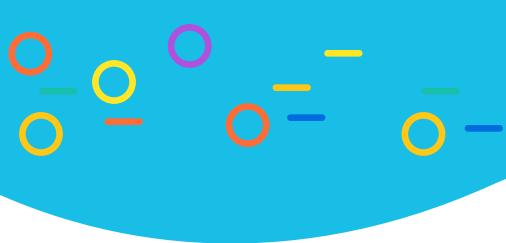




IRF2BPL-related syndrome





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 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 IRF2BPL-related syndrome.





What is IRF2BPL-related syndrome?

IRF2BPL-related syndrome happens when there are changes to the IRF2BPL gene. These changes can keep the gene from working as it should.

Key role

The IRF2BPL gene plays a key role in brain cell function.

Symptoms

Because the IRF2BPL gene is important in the development and function of brain cells, many people who have IRF2BPL-related syndrome have:

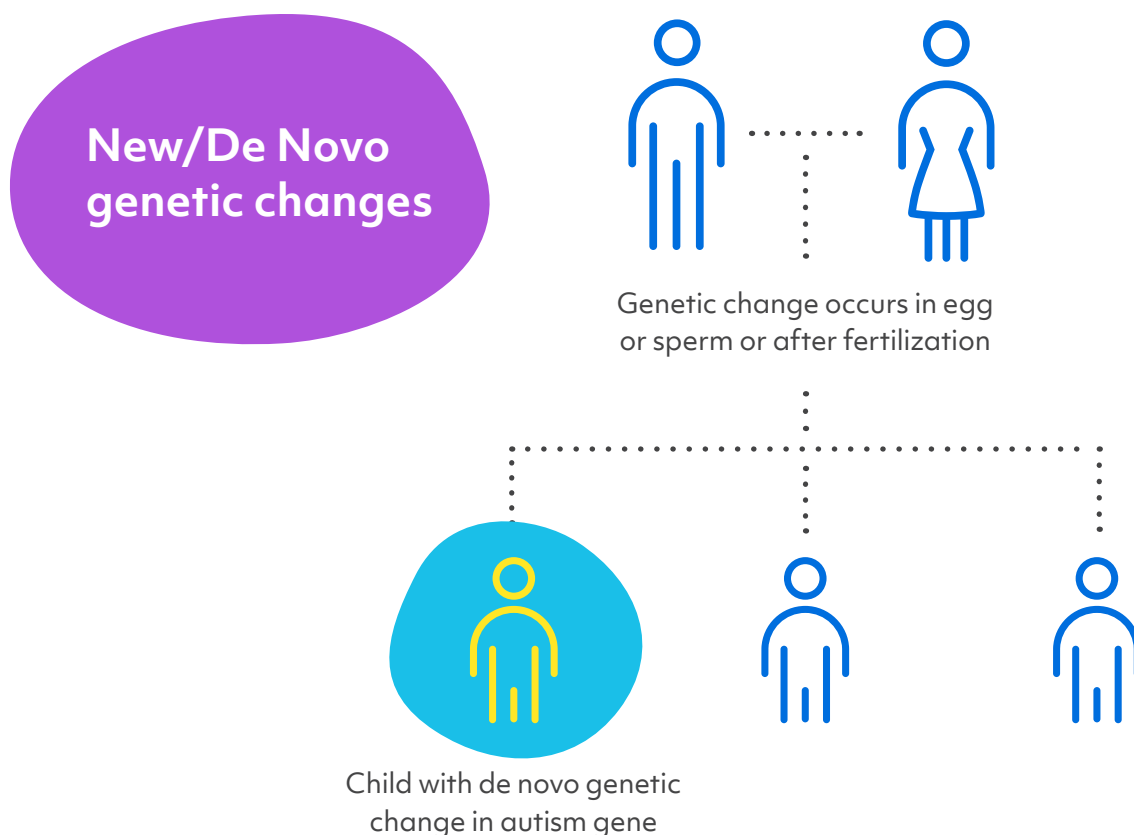
- Seizures.
- Movement issues, such as dystonia, a condition in which muscles contract uncontrollably, and ataxia, a condition that causes uncoordinated movement.
- In some cases, loss of motor skills.

People with changes in this gene are very rare and have only recently been described.

What causes IRF2BPL-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 IRF2BPL 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.



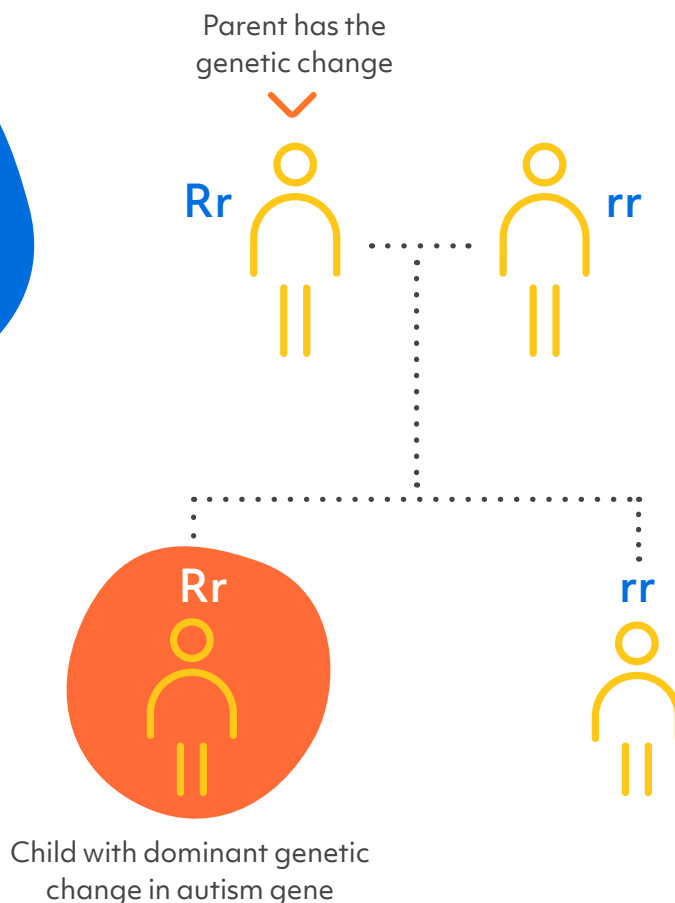
De novo changes can take place in any gene. We all have some de novo changes, most of which don't affect our health. But because IRF2BPL plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that IRF2BPL-related syndrome is often the result of a de novo change in IRF2BPL. Many parents who have had their genes tested do not have the IRF2BPL gene change found in their child who has the syndrome. In some cases, IRF2BPL-related syndrome happens because the gene change was passed down from a parent.



