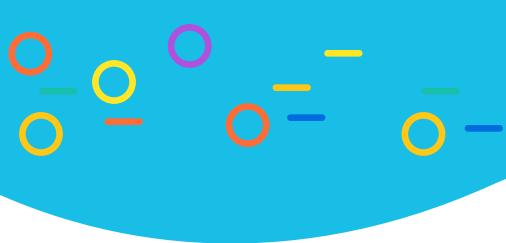




SHANK3-related syndrome *- or -* **Phelan-McDermid syndrome**





This guide is not meant to take the place of medical advice.

Please consult with your doctor about your genetic results and health care choices. The information in this guide was up to date at the time it was written in 2019. But new information may come to light with new research. You may find it helpful to share this guide with friends and family members or doctors and teachers of the person who has SHANK3-related syndrome.



What is SHANK3-related syndrome?

SHANK3-related syndrome happens when there are changes to the SHANK3 gene. These changes can keep the gene from working as it should.



Phelan-McDermid syndrome, also called PMS, is a related syndrome that is also linked to changes in the SHANK3 gene. The names PMS and SHANK3-related syndrome are sometimes used interchangeably.

People who have PMS are missing part of chromosome 22q13.3 that contains the SHANK3 gene. The amount of missing DNA can vary. Some people who have PMS have small changes in the SHANK3 gene. Others may be missing a larger piece of DNA that includes several genes.

Most of the symptoms and other information given below for SHANK3-related syndrome also apply to PMS. To read more about PMS and people who have gene changes in SHANK3, please see www.pmsf.org.

Key role

The SHANK3 gene plays a key role in the development and function of the brain. It helps to make the connections between brain cells. Changes in the SHANK3 gene may impair these connections.

Symptoms

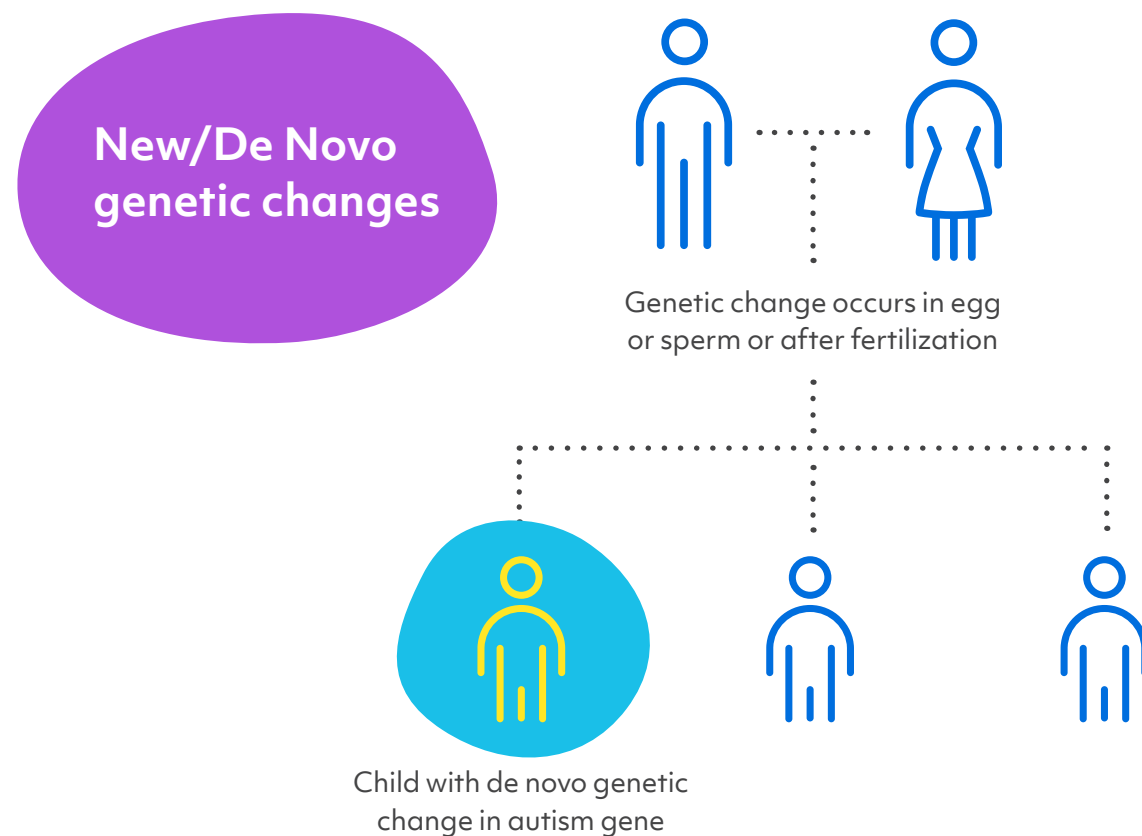
Because the SHANK3 gene is important in the development of the brain, many people who have SHANK3-related syndrome have:

- Developmental delay or intellectual disability, or both
- Autism spectrum disorder or features of autism
- Speech delay or no speech
- Low muscle tone
- Changes in facial features
- Sleep difficulties

What causes SHANK3-related syndrome?

