FACTS ABOUT HEALTH CONDITIONS
CAUSED BY CHANGES IN THE *MED13L* GENE

This fact sheet contains information about the possible impact of a change (variant) in the *MED13L* gene on your child and family. You can talk about the information in this fact sheet with your paediatrician or GP (family doctor). The links in the fact sheet may help you move forward with family life beyond receiving this rare diagnosis.

This fact sheet relates to health conditions that are due to small variants in the genetic code of the *MED13L* gene. These changes were identified by a genomic (DNA) test. It does not provide information about conditions caused by chromosome deletions or duplications that involve the *MED13L* gene.

Key points

- A change in the *MED13L* gene will usually cause developmental delay/ intellectual disability
- Changes (variants) in the *MED13L* gene that cause health problems are usually a new *('de novo')* change in a child. This means that future children are unlikely to be affected, although this may occur in rare cases. Genetic counselling before any further pregnancies is recommended
- There are not yet any specific treatments, however, supportive management is available
- You and your family are not alone in adjusting to life with the diagnosis of a change in the *MED13L* gene. Support is available from a number of different organisations and services.

When a rare condition has been diagnosed

For some families, receiving a genetic diagnosis is a relief. Others may feel overwhelmed and sad. It is very common to have a mixture of thoughts and feelings about the news, and your hopes and expectations for the future may shift and change over time.

While experiences may be shared, individuals and families can respond in different ways and have different information and support needs. Many parents describe an ongoing process of adjusting to a different focus and finding ways to celebrate their child's gains made in their own way and time. It is very important to remember that the diagnosis is only one of many things that make your child unique.

About the *MED13L* gene

Genes contain instructions that tell our body how to grow, develop and function. *MED13L* (said as med-thirteen-el) is a **gene** that plays a key role in reading and interpreting (transcribing) other genes. Changes (**variants**) in the *MED13L* gene can affect health and development by causing problems with how proteins are made, especially in the brain, muscles and heart.

The *MED13L* gene is found on chromosome 12. Usually *MED13L*-related conditions are caused by a single variant in the gene, which means the message is not read or received properly.

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In most individuals with *MED13L*-related conditions, the variant in the gene occurred when the baby was conceived (a new or *'de novo'* change), and is not seen in the parents. Based on information currently available, it would be rare (1–2% chance [1 or 2 in 100]) for the altered gene to be passed to the child from a parent.

MED13L-related conditions are **genetic conditions**. This means that the condition was not caused by anything the mother or father did before the baby was conceived, during pregnancy or birth, or after the baby was born. *MED13L*-related conditions are rare, affecting around 2 out of every 100,000 people.

What could a change in the *MED13L* gene mean for my child?

A variant in the *MED13L* gene can affect children in different ways. Some are more severely affected than others. There may be a range of signs and symptoms even in children with the same genetic variant.

Most affected children have developmental delay/intellectual disability in the moderate range. The most common problem is language difficulties, with many children speaking only a few words and some not speaking at all. Most children with a *MED13L*-related condition learn to walk later than other children, although most are walking by 2–3 years of age. Many children have low muscle tone (hypotonia) which affects their movement (motor skills). About one third of children have balance difficulties (ataxia) and some have problems with using their mouth and tongue to speak (dysarthria). Problems with balance may worsen with time. Around a quarter of individuals will have an autism spectrum disorder (ASD).

Around one fifth of children with *MED13L* variants have heart defects, particularly switching of the great blood vessels leaving the heart (transposition of the great arteries), hole in the wall of the heart (ventricular septal defect), narrowing of one of the large arteries (pulmonary valvular stenosis), or holes (persistent connections) between certain arteries and veins (these are generally mild: patent foramen ovale, patent ductus arteriosus). If your child has had a heart assessment and no defects were found, they would not be expected to develop these in the future.

Approximately one third of individuals will have problems with their eyesight, which are usually mild. Visual problems can include squint (strabismus), long sightedness (hypermetropia), short sightedness (myopia), and droopy eyelids (ptosis).

Although most individuals do not have seizures (epilepsy), seizures can occur, most often in children with a specific type of *MED13L* variant (known as a 'missense' variant).

Many children with *MED13L* variants have distinctive facial features that may be different from other people in the family e.g. broad, prominent forehead. Sometimes there may be minor differences in the hands and feet. These differences do not usually cause any problems for the child.

At this point in time, it is not possible to reverse or repair this gene variant. It is also not possible to accurately predict the level of care your child will require through to adulthood. Your child's individual needs and strengths will become more obvious over time, which will help with planning for the future.

