Why did this happen?

In most families, the genetic change affecting *MED13L* happens out of the blue (*de novo*). We have two copies of each gene, as we inherit one from our mother and one from our father. When children are conceived, the genetic material of the parents is copied in the egg and sperm that makes a new child. The biological copying machine is not perfect and occasionally random, rare changes (mutations) occur in the genetic code of children that are not seen in the DNA of their parents. This happens naturally in plants and animals and is not due to your lifestyle or anything you did.

Some affected individuals have a deletion on chromosome 12 that involves this gene so only one copy is present instead of two.

Inheriting MED13L syndrome from a parent is unusual, but there have been cases of a parent passing on an extra copy of the gene to their child. Gaining an extra copy of all or part of the *MED13L* gene appears to cause a milder form of the condition. There are also a few reports of families where more than one child has been diagnosed with MED13L syndrome, and both parents are unaffected. This is due to a phenomenon called gonadal mosaicism. Although both parents do not have MED13L syndrome, one parent carried a copy of the altered *MED13L* gene in a proportion of their eggs or sperm. This is what leads to a sibling being born with the same condition. The chances of this happening are low overall, around 1-2%.

Can it happen again?

The probability of having another child affected by a rare gene disorder depends on the genetic code of the parents. For *MED13L* defects where parents do not carry the mutation, the chance of having another affected child is very low. If genetic analyses of the parents show that one of them carries the same variant, the chance of it happening again is much higher. Each family situation is different and a clinical geneticist can give you specific advice for your family.

Families say ...

“ My son is an active and adventurous little boy. His respiratory problem is the main hurdle that makes it difficult for him to do what he wants to do. He is at a mainstream school with support and understands quicker than some of the other children in his class, but he struggles to get the words out. ”

“ He is very sociable and has lots of friends. ”

Inform Network Support

Rare Chromosome Disorder Support Group,
The Stables, Station Road West, Oxted, Surrey RH8 9EE, UK
Tel: +44(0)1883 723356
info@rarechromo.org | www.rarechromo.org

Websites, Facebook groups and other links

https://www.facebook.com/pg/MED13L-SYNDROME-1677270665898160/about/

https://www.simonsvipconnect.org/what-we-study/single-genes.html?id=557

Not specific for MED13L, but MED13L has its own page on this website along with patient stories.

https://www.facebook.com/groups/MED13L/?ref=br_rs

This guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. Unique does its best to keep abreast of changing information and to review its published guides as needed. This guide was written by Dr Rhoda Akilapa, North West Thames Regional Genetics Service, London NW University Healthcare NHS Trust, UK.

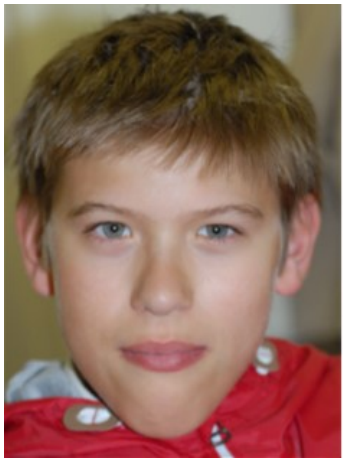
2019 Version 1 (CA)

Rare Chromosome Disorder Support Group
Registered in England and Wales

Charity Number 1110661
Company Number 5460413

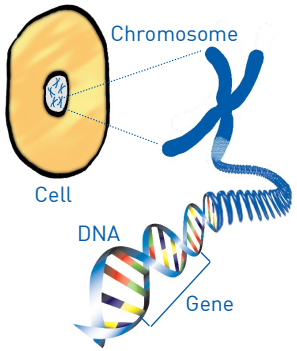
Understanding Chromosome & Gene Disorders

MED13L syndrome



rarechromo.org

What is MED13L syndrome?



MED13L syndrome is an increasingly recognised disorder associated with developmental delay; a speech delay, which is often significant; and distinctive facial features. Other features can include heart problems, feeding difficulties and additional medical concerns.

What causes MED13L syndrome?

The *MED13L* gene is found on the long arm of chromosome 12, in a band known as 12q24.21. It was first discovered in children born with heart defects and was subsequently recognised to be important in the development of the heart and the brain. Over time, it has become clear that heart defects are present in only a proportion of children with MED13L syndrome.

Most people with MED13L syndrome have:

- Developmental delay with significant speech and language delay
- Distinctive facial features including arched eyebrows, synophrys (eyebrows meeting in the middle) and macroglossia (large tongue)
- Feeding difficulties in infancy

Less common feature include:

- Heart defects
- A tendency to be overweight
- Small head size (microcephaly)
- Seizures
- Brain abnormalities on an MRI scan
- Some form of orthopaedic problem, most commonly affecting the lower limbs

Medical concerns

Heart problems

Of the first 15 children identified with this condition through the Deciphering Developmental Disorders (DDD) project, 4/15 were born with a structural heart problem. These included ASD (atrial septal defect - a hole between the top two chambers of the heart); VSD (ventricular septal defect - a hole between the bottom two chambers of the heart); pulmonary stenosis (narrowing of the vessel carrying blood from the heart to the lungs); PDA (persistent ductus arteriosus - failure of closure of the tube that carries blood between the aorta and the pulmonary artery during the foetal period); and Tetralogy of Fallot. Other heart anomalies reported in the literature include transposition of the great arteries and total anomalous pulmonary venous drainage.

Brain abnormalities

Of the first 10 children known to have had an MRI brain scan, six were found to have an abnormal result. The changes seen varied but included focal cortical dysplasia; agenesis of the corpus callosum and communicating hydrocephalus.

Orthopaedic problems

From the preliminary data, just under half of those affected had some form of orthopaedic problem, most commonly affecting the feet. The problems reported include talipes (abnormal positioning of the feet at birth); metatarsus adductus (where the front half of the foot turns inwards); prominent big toes; and a shortened foot. Under-development of the hip joint has also been reported (developmental dyplasia of the hip).

Visual impairment

Almost one third of children (27%) had some form of eye or visual anomaly. These included: Duane anomaly (misalignment of the eyes that varies with gaze direction); hyperopic astigmatism (an error of the cornea or lens causes the rays of light to focus behind the retina affecting vision); hypermetropia (long-sightedness); and retinal dystrophy (a range of chronic and progressive eye conditions affecting vision).

Seizures

Around one quarter (27%) of affected children developed seizures. They usually respond well to therapy.

Other less common medical conditions

Less common conditions include scoliosis (a sideways curvature of the spine); hearing loss (sensorneural as well as conductive); inguinal hernias; cryptorchidism (undescended testes, which can often be corrected by surgery) and micropenis (an unusually small penis). One child had severe portal hypertension.

Development

Physical development

Some degree of developmental delay is to be expected. While some children took their first steps by 12 months other were still not walking at four years.

Speech and language

A significant speech and language delay is one of the major concerns associated with MED13L syndrome. While some children said their first words after their 5th birthday, a significant proportion of children were still non-verbal by 9 years of age. As more data becomes available the progression of speech in older people with MED13L syndrome will become clearer.

Behaviour

In general, children with MED13L syndrome find enjoyment in many activities that unaffected children enjoy, such as playing with toys and looking at books. Some children appear to have a greater understanding of language, despite struggling with expressive speech. Significant behavioural concerns do not appear to be associated with MED13L syndrome, although a proportion of children have been diagnosed with autistic spectrum disorder.