IQSEC2-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 IQSEC2-related syndrome.
What is IQSEC2-related syndrome?

IQSEC2-related syndrome happens when there are changes to the IQSEC2 gene. These changes can keep the gene from working as it should.

**Key role**
The IQSEC2 gene plays a key role in brain cell growth and communication between brain cells.

**Symptoms**
Because the IQSEC2 gene is important in the development and function of brain cells, many people who have IQSEC2-related syndrome have:

- Intellectual disability
- Seizures
- Autism
What causes IQSEC2-related syndrome?

Our genes contain the instructions, or code, that tell our cells how to grow, develop, and work. Genes are arranged in structures in our cells called chromosomes. Chromosomes and genes usually come in pairs, with one copy from the mother, from the egg, and one copy from the father, from the sperm.

We each have 23 pairs of chromosomes. One pair, called the X and Y chromosomes, differs between biological males and biological females. Biological females have two copies of the X chromosome and all its genes, one from their mother and one from their father. Biological males have one copy of the X chromosome and all its genes, from their mother, and one copy of the Y chromosome and its genes, from their father.

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.

The IQSEC2 gene is located on the X chromosome, so changes in this gene can affect biological males and biological females in different ways. Biological males who have changes in this gene will likely have IQSEC2-related syndrome. Biological females who have changes in this gene may or may not have symptoms of IQSEC2-related syndrome.

Biological females who have one working copy of the gene and one non-working copy and do not have symptoms are considered to be ‘carriers’. This means that they may not have signs or symptoms of the syndrome, but they can pass it along to their children.
In some cases, IQSEC2-related syndrome is inherited. In other cases, it results from a random change in the IQSEC2 gene in the sperm or egg during development. 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. Biological females who inherit the IQSEC2 gene change tend to have milder symptoms than those who have a de novo 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 IQSEC2 plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that IQSEC2-related syndrome is often the result of a de novo change in IQSEC2. Many parents who have had their genes tested do not have the IQSEC2 gene change found in their child who has the syndrome. In some cases, IQSEC2-related syndrome happens because the gene change was passed down from a parent.
Why does my child or I have a change in the IQSEC2 gene?

No parent causes their child’s IQSEC2-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 IQSEC2-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 IQSEC2-related syndrome depends on the genes of both birth parents.

- Biological females who have changes in the IQSEC2 gene and are pregnant with a daughter have a 50 percent chance of passing on the gene change and a 50 percent chance of passing on the working copy of the gene. If they are pregnant with a son, the child has a 50 percent chance of inheriting the gene change and the syndrome.

For a symptom-free sibling, a brother or sister, of someone who has IQSEC2-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 IQSEC2-related syndrome.

- If the mother has the same gene change found in her 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 son who has IQSEC2-related syndrome is 50 percent.

For a person who has IQSEC2-related syndrome, the risk of having a child who has the syndrome is about 50 percent.
How many people have IQSEC2-related syndrome?

As of 2020, more than 130 people in the world with changes in the IQSEC2 gene had been described in the medical literature. The first case of IQSEC2-related syndrome was described in 2008. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

Do people who have IQSEC2-related syndrome look different?

People who have IQSEC2-related syndrome may look different. Appearance can vary and can include some but not all of these features:

- Small head
- Changes in head shape
How is IQSEC2-related syndrome treated?

Scientists and doctors have only just begun to study IQSEC2-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 IQSEC2-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.
IQSEC2-related syndrome is very rare. Doctors and scientists have just recently begun to study it. This section includes a summary of information from major published articles describing more than 130 people who have IQSEC2-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.

Symptoms of IQSEC2-related syndrome vary based on sex and whether the gene change is inherited or new.

**In males with inherited IQSEC2 changes**
- 30% have seizures
- 28% have autism or features of autism
- 20% have speech issues

**In males with new, or de novo, IQSEC2 changes**
- 90% have seizures
- 87% have speech issues
- 34% have autism or features of autism
In females with inherited IQSEC2 changes

- 27% have seizures
- 22% have speech issues
- 9% have autism or features of autism

In females with new, or de novo, IQSEC2 changes

- 72% have seizures
- 66% have speech issues
- 36% have autism or features of autism
Where can I find support and resources?

IQSEC2 Mutation  
www.facebook.com/groups/iqsec2mutation

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 IQSEC2  
  www.simonssearchlight.org/research/what-we-study/iqsec2

- Simons Searchlight IQSEC2 Facebook community  
  www.facebook.com/groups/741231356324192
Sources and References

The content in this guide comes from published studies about IQSEC2-related syndrome. Below you can find details about each study, as well as links to summaries or, in some cases, the full article.


  www.mdpi.com/1422-0067/20/12/3038/htm

  www.pubmed.ncbi.nlm.nih.gov/30328660