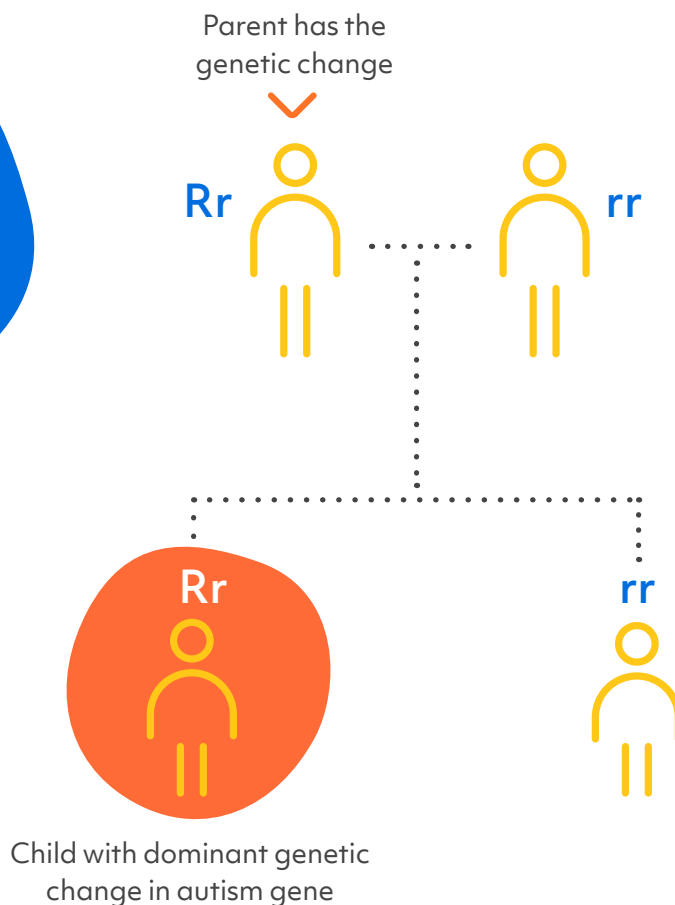
Our genes contain the instructions, or code, that tell our cells how to grow, develop, and work. Every child gets two copies of the SHANK3 gene: one copy from their mother, from the egg, and one copy from their father, from the sperm. In most cases, parents pass on exact copies of the gene to their child. But the process of copying genes is not perfect. A change in the genetic code can lead to physical issues, developmental issues, or both.

Sometimes a random change happens in the sperm or egg. This change to the genetic code is called a 'de novo', or new, change. The child can be the first in the family to have the gene change.



Dominant inheritance

Children have a 50% chance of inheriting the genetic change



De novo changes can take place in any gene. We all have some de novo changes, most of which don't affect our health. But because SHANK3 plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that SHANK3-related syndrome is often the result of a de novo change in SHANK3. Many parents who have had their genes tested do not have the SHANK3 gene change found in their child who has the syndrome. In some cases, SHANK3-related syndrome happens because the gene change was passed down from a parent.



Why does my child have a change in the SHANK3 gene?

No parent causes their child's SHANK3-related syndrome. We know this because no parent has any control over the gene changes that they do or do not pass on to their children. Please keep in mind that nothing a parent does before or during the pregnancy causes this to happen. The gene change takes place on its own and cannot be predicted or stopped.

What are the chances that other family members or future children will have SHANK3-related syndrome?

Each family is different. A geneticist or genetic counselor can give you advice on the chance that this will happen again in your family.

The risk of having another child who has SHANK3-related syndrome depends on the genes of both birth parents.

- If neither birth parent has the same gene change found in their child, the chance of having another child who has the syndrome is on average 1 percent. This 1 percent chance is higher than the chance of the general population. The increase in risk is due to the very unlikely chance that more of the mother's egg cells or the father's sperm cells carry the same change in the gene.
- If one birth parent has the same gene change found in their child, the chance of having another child who has the syndrome is 50 percent.

For a symptom-free sibling, a brother or sister, of someone who has SHANK3-related syndrome, the risk of having a child who has the syndrome depends on the symptom-free sibling's genes and their parents' genes.

- If neither parent has the same gene change found in their child who has the syndrome, the symptom-free sibling has a nearly 0 percent chance of having a child who has SHANK3-related syndrome.
- If one birth parent has the same gene change found in their child who has the syndrome, the symptom-free sibling has a small chance of also having the same gene change. If the symptom-free sibling has the same gene change as their sibling who has the syndrome, the symptom-free sibling's chance of having a child who has SHANK3-related syndrome is 50 percent.

