TRIP12-related syndrome

SPARK
Simons Powering Autism Research

SIMONS SEARCHLIGHT
Driven by science. United by hope.

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 TRIP12-related syndrome.

What is TRIP12-related syndrome?

TRIP12-related syndrome happens when there are changes to the TRIP12 gene. These changes can keep the gene from working as it should.

Key role

The TRIP12 gene plays a key role in the basic function of the cell.

Symptoms

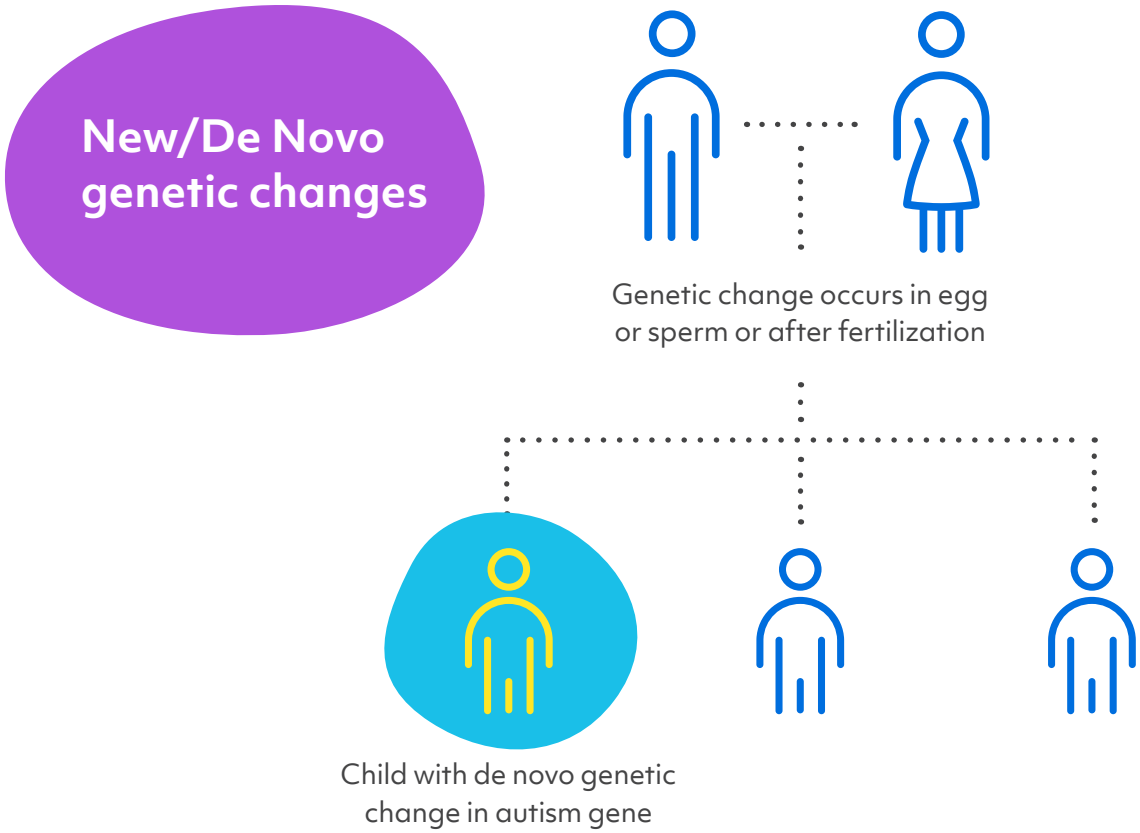
Because the TRIP12 gene is important in the development and function of brain cells, many people who have TRIP12-related syndrome have:

- Intellectual disability
- Speech delay
- Autism

What causes TRIP12-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 TRIP12 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.

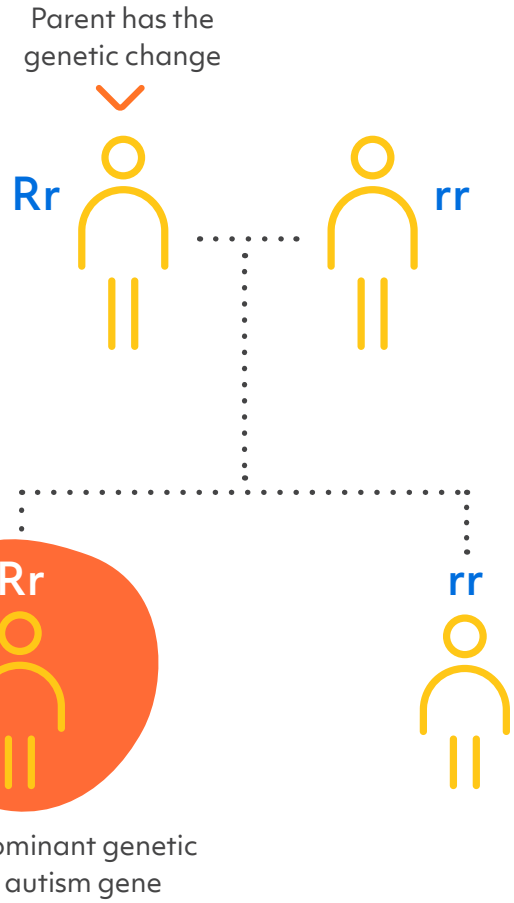


De novo changes can take place in any gene. We all have some de novo changes, most of which don't affect our health. But because TRIP12 plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that TRIP12-related syndrome is often the result of a de novo change in TRIP12. Many parents who have had their genes tested do not have the TRIP12 gene change found in their child who has the syndrome. In some cases, TRIP12-related syndrome happens because the gene change was passed down from a parent. This is called dominant inheritance.

