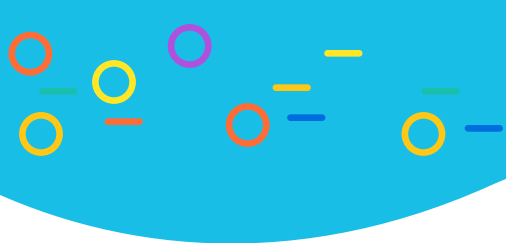




## SOX5-related syndrome





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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 SOX5-related syndrome.





## What is SOX5-related syndrome?

SOX5-related syndrome happens when there are changes to the SOX5 gene. These changes can keep the gene from working as it should.

### Key role

The SOX5 gene plays a key role in brain development.

### Symptoms

Because the SOX5 gene is important in the development and function of brain cells, many people who have SOX5-related syndrome have:

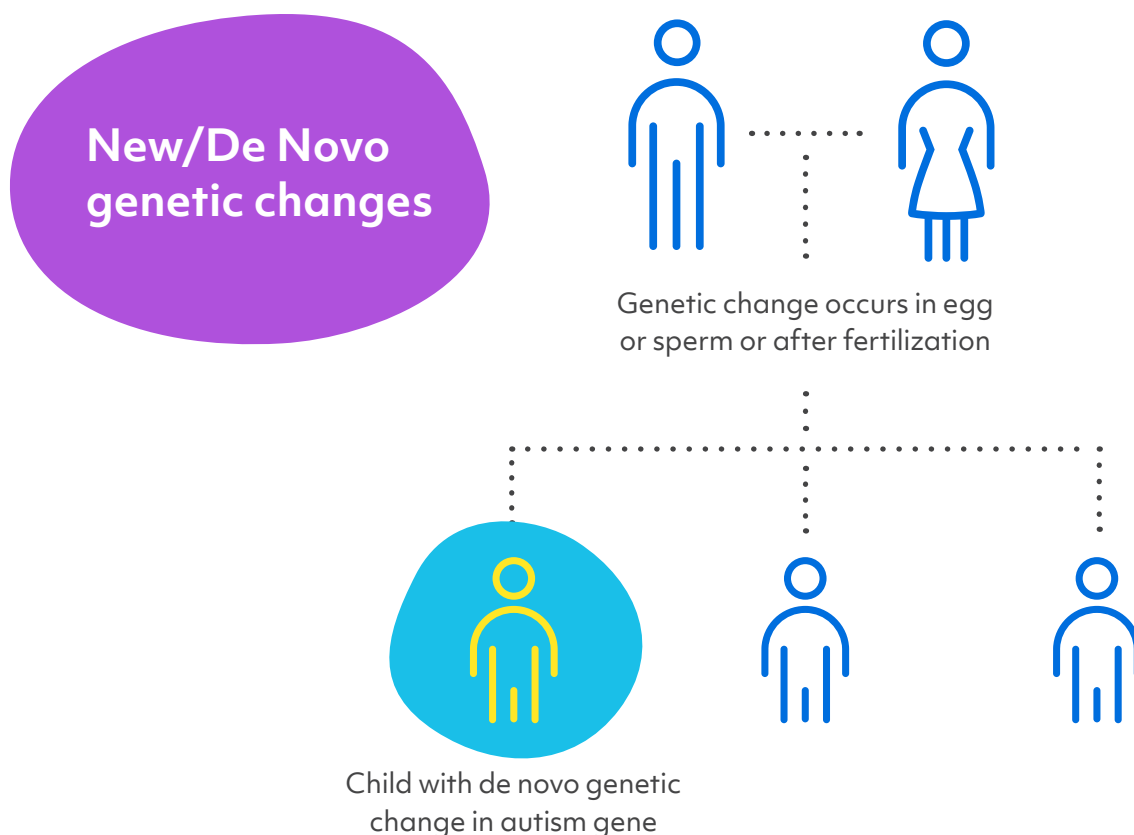
- Speech delay
- Behavior issues
- Low muscle tone
- Motor delay
- Developmental delay
- Vision issues

Our genes are arranged in long threads called chromosomes. The SOX5 gene is located on chromosome 12. Some people are missing a part of DNA on chromosome 12 that includes the SOX5 gene. This is called Lamb-Shaffer syndrome. Others have a small change within the SOX5 gene itself. These two groups have overlapping symptoms.