For a person who has SHANK3-related syndrome, the risk of having a child who has the syndrome is about 50 percent.

How many people have SHANK3-related syndrome?

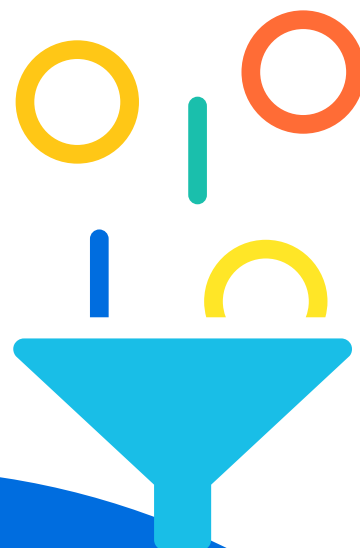
As of 2018, doctors had found more than 1,800 people in the world with PMS. Most of these people have changes in the SHANK3 gene. The first case of PMS was described in 1985. But the important role that the SHANK3 gene plays in this condition was not known until 2007.

Changes in the SHANK3 gene are rare. But these changes are one of the most common genetic causes of autism. Scientists think that changes in this gene are present in nearly 1 percent of people who have autism. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

Do people who have SHANK3-related syndrome look different?

People who have SHANK3-related syndrome have minor differences in appearance. These differences can vary and may include:

- Long head
- Flattened back of the head
- Thick eyelashes
- Folds in the corner of the eyelids
- Distinctive nose





How is SHANK3-related syndrome treated?

Scientists and doctors have only just begun to study SHANK3-related syndrome. At this point, there are no medicines designed to treat the syndrome. A genetic diagnosis can help people decide on the best way to track the condition and manage therapies. Doctors can refer people to specialists for:

- Physical exams and brain studies.
- Genetics consults.
- Development and behavior studies.
- Other issues, as needed.

A developmental pediatrician, neurologist, or psychologist can follow progress over time and can help:

- Suggest the right therapies. This can include physical, occupational, speech, or behavioral therapy.
- Guide individualized education plans (IEPs).

Specialists advise that therapies for SHANK3-related syndrome should begin as early as possible, ideally before a child begins school.

Seizures happen in about 40 percent of people who have SHANK3-related syndrome. If seizures happen, consult a neurologist. There are many types of seizures, and not all types are easy to spot. To learn more, you can refer to resources such as the Epilepsy Foundation's website: [epilepsy.com/learn/types-seizures](https://www.epilepsy.com/learn/types-seizures).

SHANK3-related syndrome is rare. As of 2018, more than 1,800 people had registered in the International PMS registry: pmsf.org.

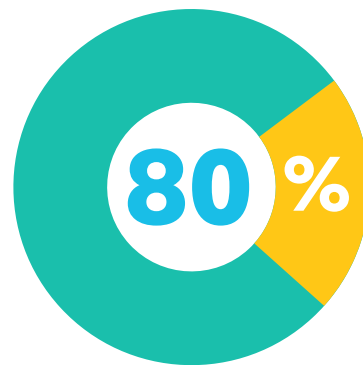
This section includes a summary of information from major published articles. It highlights how many people have different symptoms. To learn more about the articles, see the [Sources and references](#) section of this guide.

Behavior and development concerns linked to SHANK3-related syndrome

Behavior

Autism and features of autism are common among people who have SHANK3-related syndrome. Features of autism include lack of eye-to-eye contact and repetitive movements.

Studies suggest that more than 80% have **autism or features of autism**.



Speech

Speech problems are common. Many people are nonverbal and have no speech. Others use only a few words or have learned other ways to communicate.

Learning

Learning disabilities and intellectual disabilities are common.

Mental health

Several studies have found that people who have PMS have higher rates of a type of bipolar disorder, a mental health condition that causes unusual shifts in mood, energy and activity levels. Some studies have found that people who have PMS may lose skills over their lifetime.

Medical and physical concerns linked to SHANK3-related syndrome

Muscle tone

Many people who have changes in the SHANK3 gene have low muscle tone. This may be linked to feeding difficulties.

Feeding and digestion issues

People who have changes in the SHANK3 gene often have trouble with feeding. This may be caused by weaker muscle tone in the mouth and throat. Reflux or heartburn is also common.



Brain

Brain scans show that nearly three-quarters of people who have PMS have changes in brain structure.



**Where can I
find support
and resources?**

Phelan-McDermid Syndrome Foundation
pmsf.org



Phelan-McDermid Syndrome Facebook page
www.facebook.com/PMSF22q13

Sources and References

The content in this guide comes from published studies about SHANK3-related syndrome. Below you can find details about each study, as well as links to summaries or, in some cases, the full article.

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