FACTS ABOUT HEALTH CONDITIONS
CAUSED BY CHANGES IN THE *ARID1B* GENE

This fact sheet contains information about the possible impact of a change (variant) in the *ARID1B* 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 *ARID1B* 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 *ARID1B* gene. This fact sheet does not relate to cancers that are due to acquired variants in the *ARID1B* gene (changes that occur after a person is born).

Key points

- The *ARID1B* gene is one of the most common genetic causes of developmental delay/intellectual disability. Changes (variants) in the *ARID1B* gene are seen in about 1 in 100 children (1%) who receive a genetic diagnosis of intellectual disability
- Children with variants in *ARID1B* may have intellectual disability that varies from mild to very severe
- Many children with changes in the *ARID1B* gene have Coffin-Siris syndrome (CSS). Symptoms of CSS include having missing or under-developed fifth fingers/toes and nails, distinctive facial features, increased body hair and low muscle tone
- Variants in the *ARID1B* gene that cause health problems may be inherited from a parent or may be a new (*'de novo'*) change in a child. This means that future children may also have this variant. Genetic counselling before any further pregnancies is recommended
- Supportive management is available
- You and your family are not alone in adjusting to life with the diagnosis of a change in the *ARID1B* gene. Support is available from a number of different organisations and services

Other names this condition may be referred to as

- Coffin-Siris syndrome (CSS)
- ARID1B–related disorder
- ARID1B intellectual disability

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.

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About the *ARID1B* gene

Genes contain instructions that tell our body how to grow, develop and function. *ARID1B* (said as 'arid-1-bee' and also known as AT-rich interaction domain-containing protein 1B) is a **gene** that makes a protein involved in controlling how cells grow. Changes (**variants**) in the *ARID1B* gene can affect many parts of the body.

The *ARID1B* gene is found on chromosome 6. Usually *ARID1B*-related conditions are caused by a single spelling variation in the gene, which means the message is not read or received properly. In most *ARID1B*-related conditions, the change occurred when the baby was conceived (a new or *'de novo'* variant), and is not seen in the parents. In some of the milder forms, the variant can be passed to the child from a parent.

Individuals with an *ARID1B*-related condition may have a number of different features, which can vary even within the same family. Whether the features of the condition are mild or more severe often depends on the particular variant and its location within the *ARID1B* gene (known as the genotype). Variants in the *ARID1B* gene are the most common genetic cause of Coffin-Siris Syndrome (CSS). Around 50–75% of CSS cases are caused by changes in *ARID1B*.

ARID1B-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. *ARID1B*-related conditions are rare. Less than 300 people worldwide are known to have an *ARID1B*-related condition.

What could a change in the *ARID1B* gene mean for my child?

A change in the *ARID1B* 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 variant.

Children with *ARID1B*-related conditions may be slower to reach their physical milestones (sitting, crawling, walking, running). They may have problems with learning and most will have problems with speaking. Many children will grow slowly, and more often are slow to grow taller rather than to put on weight. A small number of children experience seizures (epilepsy).

Some children have an increased amount of body hair and thick eyebrows. Often children have missing or underdeveloped fifth fingers or toes and nails. Many children with *ARID1B*-related conditions have similar facial features.

At this point in time, it is not possible to reverse or directly 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 at least every year or more often if needed. The list on the next page 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) (80%)	• At least yearly checks by GP/paediatrician • Early intervention, including occupational therapy and physiotherapy
Flexible joints (hyperflexibility) (60%)	• Physiotherapy may be helpful
Speech delay (>90%)/absence of speech (20%)	• Speech therapy to help with language development, and speech aids
Autism spectrum disorder (50–70%)	• Diagnosis and management by paediatrician as appropriate
Attention-deficit/hyperactivity disorder (ADD/ADHD) (30%)	• Diagnosis and management by paediatrician as appropriate
Feeding difficulties (70%)	• Investigation for swallowing difficulties or reflux where appropriate • Children with severe feeding problems may need to be referred to a paediatric gastroenterologist and may need a feeding (nasogastric or gastrostomy) tube
Constipation (30%)	• Constipation can be treated with a high fibre diet, adequate fluid intake and/or laxatives
Curved spine (scoliosis) (25%)	• May develop over time. Yearly review by GP/paediatrician until the child has finished growing
Dental problems (40%)	• At least yearly review by a dentist
Slow growth (30%)	• At least yearly review by GP/paediatrician • Consider screening for hypothyroidism and growth hormone deficiency • Bone maturation (bone age) may be delayed
Abnormal heart structure, most commonly atrial or ventricular septal defects (cardiac malformations) (20%)	• Consultation with a cardiologist including a baseline ultrasound (echocardiogram) of the heart
Brain structural malformations (40%), including absence/under development of the corpus callosum (30%)	• Brain MRI if clinically indicated. Most structural problems do not require any specific treatment
Epilepsy, most commonly seizures where the body stiffens then the arms and legs jerk (generalised tonic-clonic seizures) (30%)	• Standard investigations and treatments, including EEG and anti-epileptic medications • Most children respond well to standard treatments. • Consultation with a paediatric neurologist if seizures are difficult to control
Visual (eyesight) problems (50%)	• Yearly eye review by ophthalmologist • A squint (strabismus) may require patching or glasses • Long- or near-sightedness (refractive error) may require glasses
Hearing problems (80%)	• Newborn screening hearing test to identify sensorineural hearing loss (caused by damage to the nerves in the ear). Treatment with hearing aids and/or cochlear implant • 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
Hormone (endocrine) problems (<20%)	• Hypothyroidism has been reported and should be tested for if suspected clinically • Type 2 diabetes (mostly non-insulin-dependent diabetes mellitus [NIDDM]) has been reported infrequently and should be tested for if suspected clinically

Detailed management recommendations for healthcare professionals can be found in the **GeneReviews article**.

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 an *ARID1B*-related condition. You can make these connections through:

- Social media (e.g. **ARID1B-related intellectual disability Facebook support group**)
- 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 *ARID1B*-related conditions

You can find further information about *ARID1B*-related conditions by following the links below.

- UNIQUE: **ARID1B syndrome**
- MedlinePlus: **Coffin-Siris Syndrome**
- NORD: **Coffin-Siris 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 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. **The Children's Hospital of The King's Daughters** in Norfolk, Virginia, USA, has a clinical registry for CSS and related disorders.

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 'ARID1B'.

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