Your child's development may be helped through early use of therapy services such as physiotherapy, and treating symptoms if/when they arise. It is likely that many different health professionals will be involved in caring for your child. Your paediatrician or GP will arrange referrals to other health professionals as needed and help with applications for service funding through the **National Disability Insurance Scheme (NDIS)**.

Good communication with the health professionals caring for your child is important to establish common goals, trust and shared responsibility. We encourage you to ask questions and express your concerns as the expert carer for your child.

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Management recommendations

As many health or developmental problems are not immediately obvious, your child will need to be checked by their paediatrician at diagnosis and then seen each year, or more often if needed, depending on their symptoms. The list below includes many of the common problems, but others may arise. If you have any concerns about your child's health, please speak with your family doctor (GP) or paediatrician.

Possible health problems (% of children affected)	Management
Developmental delay/intellectual disability (>90%), including low muscle tone (hypotonia) (70%) and speech delay (most)	• Early intervention, including speech therapy, occupational therapy and physiotherapy • Consider a formal developmental assessment before starting school or by school counsellor for school age children • At least yearly checks by GP/paediatrician • Special education programs
Difficulty/delayed walking (most), balance difficulties (ataxia) (30%)	• Physiotherapy and occupational therapy, as well as assistance with using medical devices such as wheelchairs, if needed
Autism spectrum disorder (25%)	• Diagnosis and management by paediatrician as appropriate
Abnormal heart structure (cardiac malformations) (20%)	• Consultation with a cardiologist including a baseline ultrasound (echocardiogram) of the heart. If no abnormalities are found, these will not develop later
Brain structural malformations/ developmental differences of brain (45%)	• Brain MRI if clinically indicated. Most structural problems do not require any specific treatment
Seizures (epilepsy) (5%)	• Standard investigations and treatments, including EEG and anti-epileptic medications • Consultation with paediatric neurologist if seizures are difficult to control
Visual (eyesight) problems (30%), including droopy eyelids (ptosis) (rare)	• Review by ophthalmologist for assessment of vision and ptosis • A squint (strabismus) may require patching or glasses • Long or near sightedness (refractive error) may require glasses
Talipes (clubfoot) (<10%)	• This is not a common problem, but if it occurs, physiotherapy/use of splints may be needed • May require a review by an orthopaedic specialist if severe

Resources, support and connecting with others

You may find it helpful to connect with other people who have personal experience of day-to-day life with a child who has a *MED13L*-related condition. You can make these connections through:

- Social media (e.g. closed Facebook groups)
- Umbrella groups (e.g. **Genetic Alliance Australia** and **Rare Voices Australia**)
- Condition-specific groups
- Groups for individuals with common symptoms that may have many different causes (e.g. intellectual disability, hearing loss, autism).

The **MED13L Foundation** website offers support specifically for families with a *MED13L*-related condition. You can also connect with them via their **Facebook page**.

Many organisations (e.g. **Carers NSW** and **Reframing Disability**) can also offer general advice and support in caring for a family member with long-term needs.

It is important to know that you are not alone on this journey

More information about *MED13L*-related conditions

You can find further information about *MED13L*-related conditions by following the links below.

- UNIQUE: **MED13L syndrome**
- MedlinePlus: **MED13L syndrome**
- Genetic and Rare Diseases Information Center (GARD): **MED13L haploinsufficiency syndrome**

For more information about genetic conditions and to find your local Clinical Genetics services, visit the **NSW Centre for Genetics Education**.

Family planning

Genetic conditions are sometimes passed from a parent to their child. Even if the same variant was not found in one of the parents, it is still possible to have another child with the same condition. The chance of this happening is low (about 1–2%).

If you are thinking about having more children, it is recommended that you talk with your local **Clinical Genetics service**. Some people may choose to have **genetic testing** before or during a pregnancy. Specialised health professionals such as **genetic counsellors** can advise you on your options.

You can also speak with your GP about options for **reproductive genetic carrier screening**. When planning a family, it is best to explore your options before becoming pregnant.

Research, registries and clinical trials

Some people with rare conditions are able to participate in **research**, which may be of benefit to your child. This may investigate how a particular variant causes health problems or it may be a clinical trial testing new treatments. Sharing information about your child's signs and symptoms through registries such as **FaceMatch** and **IAMRARE** can help build further knowledge about this condition.

Information about current clinical trials can be found by searching the international databases **ClinicalTrials.gov** or **EudraCT**.

To print more copies of this fact sheet and access links to the underlined topics, go to **www.genetics.edu.au** and search for 'MED13L'.

This fact sheet should not replace a consultation with a specialist healthcare professional.

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