SETD5-related 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 SETD5-related syndrome.

What is SETD5-related syndrome?

SETD5-related syndrome happens when there are changes to the SETD5 gene. These changes can keep the gene from working as it should.

Key role

The SETD5 gene plays a key role in controlling other genes.

Symptoms

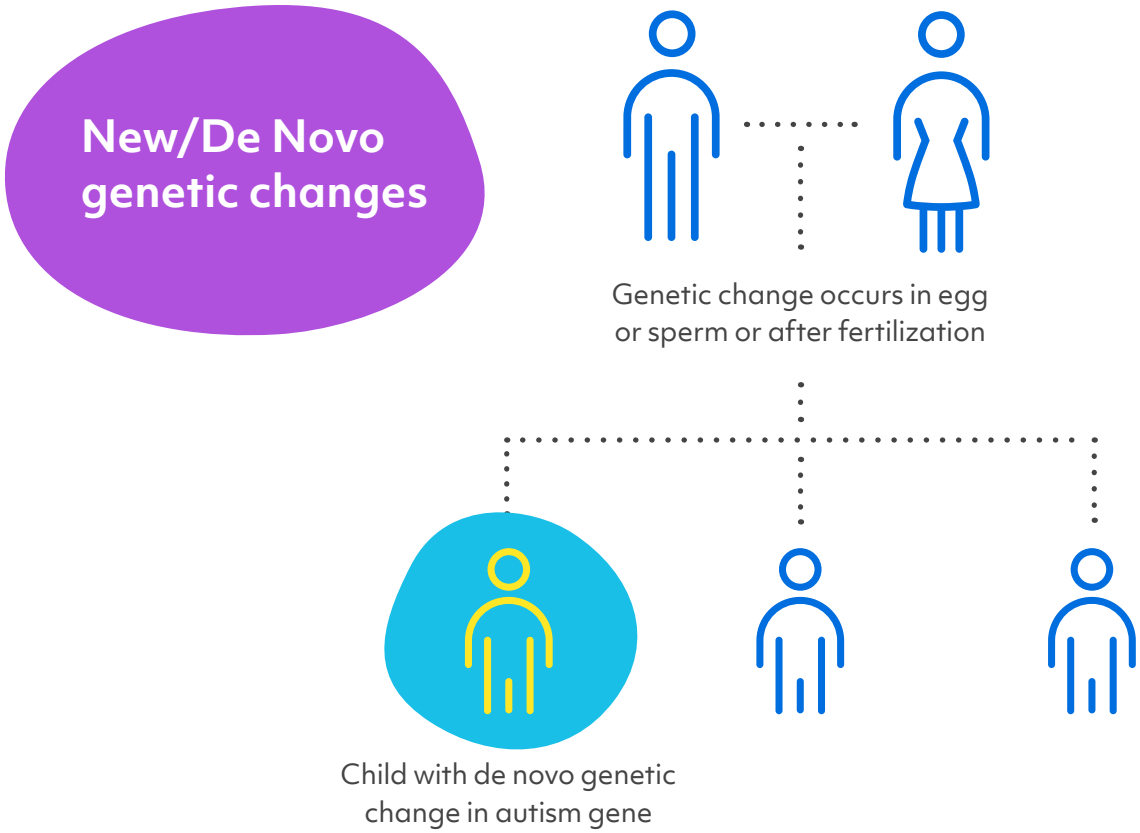
Many people who have SETD5-related syndrome have:

- Intellectual disability
- Language delay
- Differences in facial features

What causes SETD5-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 SETD5 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.

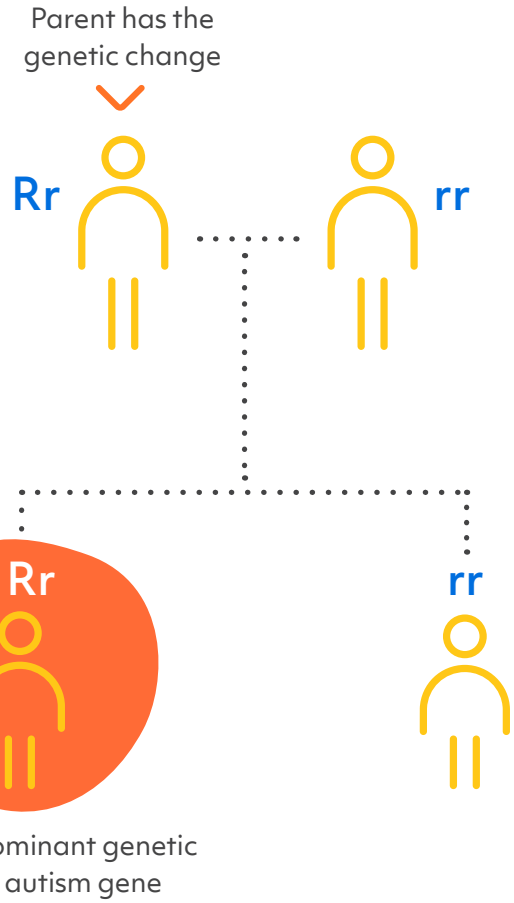


De novo changes can take place in any gene. We all have some de novo changes, most of which don't affect our health. But because SETD5 plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that SETD5-related syndrome is often the result of a de novo change in SETD5. Many parents who have had their genes tested do not have the SETD5 gene change found in their child who has the syndrome. In some cases, SETD5-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 SETD5 gene?