## What causes SOX5-related syndrome?

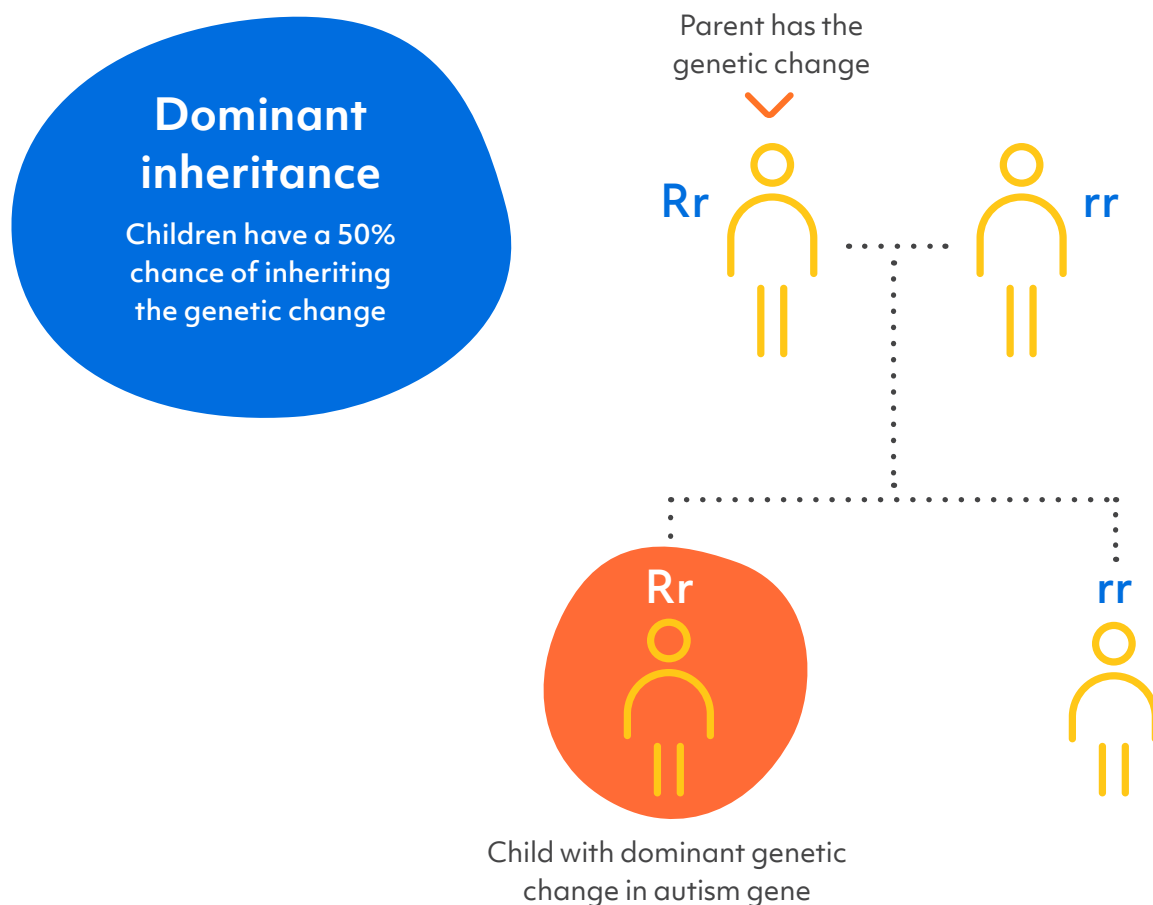
Our genes contain the instructions, or code, that tell our cells how to grow, develop, and work. Every child gets two copies of the SOX5 gene: one copy from their mother, from the egg, and one copy from their father, from the sperm. In most cases, parents pass on exact copies of the gene to their child. 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 SOX5 plays a key role in development, de novo changes in this gene can have a meaningful effect.

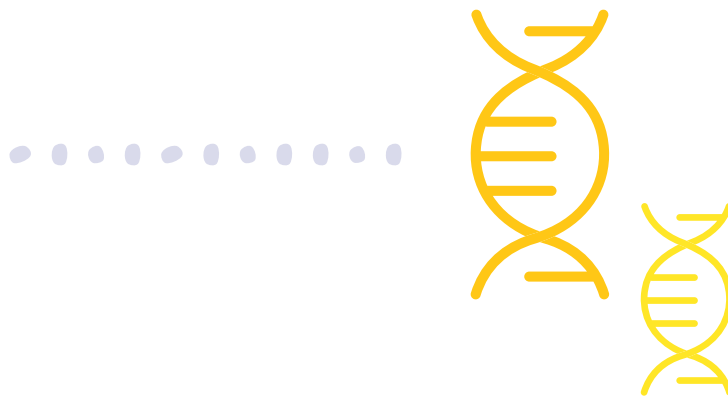
Research shows that SOX5-related syndrome is often the result of a de novo change in SOX5. Many parents who have had their genes tested do not have the SOX5 gene change found in their child who has the syndrome. In some cases, SOX5-related syndrome happens because the gene change was passed down from a parent. This is called dominant inheritance.




