EBF3-related 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 2020. 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 EBF3-related syndrome.
What is EBF3-related syndrome?

EBF3-related syndrome happens when there are changes to the EBF3 gene. These changes can keep the gene from working as it should.

**Key role**
The EBF3 gene plays a key role in the growth of brain cells.

**Symptoms**
Because the EBF3 gene is important in the development and function of brain cells, many people who have EBF3-related syndrome have:

- Developmental delay
- Intellectual disability
- Low muscle tone
- Certain facial features, including a triangular face
- Autism, or attention deficit hyperactivity disorder, also called ADHD, or both
Our genes contain the instructions, or code, that tell our cells how to grow, develop, and work. Every child gets two copies of the EBF3 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.

What causes EBF3-related syndrome?

![Diagram showing genetic change in egg or sperm or after fertilization leading to a child with de novo genetic change in autism gene.](image-url)
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 EBF3 plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that EBF3-related syndrome is often the result of a de novo change in EBF3. Many parents who have had their genes tested do not have the EBF3 gene change found in their child who has the syndrome. In some cases, EBF3-related syndrome happens because the gene change was passed down from a parent. This is called dominant inheritance.
Why does my child or I have a change in the EBF3 gene?

No parent causes their child’s EBF3-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 EBF3-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 EBF3-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 EBF3-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 EBF3-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 EBF3-related syndrome is 50 percent.

For a person who has EBF3-related syndrome, the risk of having a child who has the syndrome is about 50 percent.
How many people have EBF3-related syndrome?

As of 2020, about 30 people in the world with changes in the EBF3 gene had been described in medical research. The first case of EBF3-related syndrome was described in 2017. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

Do people who have EBF3-related syndrome look different?

People who have EBF3-related syndrome may look different. Appearance can vary and can include some but not all of these features:

- Triangular face
- Single connected eyebrow, also called synophrys
- Small ears
- Roof of the mouth that is highly arched
- Crowded teeth
- Single crease on the palms of hands
How is EBF3-related syndrome treated?

Scientists and doctors have only just begun to study EBF3-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 EBF3-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: www.epilepsy.com/learn/types-seizures.
EBF3-related syndrome is very rare. Doctors and scientists have just recently begun to study it. As of 2020, studies described around 30 people who have EBF3-related syndrome.

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 EBF3-related syndrome

Speech
- Speech delay is common.

Learning
- Intellectual disability is common.

Behavior
- Some people have autism, attention deficit hyperactivity disorder, also called ADHD, and behavioral differences, including poor eye contact, self-injurious behavior, or altered pain sensitivity.
Medical and physical concerns linked to EBF3-related syndrome

**Sitting and walking**
Motor delay is common.

**Eyes and eyesight**
Eye issues are common. These can include near sightedness or crossed eyes, also called strabismus.

**Muscle tone**
Some people have low muscle tone.

**Growth**
Some people are short.

**Other motor concerns**
Some people have impaired coordination, also called ataxia.
Where can I find support and resources?

**EBF3-HADDS Foundation**
www.hadds.org

*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 200 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 EBF3
  www.simonssearchlight.org/research/what-we-study/ebf3

- Simons Searchlight EBF3 Facebook community
  www.facebook.com/groups/407663279857755
Sources and References

The content in this guide comes from published studies about EBF3-related syndrome. Below you can find details about each study, as well as links to summaries or, in some cases, the full article.


- Tanaka AJ. et al. Cold Spring Harbor Molecular Case Studies, a002097, 3, (2017). De novo variants in EBF3 are associated with hypotonia, developmental delay, intellectual disability, and autism. [www.molecularcasestudies.cshlp.org/content/3/6/a002097.long](www.molecularcasestudies.cshlp.org/content/3/6/a002097.long)