What causes *ARID1B*-RD?

ARID1B-RD is caused by changes in the DNA (genetic material) of the *ARID1B* gene, or by loss of one copy of the gene. Genes provide the instructions to make proteins. The ARID1B protein is one component of a large assembly of proteins called the BAF-complex. This complex plays an important role in the formation of nerve cells (neurons). It is not yet understand the precise way this causes intellectual disability or the other features of *ARID1B*-RD, but research is ongoing.

Why did this happen?

In most families the DNA change in *ARID1B* occurs out of the blue (de novo). When children are conceived their parents' genetic material is copied in the egg and sperm that makes a new child. The biological copying method is not perfect and occasionally random rare changes occur in the genetic code of children that are not seen in the DNA of their parents. These types of change happen naturally in everyone and are not due to environmental factors or lifestyle choices.

In a few families, one parent may have the same genetic change as their child, but this is very rare.

Can it happen again?

The risk of having another child affected by a rare gene disorder depends on the genetic code of the parents. For *ARID1B*-RD where parents are not found to carry the same *ARID1B* change as their child, by testing their DNA from a blood sample, the chances of having another child with *ARID1B*-RD are very small, at about 1-2%. The reason there is still a small chance is due to a phenomenon known as germline mosaicism. This is when a parent has the genetic change in a few of their egg or sperm cells, but not in the cells of their body. If the genetic analysis of the parents of a child with *ARID1B*-RD shows that one of them carries the same change in the *ARID1B* gene, the chances of having another child with *ARID1B*-RD are much higher.

Every family situation is different and a clinical geneticist or genetic counsellor can give specific advice for each family.

Families say ...

❝ There is a strong possibility that other children will be diagnosed with the same condition and it is a help to share experiences with other parents to find out what works, and what doesn't. We have hopes that if there is a similar adult case we may have some idea of her future outcomes or whether specialist training may prevent her having future problems. She is an incredibly happy child and brings joy to family and school, popular with the other children, and has started to become more engaged and to cuddle, hug and laugh with us demonstrating a sense of humour. ❞ - 6 years

❝ Happy, friendly. Loves exploring, being busy. ❞ - 8 years

Inform Network Support

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Surrey. RH8 9EE. UK
Tel: +44(0)1883 723356
info@rarechromo.org | www.rarechromo.org

Websites and Facebook groups

FAR - Foundation for ARID1B Research
www.arid1b.org

Coffin-Siris Syndrome Foundation
www.coffinsiris.org

https://www.facebook.com/groups/1092529431567496
https://www.facebook.com/groups/searchlight.arid1b
There are also many country specific Coffin-Siris syndrome Facebook groups

Unique lists other organisations' message boards and websites in order to be helpful to families looking for information and support. This does not imply that we endorse their content or have any responsibility for it.

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.

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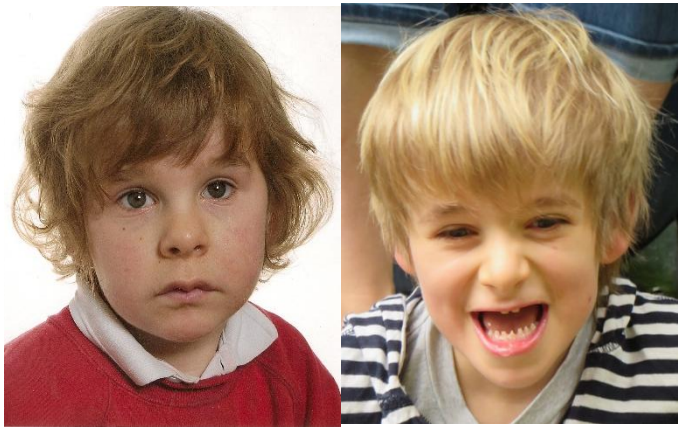
Understanding Chromosome & Gene Disorders

ARID1B-related disorder



rarechromo.org

What is *ARID1B*-related disorder?

