PHF21A-related syndrome
This guide is not meant to take the place of medical advice.

Please consult with your doctor about 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 PHF21A-related syndrome.
What is PHF21A-related syndrome?

PHF21A-related syndrome happens when there are changes to the PHF21A gene. These changes can keep the gene from working as it should.

**Key role**
The PHF21A gene helps to control other genes and is important for the development of the brain.

**Symptoms**
Because the PHF21A gene is important in brain development, many people who have PHF21A-related syndrome have:

- Autism
- Intellectual disability
- Seizures
- Increased weight, height, head size

Some people are missing a large segment of DNA that includes the PHF21A gene. This is called Potocki-Shaffer syndrome or 11p11.2-related syndrome, because the missing segment is on part of chromosome 11. Other people have a small change within the PHF21A gene itself. People who have these different syndromes have symptoms that overlap.
What causes PHF21A-related syndrome?

Our genes contain the instructions, or code, that tell our cells how to grow and work. Every child gets two copies of the PHF21A gene: one copy from the mother, via the egg, and one copy from the father, via 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 occurs 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.
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 PHF21A plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that PHF21A-related syndrome is often the result of a de novo change in PHF21A. Many parents who have had their genes tested do not carry the PHF21A gene change found in their child. In some cases, PHF21A-related syndrome happens because the gene change is passed down from a parent.
No parent causes their child’s PHF21A-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 foreseen or stopped.
What are the chances that other family members or future children will have PHF21A-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 PHF21A-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 with the syndrome is on average 1 percent. This 1 percent chance is higher than that for 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 with the syndrome is 50 percent.

For a symptom-free sibling (brother or sister) of someone with PHF21A-related syndrome, the risk of having a child with 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 with the syndrome, the symptom-free sibling has a nearly 0 percent chance of having a child with PHF21A-related syndrome.
- If one birth parent has the same gene change found in their child with 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 with the syndrome, the symptom-free sibling’s chance of having a child who has PHF21A-related syndrome is 50 percent.

A person who has PHF21A-related syndrome has about a 50 percent risk of having a child with the syndrome.
How many people have PHF21A-related syndrome?

As of 2019, doctors had found fewer than 10 people in the world with changes in just the PHF21A gene. Potocki-Shaffer syndrome is more common, but also very rare. In Potocki-Shaffer syndrome, people are missing a large segment of DNA that includes PHF21A. The first case of PHF21A-related syndrome was described in 2012. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

Do people who have PHF21A-related syndrome look different?

People who have PHF21A-related syndrome may look different. One study of four people who have the syndrome found that two had flat foreheads and two had large heads.
How is PHF21A-related syndrome treated?

Scientists and doctors have only just begun to study PHF21A-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 PHF21A-related syndrome should begin as early as possible, ideally before a child begins school.

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.
PHF21A-related syndrome is very rare. Doctors and scientists have just recently begun to study it. As of 2019, studies had found fewer than 10 people who have PHF21A-related syndrome.

This section includes a summary of information from two published articles describing symptoms in four people. To learn more about the articles, see the Sources and references section of this guide.

**Behavior and development concerns linked to PHF21A-related syndrome**

**Speech**
4 out of 4 had speech delay.

**Learning**
4 out of 4 had some degree of intellectual disability.

**Behavior**
1 out of 3 seem to require lots of sleep.
1 out of 3 had autism.
Medical and physical concerns linked to PHF21A-related syndrome

Growth
3 out of 3 had larger than average weight, height, and head size.

Motor issues
3 out of 4 had low muscle tone.

Brain
1 out of 4 had seizures.
Simons Searchlight is another research program sponsored and run by the Simons Foundation Autism Research Initiative, also known as SFARI. As part of the next step in your research journey, Simons Searchlight offers you the opportunity to partner with scientists and other families who have the same gene change. Simons Searchlight is a registry for more than 150 genetic changes that are associated with neurodevelopmental conditions, including autism spectrum disorder. Simons Searchlight makes it easier for researchers to access the information they need to advance research on a condition.

To register for Simons Searchlight, go to the Simons Searchlight website at www.simonssearchlight.org and click “Join Us Today”.

- Learn more about Simons Searchlight
  www.simonssearchlight.org/frequently-asked-questions

- Simons Searchlight webpage with more information on PHF21A
  www.simonssearchlight.org/research/what-we-study/phf21a

- Simons Searchlight Facebook group
  www.facebook.com/groups/496201247823592
Sources and References

The content in this guide comes from published studies about PHF21A-related syndrome. Below you can find details about each study, as well as links to summaries or, in some cases, the full article.