Dominant inheritance


Children have a 50% chance of inheriting the genetic change



Why does my child have a change in the IRF2BPL gene?

No parent causes their child's IRF2BPL-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 IRF2BPL-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 IRF2BPL-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 IRF2BPL-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 IRF2BPL-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 IRF2BPL-related syndrome is 50 percent.

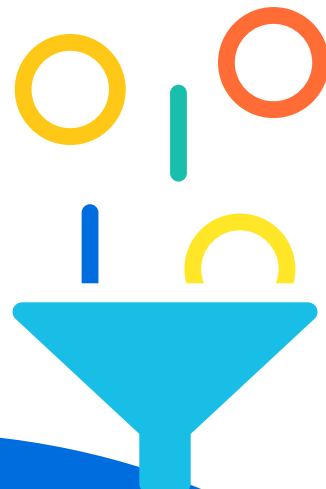
For a person who has IRF2BPL-related syndrome, the risk of having a child who has the syndrome is about 50 percent.

How many people have IRF2BPL-related syndrome?

As of 2019, about 20 people in the world with changes in the IRF2BPL gene had been described in the medical literature. The first case of IRF2BPL-related syndrome was described in 2018. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

Do people who have IRF2BPL-related syndrome look different?

People who have IRF2BPL-related syndrome do not look very different.





How is IRF2BPL-related syndrome treated?

Scientists and doctors have only just begun to study IRF2BPL-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 IRF2BPL-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.

IRF2BPL-related syndrome is very rare. Doctors and scientists have just recently begun to study it. As of 2019, studies described around 20 people who have IRF2BPL-related syndrome.

This section includes a summary of information from major published articles. It focuses on a research study that included five people who had a change at the end of the IRF2BPL gene. These types of gene changes are linked to neurodevelopmental symptoms. To learn more about the articles, see the [Sources and references](#) section of this guide.

Behavior and development concerns linked to IRF2BPL-related syndrome

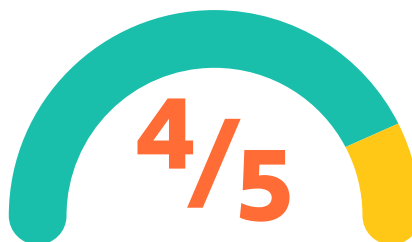
Behavior

Autism and developmental delay are common in people who have this type of gene change in IRF2BPL.



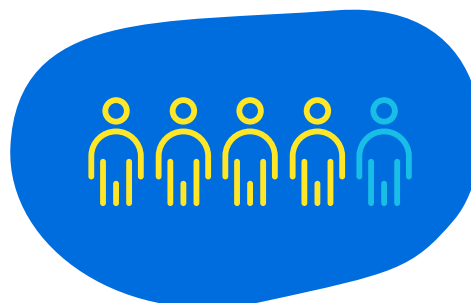
Speech

Four out of five people in the small study had **speech delay**.



Development

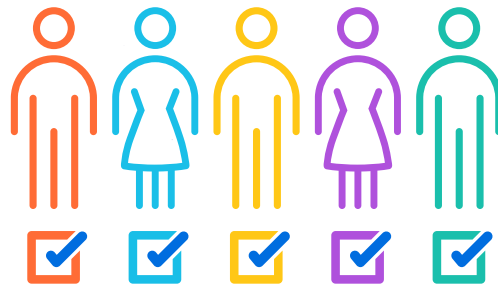
Four out of five lost some motor or verbal skills in the first years of life, which is called **regression**.



Medical and physical concerns linked to IRF2BPL-related syndrome

Motor concerns

All five of the people who have this type of gene change had **low muscle tone**.



Brain

Three out of five people who have this type of gene change had **seizures**.

Sitting and walking

Two out of five had **difficulty walking**.





Where can I find support and resources?

Stand by Eli Foundation
www.standbyeli.org

IRF2BPL Foundation
www.irf2bpl.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 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 IRF2BPL**
www.simonssearchlight.org/research/what-we-study/irf2bpl
- **Simons Searchlight IRF2BPL Facebook community**
www.facebook.com/groups/229525617935154

Sources and References

The content in this guide comes from published studies about IRF2BPL-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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www.ncbi.nlm.nih.gov/pubmed/30057031
- Tran Mau-Them F. *et al. Genetics in Medicine: Official Journal of the American College of Medical Genetics*, **21**, 1008-1014, (2019). De novo truncating variants in the intronless IRF2BPL are responsible for developmental epileptic encephalopathy
www.ncbi.nlm.nih.gov/pubmed/30166628



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