What causes SETD5 syndrome?

When children are conceived their parents' genetic material is copied in the egg and sperm that makes a new child. The biological copying method is not perfect and occasionally random, rare changes occur in the genetic code of children that are not seen in the DNA of their parents. SETD5 syndrome occurs when one of these random, rare changes affects the *SETD5* gene on chromosome 3. These types of change happen naturally in all species - humans, plants and animals - and are not due to your lifestyle or anything you did.
In most families the DNA change in *SETD5* occurs out of the blue (de novo). In a minority of families, one parent may have the same genetic change as their child, but this is very rare.

Can it happen again?

The possibility of having another child affected by a rare gene disorder depends on the genetic code of the parents. For SETD5 syndrome where parents do not carry the same *SETD5* change as their child, the chances of having another child are little higher than for anyone else in the population. If the genetic analysis of the parents of a child with SETD5 syndrome shows that they carry the same change in the *SETD5* gene, the chances of it happening again are much higher. Each family situation is different and a clinical geneticist or genetic counsellor can give you specific advice for your family.

How common is SETD5 syndrome?

SETD5 syndrome is a rare condition and was only identified for the first time in 2014. The first study identified changes (mutations) in the *SETD5* gene as one of the commoner causes of intellectual disability with autism and behavioural problems. In a recent study of 1000 children with moderate to severe intellectual disability a change in the *SETD5* gene was found in 6 individuals (0.7%).

Families say ...

"Our daughter made us see the world through different eyes. She is a gift to us." - 11 years

"Our son is very fond of electronics, seems to know a lot and gets excited to help others. He loves all special Olympics activities he participates in. Always excited to go and be part of the group. Always keeps us on our toes, very loving and loves to talk. One of the most special boys we have ever known." - 15 years

Inform Network Support

Understanding chromosome disorders Unique

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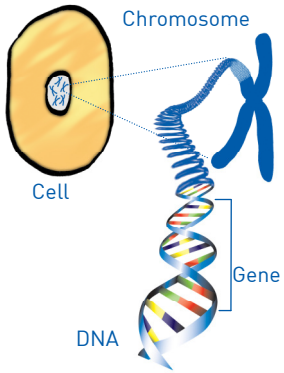
SETD5 and 3p25 deletion syndrome

rarechromo.org

What is SETD5 syndrome?

SETD5 syndrome was first identified in 2014 so what we know about it is still a little limited. However the *SETD5* gene is on the band known as p25 on chromosome 3, and is one of the genes that is missing in the 3p25 microdeletion syndrome. When you study children with 3p25 microdeletion syndrome and those with changes in the *SETD5* gene, many of the features of the children are similar. So it is now thought that the key features of 3p25 microdeletion syndrome are due to absence of *SETD5*.



Frequent features

The most common features in children with SETD5 syndrome are also found in many other genetic conditions that cause learning problems so children may not be easily recognized without genetic investigations.

The first three features are found in almost all children with SETD5 syndrome. The other features may or may not be present.

- Intellectual disability or slow learning or developmental delay
- Language delay and /or stammer
- Ritualised behaviour and /or autism
- Small head
- Poor feeding and slow growth
- Prominent eyebrows that meet or nearly meet over the midline (synophrys)
- Heart condition
- Hearing problems
- Ptosis (an inability to fully raise the upper eyelid)
- Curvature of the spine

Development

Growth

Almost all babies are small for dates and some are also born one or two months early. While many babies remain small and are short as children, some babies grow well and are of average height.

Feeding

Parents are likely to need support as feeding difficulties can be considerable at first. Typically, babies suck weakly and some need high energy milks to encourage weight gain. Many babies readily bring feeds back (gastro oesophageal reflux) and need careful positioning for feeding and while sleeping. Some babies are helped by medicines for reflux. Occasionally surgery is helpful to improve the effectiveness of the valve between the stomach and the food pipe (a fundoplication). Some babies need to be fed temporarily through a tube direct into the stomach (gastrostomy). Older children typically have chewing difficulties.

Sitting, moving, walking

Babies are usually quite late to become mobile. With the help of standing and walking aids, some children learn to walk and eventually to swim, run and dance but for others this is not possible.

Speech

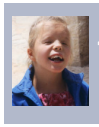
Children typically experience delay in communicating and learning to use words. The eventual range of achievement is very broad, from a few children who have a large vocabulary to others who use signing, gestures and vocal noises to express their needs.

Learning difficulties

Most children need very considerable support with learning. A few learn to write and read but non-academic skills will be more important in their lives.

Behaviour

As a group, children appear to have a happy disposition. Some families have noticed autistic tendencies in young children and hyperactivity at school age. This can be controlled with medication in some, but others may continue to have quite challenging behaviour requiring specialist advice and support.



"Happy, non-verbal, very social. Very good social reading and loves people." 13 years

Medical concerns

These disorders have been found in a group of babies and children with a *SETD5* deletion. They are not found in all babies and your child may not be affected.

Heart conditions

Around one baby in three is born with a heart condition, typically an atrioventricular septal defect (AVSD). This is a group of defects (also known as endocardial cushion defects) affecting the development of the walls between the two upper and the two lower chambers of the heart (the atria and ventricles) and the valves that control the blood flow between them. Many babies will need open heart surgery but Unique's experience is that they thrive afterwards.

Seizures

Quite a few babies will have seizures, although these may be rare or occasional.

Ptosis

Some babies will not be able to open their upper eyelids fully on one side or both. Very mild ptosis does not need treatment but if vision is obscured, surgery can be performed to hold the eyelid up.

Eyesight

In Unique's experience, many babies have eyesight problems. However, the great majority can be corrected with surgery (such as strabismus, a squint) or with glasses (such as short sight).

Hearing

Hearing impairment, either temporary or permanent, affects many children.

Extra fingers and/ or toes

These are fairly common but can be removed and do not usually cause any long-term problems.

Genitals

Some boys have hypospadias, where the hole usually at the end of the penis is on the underside, and some are born with undescended testicles. Both conditions may need no treatment but if they do, they can usually be corrected with straightforward surgery.