FACTS ABOUT HEALTH CONDITIONS
CAUSED BY CHANGES IN THE *SETD5* GENE

This fact sheet contains information about the possible impact of a change (variant) in the *SETD5* 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 *SETD5* gene. These changes were identified by a genomic (DNA) test. The *SETD5* gene is located on chromosome 3, at band p25, and is one of the genes that is missing in the **3p25 deletion syndrome**. It is thought that most of the health problems that occur in the *3p25 deletion syndrome* are caused by the loss of the *SETD5* gene, and there is overlap between the two conditions. This fact sheet is not about cancers that are due to acquired variants in the *SETD5* gene (changes that occur after a person is born) or the 3p25 deletion syndrome.

Key points

- A change in the *SETD5* gene will usually cause developmental delay/ intellectual disability, delayed language and autism spectrum disorder (ASD). Other features that are present in some individuals are poor feeding, slow growth and prominent eyebrows
- Changes (variants) in the *SETD5* gene that cause health problems are nearly always new (*'de novo'*) changes in a child. Rarely, a *SETD5* variant in a child is inherited from a parent who also carries the variant
- Supportive management is available
- You and your family are not alone in adjusting to life with the diagnosis of a change in the *SETD5* gene. Support is available from a number of different organisations and services.

Other names this condition may be referred to as:

- Overlap with 3p25 deletion syndrome. This condition is not discussed in this fact sheet

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.

Content updated November 2021
NOV21/V1 NS12695
SHPN: (HETI) 241001

About the *SETD5* gene

Genes contain instructions that tell our body how to grow, develop and function. *SETD5* is a **gene** that helps to control whether many other genes in the body are 'switched on' or 'switched off'. *SETD5* can be viewed as a gene that 'fine tunes' the function of other genes in the body. Changes (**variants**) in the *SETD5* gene can alter how many parts of the body develop and function, but the role of *SETD5* is most important in the brain.

The *SETD5* gene is found on chromosome 3. Usually *SETD5*-related conditions are caused by a single spelling variation in the gene, which means the message is not read or received properly.

In nearly all individuals with *SETD5*-related conditions, the gene variant occurred when the baby was conceived (a new or *'de novo'* variant), and is not seen in the parents. Rarely, the variant is passed to the child from a parent who may be only mildly affected.

SETD5-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. *SETD5*-related conditions are rare, with fewer than 50 individuals described in the medical literature. However *SETD5*-related conditions have only been recognised since 2014, and it is likely that there are many affected individuals who have not been diagnosed.

What could a change in the *SETD5* gene mean for my child?

A change in the *SETD5* 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.

Almost all children with a change in the *SETD5* gene have developmental delay. Most children have intellectual disability, which can range from mild to severe. Delays in learning to understand and communicate are particularly common, and some children with *SETD5*-related conditions show signs of autism spectrum disorder (ASD) or hyperactivity.

Some children with a change in the *SETD5* gene have physical health problems, such as heart disease that is present from birth (congenital heart disease) and seizures (epilepsy). Children often grow at a slower rate than other children. Some children with *SETD5*-related conditions have facial differences, in particular prominent eyebrows and drooping eyelids (ptosis).

At this point in time, it is not possible to reverse or repair this gene change. 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 primary carer for your child.

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 every 6 months, or more often if needed.

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 [>50%])	• Early intervention including speech therapy, physiotherapy and occupational therapy; special education programs • At least yearly checks by paediatrician
Attention-deficit/hyperactivity disorder (ADD/ADHD) (frequency unknown)	• Diagnosis and management by paediatrician as appropriate
Autism spectrum disorder (ASD) (~30%)	• Diagnosis and management by paediatrician as appropriate
Feeding difficulties, including gastrointestinal reflux (~50%)	• Investigation for swallowing difficulties or reflux where appropriate
Curved spine (scoliosis) (~40%)	• May develop over time • Yearly review by paediatrician until the child has finished growing
Slow growth (~35%)	• At least yearly review by paediatrician
Abnormal heart structure (cardiac malformations) (~40%)	• Non-urgent consultation with a cardiologist including a baseline ultrasound (echocardiogram) of the heart
Genital differences in males (~25%)	• Physical examination by paediatrician
Seizures (epilepsy) (~25%)	• Standard investigations and treatments, including EEG and anti-epileptic medications
Visual (eyesight) problems/ loss of sight (~50%)	• Initial review by ophthalmologist for assessment of vision and squint (strabismus)
Hearing loss (~15%)	• Additional hearing assessment if there are concerns about hearing loss, as conductive hearing loss (when problems with the ear prevent sound from passing into it) may occur
Limb abnormalities including different sized legs (leg length discrepancy) and extra fingers or toes (polydactyly) (uncommon)	• Orthopaedic review and/or physiotherapy, shoe raiser

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 *SETD5*-related condition. You can make these connections through:

- Social media (e.g. closed Facebook groups: **SETD5 Simon's Searchlight Community**)
- 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).

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 *SETD5*-related conditions

You can find further information about *SETD5*-related conditions by following the links below.

- Unique: **SETD5 and 3p25 deletion syndrome**
- Simon's Searchlight: **SETD5**

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 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**.

You may like to discuss this research with your child's healthcare team.

To print more copies of this fact sheet and access links to the underlined topics, go to **www.genetics.edu.au** and search for 'SETD5'.

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