MAP2K1 gene in lung cancer
- if there are any drugs that might work better if you have certain changes in the MAP2K1 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 MAP2K1?

MAP2K1 (pronounced “Măp-2-K-1”) is the name of both a gene<sup>🧬</sup> and protein<sup>🧬</sup>. The MAP2K1 gene contains the instructions for making the MAP2K1 protein. MAP2K1 used to be called MEK1. It is a member of the MAP kinase<sup>🧬</sup> family of proteins. Their main job is to help control cell growth as part of a pathway. Proteins in pathways work together to do specific jobs within the cell. Many pathways relay signals from outside the cell to the cell’s nucleus. The nucleus is the control center of the cell. These signals may tell the cell to grow, divide, or die. The body turns the signals on and off as needed.

In healthy cells, MAP2K1 is a key protein in a growth pathway (Figure 1). As the growth signal reaches each protein in the pathway, it turns on the protein. When the RAS protein receives the signal, it passes it on to a RAF protein. RAF passes it on to MAP2K1, and MAP2K1 passes it on to ERK. ERK is the last protein in the pathway. When ERK is on, it turns on genes in the nucleus that help cells grow. When the signal stops, the proteins turn off.

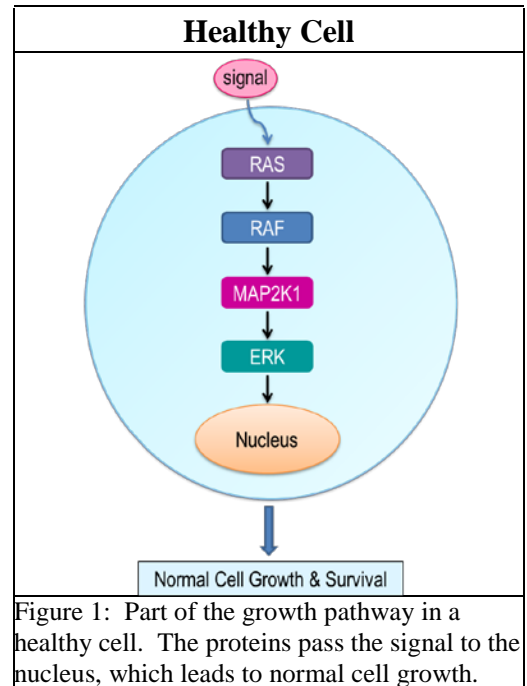


Figure 1: Part of the growth pathway in a healthy cell. The proteins pass the signal to the nucleus, which leads to normal cell growth.

## How do mutations in proteins affect pathways?

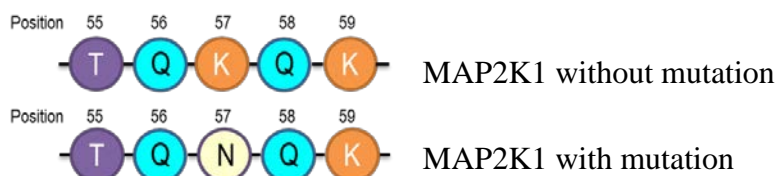
If a mutation<sup>🧬</sup> affects one or more proteins<sup>🧬</sup> in a pathway, the proteins may not be able to be turned on or off as expected. This can cause cells to grow out of control and lead to cancer.

## How common are MAP2K1 mutations in lung cancer?

About 1 in 100 non-small cell lung cancers (NSCLCs) have a mutation<sup>🧬</sup> in the MAP2K1 gene<sup>🧬</sup> that changes the MAP2K1 protein<sup>🧬</sup>. MAP2K1 mutations are most common in smokers or former smokers with adenocarcinoma, a type of NSCLC. But, MAP2K1 mutations can be found in all types of NSCLCs, regardless of smoking status.

## What is the MAP2K1 K57N mutation?

MAP2K1 K57N is a specific variation in the MAP2K1 protein<sup>🧬</sup>. Proteins are long chains of amino acids<sup>🧬</sup>. The MAP2K1 protein has 393 amino acids. MAP2K1 with no mutation<sup>🧬</sup> at amino acid position 57 has a lysine, or K for short. The amino acid at position 57 in MAP2K1 with the K57N mutation is an asparagine, or N for short.



### What is the effect of this mutation?

The K57N mutation is in the part of MAP2K1 that controls if the protein is on or off. In cells with this mutation, MAP2K1 can always turn on ERK. This keeps the growth pathway on. This could cause cells to grow out of control and may lead to cancer.

### Are there targeted therapies for MAP2K1 K57N?

At this time, it is unclear if any drugs target MAP2K1 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 MAP2K1 or “no mutation”?

Your cancer cells might still have other 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.

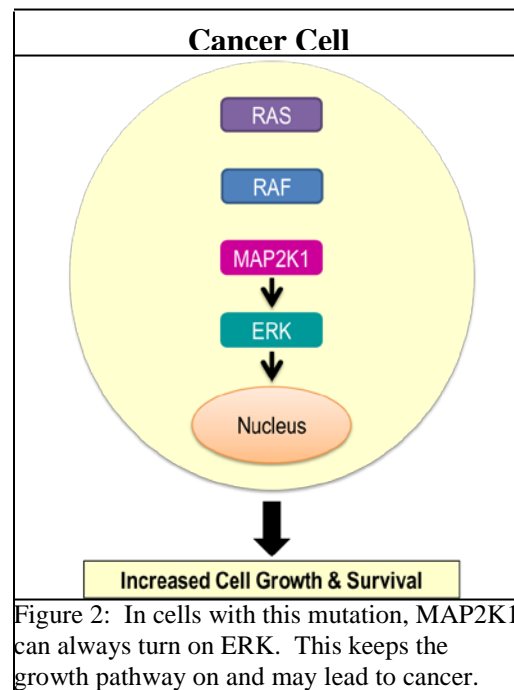


Figure 2: In cells with this mutation, MAP2K1 can always turn on ERK. This keeps the growth pathway on and may lead to cancer.