ASXL3-Related Syndrome

- or -

Bainbridge-Ropers Syndrome

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Simons Powering Autism Research

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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 ASXL3-related syndrome.

What is ASXL3-related syndrome?

ASXL3-related syndrome happens when there are changes to the ASXL3 gene. These changes can keep the gene from working as it should. ASXL3-related syndrome is also known as Bainbridge-Ropers syndrome or BRPS.

Key role

The ASXL3 gene plays a key role in development of the brain and the body. It affects parts of the body including the spinal cord, liver, kidneys, and bone marrow.

Symptoms

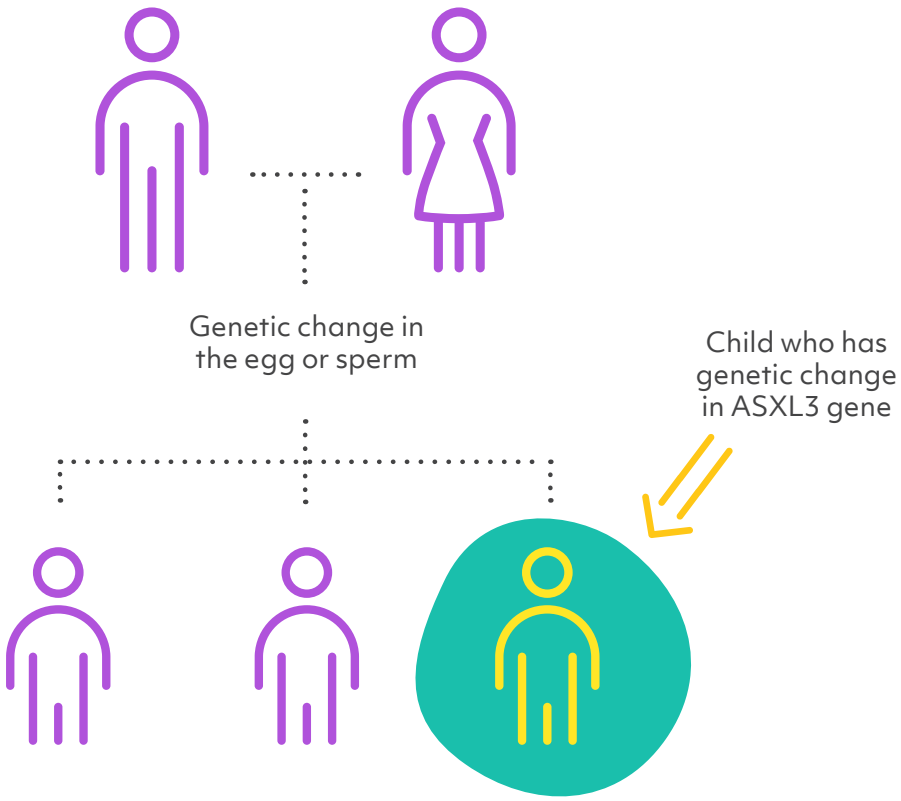
ASXL3-related syndrome can affect communication, social, and learning skills. The effects can be moderate to severe. Because the ASXL3 gene plays a key role in how cells work, many people who have ASXL3-related syndrome have:

- Intellectual disability
- Changes in skull and facial features
- Feeding problems
- Delayed growth
- Curved spine, also called scoliosis

What causes ASXL3-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 ASXL3 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.



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 ASXL3 plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that ASXL3-related syndrome is often the result of a de novo change in ASXL3. Many parents who have had their genes tested do not have the ASXL3 gene change found in their child who has the syndrome. In some cases, ASXL3-related syndrome happens because the gene change was passed down from a parent.

Why does my child have a change in the ASXL3 gene?

No parent causes their child's ASXL3-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 ASXL3-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 ASXL3-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 ASXL3-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 ASXL3-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 ASXL3-related syndrome is 50 percent.

For a person who has ASXL3-related syndrome, the risk of having a child who has the syndrome is about 50 percent.

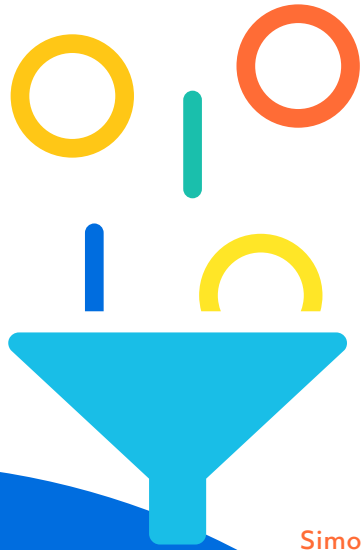
How many people have ASXL3-related syndrome?

As of 2018, doctors had found about 24 people in the world with changes in the ASXL3 gene. The first case of ASXL3-related syndrome was described in 2013. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

Do people who have ASXL3-related syndrome look different?

