Why did this happen?

To answer this question, the parents' and affected child's chromosomes need to be tested. What is certain is that, as a father or mother, there is nothing you did to cause the duplication and nothing you could have done which would have prevented it. Chromosome rearrangements affect children from all parts of the world and from all types of background. No environmental, dietary or lifestyle factors are known to cause 5q35 duplications. There is nothing that either parent did before, during or after pregnancy that caused the duplication.

5q35 duplications are known to be either inherited from a parent or to occur *de novo* (dn), which means the duplication has occurred as a new event in the child. In the majority of cases, *Unique* members' 5q35 duplications were *de novo*, but there have been some cases where the duplication was inherited from the mother or father. Based on our current knowledge of 5q35 duplications, roughly equal numbers of females and males are affected.

Can it happen again?

The possibility of having another pregnancy with a 5q35 duplication depends on the parents' chromosomes.

Where both parents have "normal" chromosomes, it is very unlikely that another child will be born with a 5q35 duplication or any other chromosome disorder. Very rarely (less than 1%), both parents have normal chromosomes by a blood test, but a few of their egg or sperm cells carry a chromosomal change. This is called germline (gonadal) mosaicism and it means that parents whose chromosomes appear "normal" when their blood is tested can have more than one child with the duplication.

In families where the 5q35 duplication has been inherited from a parent, the possibility of having another child - either a girl or a boy - with the 5q35 duplication rises to 50% (1 in 2) in each pregnancy.

However, the effect of the duplication on the child's development, health and behaviour cannot be reliably predicted. Your genetics centre should be able to offer counselling before you have another pregnancy.

Management options might include:

- Feeding management if necessary e.g. tube feeding as a baby
- Follow up by a developmental paediatrician
- Physiotherapy/occupational therapy/speech and language therapy/assessment for behavioural concerns, as needed
- Eye examination e.g. check if glasses are needed
- An assessment to identify the most appropriate schooling
- Clinical genetics referral (to help interpret genetic test results, advice about future pregnancy etc.)

Families say ...

" Don't worry about not knowing what the future holds. Our geneticist told us not to let her diagnosis overwhelm us but to look at our daughter and SEE her. As time goes on, I don't see her diagnosis at all, but only her. She is not a medical condition, she is herself and we couldn't love her more. "

Inform Network Support

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Chromosome 5 duplication - https://www.facebook.com/groups/1548614302021901/
Reversed Sotos Syndrome - https://www.facebook.com/groups/313154342038158/

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Rare Chromosome Disorder Support Group
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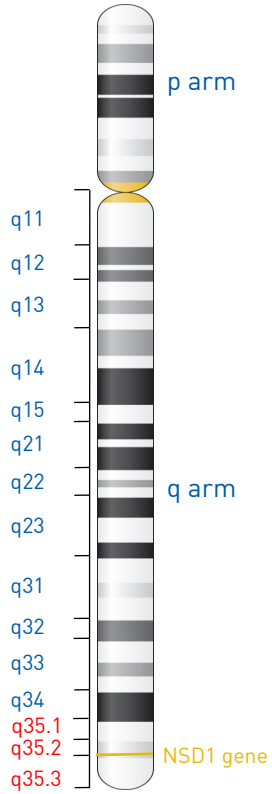
Understanding Chromosome & Gene Disorders

5q35 duplications

rarechromo.org

What are 5q35 duplications?

A chromosome 5q35 duplication is a rare genetic condition in which there is an extra copy of part of the genetic material that makes up one of the body's 46 chromosomes at band q35 on the long arm of chromosome 5 (marked in red).



For healthy development, chromosomes should contain just the right amount of genetic material (DNA) – not too much and not too little. As with other chromosome disorders, having an extra piece of genetic material may increase the risk of birth defects, affect the development and intellectual abilities of a child and be associated with a range of other individual features, to a varying degree.

It is important to remember that the outcome of having a 5q35 duplication is extremely variable and depends on a number of factors, including what and how much genetic material is duplicated.

What causes 5q35 duplications

At fertilisation, a sperm and egg cell join to form a single cell. Changes to the structure of chromosomes often occur during the cell divisions that lead to the creation of egg or sperm cells. The long (q) arm of chromosome 5 contains areas where the DNA of the chromosome is repeated at close intervals meaning "mistakes" leading to parts of a chromosome(s) being lost, duplicated and/or becoming rearranged are more likely to occur during the production of the sperm or egg cell.

The *NSD1* gene is located within this area and having extra copies of this gene due to the duplication is thought to play a crucial role in some of the features associated with 5q35 duplications (see blue box).

Most common features:

- Growth delay/a short stature (duplications including *NSD1* gene)
- A small head (microcephaly) (duplications including *NSD1* gene) or unusual head shape
- Some degree of developmental delay
- Some degree of intellectual disability/learning difficulty

Other possible features include:

- Feeding difficulties
- Speech and language delay
- Eczema
- Behavioural concerns
- Hypermobile joints
- Low muscle tone (hypotonia)
- Problems with vision/structural eye anomalies

Medical concerns

Eczema

Chronic eczema that causes the skin to become red, itchy and inflamed is a recognised feature of distal 5q duplications. You can speak with your doctor about how to relieve the symptoms of eczema.

Eyes & vision

Problems with vision and/or structural eye anomalies have been reported for about two-thirds of *Unique* members with a 5q35 duplication.

Other conditions

Very occasionally, other medical conditions such as hernias, seizures, heart conditions, brain anomalies and anomalies of the hands and feet, have been reported.

The *NSD1* gene

Location: chromosome 5q35.3 (176,560,026-176,727,216 (GRCh37/hg19))

The *NSD1* gene codes for a protein called nuclear receptor SET domain-containing protein 1. This protein regulates the expression of another gene called *APC2*, which participates in brain development, as well as a number of other genes required for the normal development of the heart, skeleton and kidneys. The presence of an extra copy (duplication) of the *NSD1* gene is believed to be responsible for many of the features associated with 5q35 duplications.

Development

Growth

Most babies had a birth weight at the lower end of the typical range and growth delay was common among children with a duplication involving *NSD1*, ranging from mild to severe. Many *Unique* parents described their children as "short and thin".

Gross and fine motor skills

Many babies and children were late to achieve their 'milestones' of sitting and walking, although the delay was often mild. Among *Unique* children, sitting was typically achieved between 8 and 11 months and walking independently between 12 months and 3 years. A delay in the development of hand use and hand-eye coordination in most children is common. Loose, hypermobile joints and low muscle tone affected some *Unique* members, which can have an impact on their physical development.

Learning

The range of learning ability is very broad, but children with a 5q35 duplication often need support with their learning. Many *Unique* children attended a mainstream school, often with 1:1 help in the classroom or other provisions. A few transferred to a special educational needs setting at a later stage in their education; others attended a special needs school throughout.

Behaviour

Alongside many positive personality traits, many *Unique* children at times demonstrated some kind of challenging behavior e.g. sudden mood swings, difficulty with social interactions and being over-emotional. Only a minority of children displayed aggressive behavior. Some have been diagnosed with/demonstrated traits associated with specific social, emotional and anxiety disorders such as autism spectrum (ASD) or attention deficit hyperactivity (ADHD) disorders.

Speech and language

While roughly half of Unique children with a 5q35 duplication including the *NSD1* gene had speech and language that was completely fluent and/or age-appropriate, others experienced speech delay, ranging from difficulties with articulation to communication without words.