Dominant inheritance

Children have a 50% chance of inheriting the genetic change



Why does my child or I have a change in the TRIP12 gene?

No parent causes their child's TRIP12-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 TRIP12-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 TRIP12-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 TRIP12-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 TRIP12-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 TRIP12-related syndrome is 50 percent.

For a person who has TRIP12-related syndrome, the risk of having a child who has the syndrome is about 50 percent.

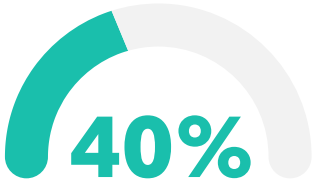
How many people have TRIP12-related syndrome?

As of 2020, about 24 people in the world with changes in the TRIP12 gene had been described in medical research. The first case of TRIP12-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 TRIP12-related syndrome look different?

People who have TRIP12-related syndrome may look different. Appearance can vary and can include some but not all of these features:

Ears



have differences in the shape of the ear, such as **large lobes**.

Eyes

have differences in the shape of the eye, such as a **skin fold of the upper eyelid that covers the inner corner**, known as an epicanthic fold.

Mouth

have a **wide mouth**.

How is TRIP12-related syndrome treated?

Scientists and doctors have only just begun to study TRIP12-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 TRIP12-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.

TRIP12-related syndrome is very rare. Doctors and scientists have just recently begun to study it. As of 2020, studies described 24 people who have TRIP12-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.

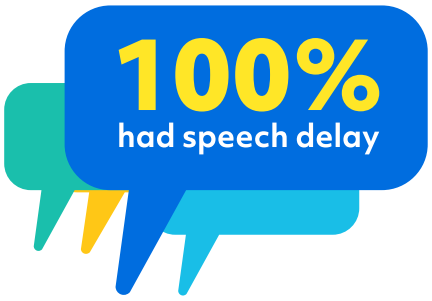
Behavior and development concerns linked to TRIP12-related syndrome

Learning

Everyone studied to date that had TRIP12-related syndrome had **intellectual disability or developmental delay**.

Speech

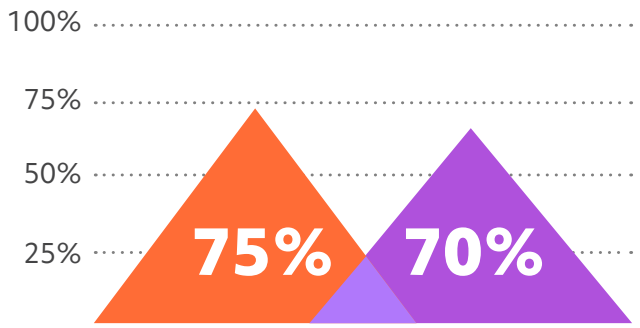
Everyone studied to date had speech delay.



Behavior

Many people had aggressive episodes. Most people had autism or signs of autism.

- 75% had **aggressive episodes**.
- 70% had **autism or signs of autism**.



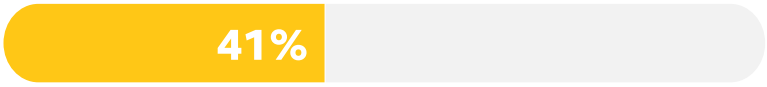
Medical and physical concerns linked to TRIP12-related syndrome

Motor concerns

Many people who had TRIP12-related syndrome had **motor delays**.

Growth

Less than one-half of people who had this syndrome were **obese**.



Brain

About one-fifth had **seizures**.

Where can I find support and resources?

TRIP12 Gene Community

www.facebook.com/groups/1131776373532604

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 TRIP12**
  www.simonssearchlight.org/research/what-we-study/trip12
- **Simons Searchlight TRIP 12 Facebook group**
  www.facebook.com/groups/391182461536247

Sources and References

The content in this guide comes from published studies about TRIP12-related syndrome. Below you can find details about each study, as well as links to summaries or, in some cases, the full article.

- Bramswig NC. *et al. Human Genetics*, **136**, 179-192, (2017). Identification of new TRIP12 variants and detailed clinical evaluation of individuals with non-syndromic intellectual disability with or without autism
  www.ncbi.nlm.nih.gov/pmc/articles/PMC5821420

- Zhang J. *et al. Human Genetics*, **136**, 377-386, (2017). Haploinsufficiency of the E3 ubiquitin-protein ligase gene TRIP12 causes intellectual disability with or without autism spectrum disorders, speech delay, and dysmorphic features
  www.ncbi.nlm.nih.gov/pmc/articles/PMC5543723

- Donoghue T. *et al. American Journal of Medical Genetics Part A*, **182**, 1801-1806, (2020). Novel de novo TRIP12 mutation reveals variable phenotypic presentation while emphasizing core features of TRIP12 variations
  www.pubmed.ncbi.nlm.nih.gov/32424948

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