People who have ASXL3-related syndrome often have different facial features. Appearance can vary and can include some but not all of these features:

- Wide mouth with full lower lip. High-arched roof of the mouth and crowded teeth.
- Eyes that are slanted down. Eyes that are slanted up are less common.
- Long nose with wide nasal bridge. Tip of nose is broad and pointed up.
- Narrow head shape with wide forehead.
- High-arched eyebrows.



How is ASXL3-related syndrome treated?

Scientists and doctors have only just begun to study ASXL3-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 ASXL3-related syndrome should begin as early as possible, ideally before a child begins school.

Surgery may be necessary for people who have issues with the roof of their mouth or severe curved spine.

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.

ASXL3-related syndrome is very rare. Doctors and scientists have just recently begun to study it. As of 2018, studies found around 24 people who have ASXL3-related syndrome.

This section includes a summary of information from major published studies. 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 ASXL3-related syndrome

Behavior

Most people who have ASXL3-related syndrome are on the autism spectrum. Many have sleep problems. Some flap their hands, rock, or breath rapidly, also known as hyperventilation. These actions are more common when a person is anxious.

Speech

Many people who have ASXL3-related syndrome do not speak.

Learning

Everyone who has ASXL3-related syndrome has some level of intellectual disability. It can range from moderate to severe, but most cases are severe. These people often require special educational support.

Mental health

People who have the syndrome may feel agitation or frustration for brief periods.

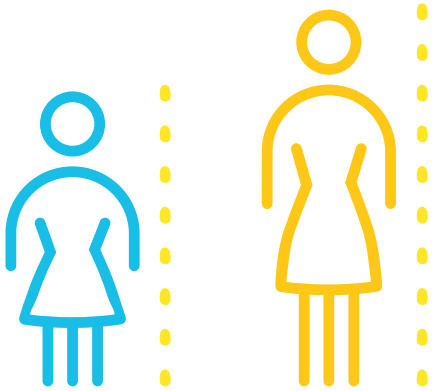
Medical and physical concerns linked to ASXL3-related syndrome

Brain

About one-third of people who have ASXL3-related syndrome have seizures. These can be of different types including absence — seizures with a lapse of awareness and blank staring spells, focal — seizures that initially affect only half the brain, and generalized tonic-clonic — seizures that involve the entire body. Seizures start very early in some people. For others, seizures can start later in life.

Growth

Height can vary. Some are short. Others are tall and slender.



Sitting and walking

Children who have ASXL3-related syndrome are often late in walking. Some never walk.

Medical and physical concerns linked to ASXL3-related syndrome

Other movement concerns

Children who have the syndrome often meet motor milestones late. They may have trouble with movement of smaller muscles, such as fingers and hands, also called fine motor skills.

Muscle tone

People often have low muscle tone.

Feeding and Digestion issues

People who have the syndrome often have feeding issues, especially during early life. Some need a feeding tube.

Eyes and eyesight

Some people have a lazy eye or trouble moving their eyes.

Joints and spine

Some people have spine issues, such as a curved spine, also called scoliosis.

Where can I find support and resources?

Simons Searchlight ASXL3 Information Page
www.simonssearchlight.org/research/what-we-study/asxl3

Simons Searchlight ASXL3 Facebook community
www.facebook.com/groups/searchlight.asxl3

Parent-run page with information about ASXL3
www.asxl3.com

Facebook group for families with children who have Bainbridge Ropers-Syndrome and ASXL3 gene mutation
www.facebook.com/groups/Bainbridge-Ropers-Syndrome-and-ASXL3-Families-288227234667517/511917542298484

On the Edge of Autism (SPARK Discover article)
www.sparkforautism.org/discover_article/on-the-edge-of-autism/

Sources and References

The content in this guide comes from published studies about ASXL3-related syndrome. Below you can find details about each study, as well as links to summaries or, in some cases, the full article.

- Bainbridge MN. *et al. Genome Medicine*, **5**, 11, (2013). De novo truncating mutations in ASXL3 are associated with a novel clinical phenotype with similarities to Bohring-Opitz syndrome
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- Balasubramanian M. *et al. Journal of Medical Genetics*, **54**, 537-543, (2017). Delineating the phenotypic spectrum of Bainbridge-Ropers syndrome: 12 new patients with de novo, heterozygous, loss-of-function mutations in ASXL3 and review of published literature
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- Myers KA. *et al. Epilepsy Research*, **140**, 166-170, (2018). Childhood-onset generalized epilepsy in Bainbridge-Ropers syndrome
  www.ncbi.nlm.nih.gov/pubmed/29367179

- Verhoeven W. *et al. Neuropsychiatric Disease and Treatment*, **14**, 867-870, (2018). Phenotypic characterization of an older adult male with late-onset epilepsy and a novel mutation in ASXL3 shows overlap with the associated Bainbridge-Ropers syndrome
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