

## Melanoma and the CTNNB1 S45F Mutation

This material will help you understand:

- the basics of melanoma
- the role of the CTNNB1 gene in melanoma
- if there are any drugs that might work better if you have certain changes in the CTNNB1 gene

### What is melanoma?

Melanoma is a type of skin cancer. It starts in the cells that make melanin, the substance that gives skin its color.

### What causes melanoma?

Cancer is caused by 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.

Melanoma usually starts on areas of the skin exposed to the sun. But melanoma can also show up in other parts of your body like the eye, the bottom of the feet, under the nails, or inside the mouth.



### What are the most common current treatments for melanoma?

Doctors may treat melanoma using one or more of these options:

- **Surgery** – operation that removes as much of a cancer tumor as possible.
- **Traditional chemotherapy** – drugs that kill growing cells. All cells grow, but cancer cells grow faster than healthy cells. So, these drugs kill more of the 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.

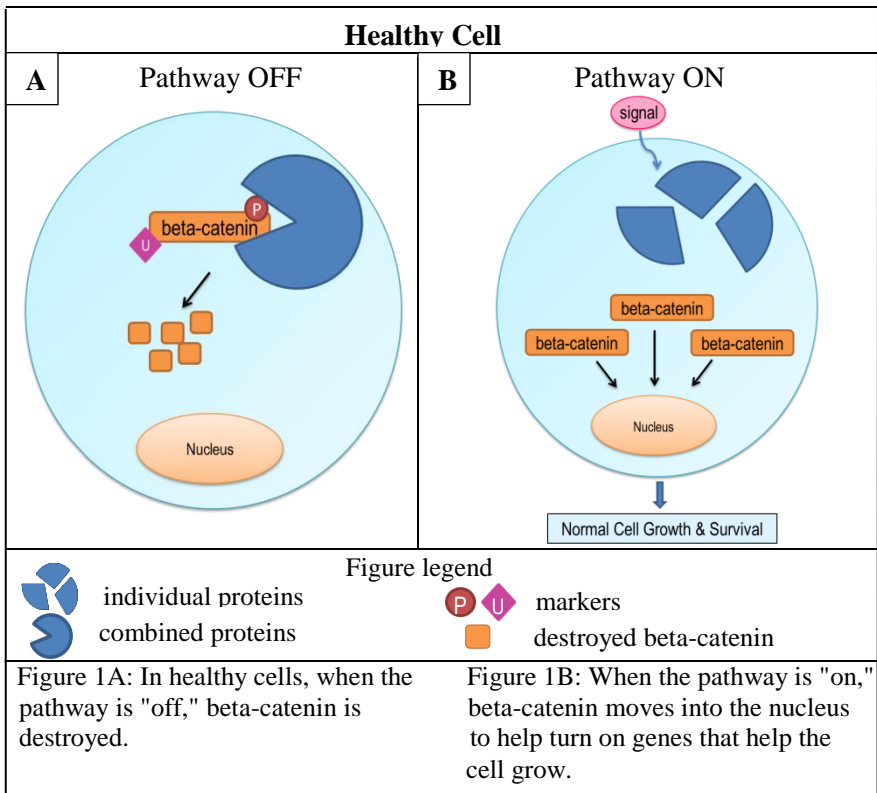


## What is CTNNB1?

CTNNB1 is the name of both a gene and a protein. The CTNNB1 gene contains the instructions for making the CTNNB1 protein. The common name for this protein is beta-catenin. Beta-catenin has many important jobs in our cells. It helps hold cells together to form our body tissues, regulate insulin levels, and control how fast cells grow.

Beta-catenin is also part of a pathway. Proteins in pathways work together to do specific jobs within the cell. This pathway relays a signal 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. These are all normal cell functions. The body turns the signals on and off as needed.

When the pathway is off, other proteins in the cell combine with beta-catenin (Figure 1A). The other proteins mark beta-catenin for destruction, and then destroy it. But when the pathway is on, the signal stops the proteins from combining (Figure 1B). This allows beta-catenin to move into the nucleus to help turn on genes that help the cell grow.

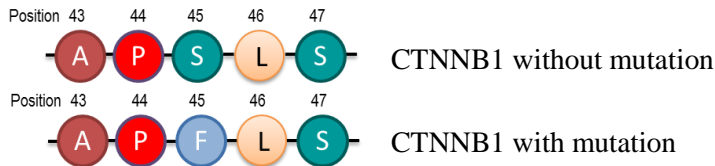


## How common are CTNNB1 mutations in melanoma?

About 1 in 25 melanomas have a mutation in the CTNNB1 gene that changes the beta-catenin protein. At this time, we do not know if sun damage plays a role in CTNNB1 mutations.

### What is the CTNNB1 S45F mutation?

CTNNB1 S45F is a specific variation in the beta-catenin protein. Proteins are long chains of amino acids. The beta-catenin protein has 781 amino acids. CTNNB1 with no mutation at amino acid position 45 has a serine, or S for short. The amino acid at position 45 in CTNNB1 with the S45F mutation is a phenylalanine, or F for short.



### What is the effect of this mutation?

The S45F mutation stops beta-catenin from being marked for destruction when there is no signal. Without the mark, beta-catenin is not destroyed and can move into the nucleus (Figure 2). This can cause cells to grow out of control, which can lead to cancer. Mutations in beta-catenin can also cause cells in tissues to detach. This means the cancer cells could move to other parts of the body.

### Are there targeted therapies for CTNNB1 mutations?

There are no drugs that target beta-catenin right now. But, you should talk to your doctor about your treatment options.

### What if I have a different mutation in CTNNB1 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.