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## Why does my child have a change in the SOX5 gene?

No parent causes their child's SOX5-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.





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## What are the chances that other family members or future children will have SOX5-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 SOX5-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 SOX5-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 SOX5-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 SOX5-related syndrome is 50 percent.

For a person who has SOX5-related syndrome, the risk of having a child who has the syndrome is about 50 percent.

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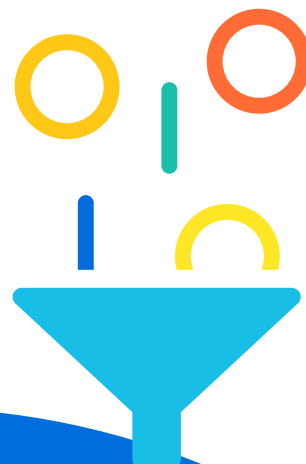
## How many people have SOX5-related syndrome?

As of 2019, fewer than 150 people in the world with changes in the SOX5 gene had been described in the medical literature. The first case of SOX5-related syndrome was described in 2012. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

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## Do people who have SOX5-related syndrome look different?

Some people who have SOX5-related syndrome have a large forehead.





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## How is SOX5-related syndrome treated?

Scientists and doctors have only just begun to study SOX5-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 SOX5-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](http://www.epilepsy.com/learn/types-seizures).

SOX5-related syndrome is very rare. Doctors and scientists have just recently begun to study it. The following information is based on published articles describing around 25 people who have SOX5-related syndrome.

This section includes a summary of information from major published articles describing 8 to 14 people who have SOX5-related syndrome. It highlights how many people have different symptoms. To learn more about the articles, see the [Sources and references](#) section of this guide.

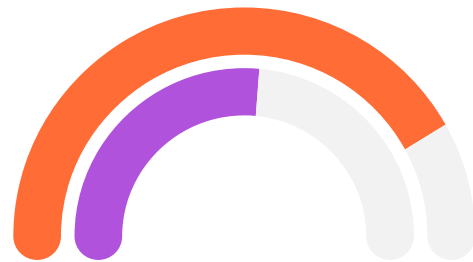
## Behavior and development concerns linked to SOX5-related syndrome

### Speech

Almost everyone who had SOX5-related syndrome had **speech delay**.

### Behavior

About one-half had behavior issues, including **aggressive behavior**, **attention deficit hyperactivity disorder**, also called ADHD, and **autism**.



8 out of 9 had speech delay

5 out of 9 had behavior issues, including autism



### Learning

Many people had some level of intellectual disability, ranging from mild to severe.

1 out of 14 No intellectual disability

5 out of 14 Mild intellectual disability

4 out of 14 Moderate to severe intellectual disability

4 out of 14 Level of intellectual disability unknown

# Medical and physical concerns linked to SOX5-related syndrome

## Eyes and eyesight

Two-thirds of people who had SOX5-related syndrome had crossed eyes.



**6 out of 9**  
had crossed eyes

## Muscle tone

One-half had low muscle tone.



**4 out of 8**  
had low muscle tone

## Brain

About one-fifth had seizures.



**2 out of 9**  
had seizures



**Where can I  
find support  
and resources?**

[www.lambshaffer.org](http://www.lambshaffer.org)

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**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](http://www.simonssearchlight.org) and click “Join Us Today”.

- **Learn more about Simons Searchlight**  
[www.simonssearchlight.org/frequently-asked-questions](http://www.simonssearchlight.org/frequently-asked-questions)
- **Simons Searchlight webpage with more information on SOX5**  
[www.simonssearchlight.org/research/what-we-study/sox5](http://www.simonssearchlight.org/research/what-we-study/sox5)
- **Simons Searchlight SOX5 Facebook community**  
[www.facebook.com/groups/549794785765854](https://www.facebook.com/groups/549794785765854)

## Sources and References

The content in this guide comes from published studies about SOX5-related syndrome. Below you can find details about each study, as well as links to summaries or, in some cases, the full article.

- Lamb AN. *et al. Human Mutation*, **33**, 728-740, (2012). Haploinsufficiency of SOX5 at 12p12.1 is associated with developmental delays with prominent language delay, behavior problems, and mild dysmorphic features  
[www.ncbi.nlm.nih.gov/pmc/articles/PMC3618980](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3618980)
- Nesbitt A. *et al. American Journal of Medical Genetics Part A*, **167a**, 2548-2554, (2015). Exome sequencing expands the mechanism of SOX5-associated intellectual disability: A case presentation with review of sox-related disorders  
[www.ncbi.nlm.nih.gov/pubmed/26111154](http://www.ncbi.nlm.nih.gov/pubmed/26111154)



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