No parent causes their child's SETD5-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 SETD5-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 SETD5-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 SETD5-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 SETD5-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 SETD5-related syndrome is 50 percent.

For a person who has SETD5-related syndrome, the risk of having a child who has the syndrome is about 50 percent.

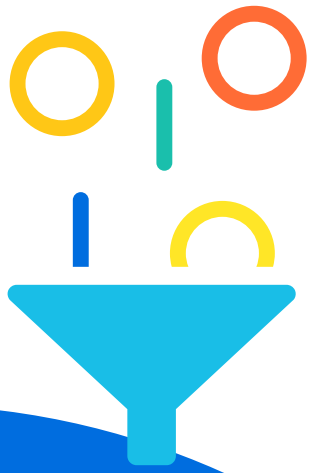
How many people have SETD5-related syndrome?

As of 2019, about 21 people in the world with changes in the SETD5 gene had been described in the medical literature. The first case of SETD5-related syndrome was described in 2014. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

Do people who have SETD5-related syndrome look different?

People who have SETD5-related syndrome may look different. Appearance can vary and can include some but not all of these features:

- Short head, also called brachycephaly
- Large, high forehead
- Eyebrows that meet in the middle of the forehead or are full and broad
- Long, thin, tube-shaped nose
- Long, narrow, up-slanting openings of the eyelids, also called palpebral fissures
- Large, fleshy, low-set ears



How is SETD5-related syndrome treated?

Scientists and doctors have only just begun to study SETD5-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 SETD5-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.

SETD5-related syndrome is very rare. Doctors and scientists have just recently begun to study it. As of 2019, studies described around 21 people who have SETD5-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 SETD5-related syndrome

Speech and Learning

Almost everyone who has the syndrome has some level of **intellectual impairment** or **developmental delay**. Most can talk and communicate their needs.

have intellectual impairment or developmental delay

have behavior issues, including autism

Behavior

Many people who have the syndrome have behavior issues. This can include **obsessive-compulsive disorder**, **hand-flapping**, or symptoms of **autism**. Some people have **involuntary movements**, but these are not long-lasting.

Medical and physical concerns linked to SETD5-related syndrome

Sitting and walking

10 out of 14 people had an **unsteady walk**.

Muscle tone

Two-thirds of people have **low muscle tone**.

Feeding and digestion issues

Many people have **feeding problems**, especially with **swallowing** and **chewing**.

Medical and physical concerns linked to SETD5-related syndrome

Ears and hearing

Ears tend to be **large and low set** with long, fleshy lobes.

More than one-half of people who have the syndrome have **skeletal changes, including a curved spine**, which may require treatment.

Joints and spine

Four out of seven had skeletal changes, including a sideways curved spine, also called **scoliosis**, an outwardly curved spine, also called **kyphosis**, and an inwardly curved spine, also called **lordosis**.

Two out of seven had **changes in the length of the legs**.

Birth defects

Two our of seven people had **heart defects** at birth.

Four out of seven people had either a **groin hernia** or a misplacement of the opening of the urethra, also called **hypospadias**.

SETD5 Gene Mutation/Deletion/Duplication Patient And Family Support Group

www.facebook.com/groups/setd5families

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 SETD5**
  www.simonssearchlight.org/research/what-we-study/setd5
- **Simons Searchlight SETD5 Facebook community**
  www.facebook.com/groups/SETD5

Sources and References

The content in this guide comes from published studies about SETD5-related syndrome. Below you can find details about each study, as well as links to summaries or, in some cases, the full article.

- Grozeva D. *et al. American Journal of Human Genetics*, **94**, 618-624, (2014). De novo loss-of-function mutations in SETD5, encoding a methyltransferase in a 3p25 microdeletion syndrome critical region, cause intellectual disability
  www.ncbi.nlm.nih.gov/pubmed/24680889

- Powis Z. *et al. Clinical Genetics*, **93**, 752-761, (2018). Expansion and further delineation of the SETD5 phenotype leading to global developmental delay, variable dysmorphic features, and reduced penetrance
  www.ncbi.nlm.nih.gov/pubmed/28881385

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