ARID1B-related disorder, or *ARID1B*-RD for short, is a genetic condition. *ARID1B* (pronounced a-rid-one-bee) is the name of the gene involved. A change in the gene or loss of the gene (a 6q25.3 microdeletion) can cause the condition.

People with *ARID1B*-RD can have different symptoms and features ranging from intellectual disability (ID) with or without distinctive facial features (*ARID1B*-ID) to those observed in classic Coffin-Siris syndrome (*ARID1B*-CSS) which also involves developmental delay and ID. Apart from the external features (such as a short fifth finger) which helps geneticists to make a clinical diagnosis of Coffin-Siris syndrome, there does not seem to be a relevant difference between ARID1B-ID and ARID1B-CSS. It has become more clear that the effect of a change in *ARID1B* is variable and a spectrum of symptoms and features are possible.

A list of the most commonly observed features is noted below. Many other features have been identified such as undescended testis in boys (cryptorchidism), a floppy voice box (laryngomalacia) and curvature of the spine (scoliosis).

Typical features in *ARID1B*-ID

- Developmental delay and or ID (mild to profound)
- Hypotonia
- Feeding difficulties
- Seizures and brain anomalies
- Behavioural difficulties (e.g., ADHD or ASD like features)
- Short sightedness
- Speech development delay

Typical features in *ARID1B*-CSS

- Developmental delay or ID
- Underdeveloped little finger or finger nail
- Hypotonia
- Unusual hair growth
- Seizures and brain anomalies

Can *ARID1B*-RD be cured?

It is not possible to repair the change in the *ARID1B* gene, but careful screening, early intervention with the right therapies and regular monitoring will give each child the best chance of reaching their full potential. Treatments can be offered for some of the symptoms such as seizures.

Medical concerns

- **Seizures** about 30% of people with *ARID1B*–RD have been reported to have had at least one seizure (2023). If there are concerns about seizures, it can be helpful to record episodes to show to a child's doctor.
- **Eyes and vision** eye and vision anomalies have been reported in 54% of people with *ARID1B*-RD (2023) with short-sightedness and a squint (strabismus) being most commonly observed. Some children are long-sighted and many other less common anomalies have been reported. Eye and vision testing is strongly recommended.
- **Hearing** about 29% of people with *ARID1B*-RD (2023) have been reported as having 'abnormal' hearing, with hearing impairment and glue ear (a build-up of fluid in the middle ear) most commonly reported. Conductive hearing loss (when sound waves cannot travel to the inner ear) appears to be more common than sensorineural (when there is damage to the inner ear, nerve or part of the brain responsible for processing signals). Hearing loss can be in one or both ears and a few children use hearing aids. If there is any doubt about a child's hearing ability, this should be tested.
- **Feeding difficulties** about 69% of children with *ARID1B*-RD reported so far (2023) experienced feeding difficulties. Usually, these difficulties show shortly after birth, and resolve within a few months. However, a few children have needed tube feeding (either via their nose or direct to the stomach). 29% of people with ARID1B-RD have constipation. Feeding difficulties should be taken seriously, and dietary advice and feeding management offered promptly.
- **Frequent infections** about 32% of people with a with *ARID1B*–RD (2023) have been found to have symptoms related to immune system functioning with recurrent respiratory tract infections being the most common. However there is no clinical evidence to support taking extra precautions to prevent infections.
- **Heart** about 25% of people with a with *ARID1B*–RD (2023) were found to have a heart anomaly with septal defects (a hole between heart chambers) being the most common diagnosis. Heart screening is therefore recommended.
- **Brain** about 30% of people with a with *ARID1B*–RD (2023) were found to have a brain anomaly, with the bundle of nerve fibres that connect the two hemispheres of the brain (corpus callosum) being most commonly affected. There is no recommended screening.
- **Malignancies** although mutations in *ARID1B* have been described in cancer, there is no clinical evidence to support an increased risk of malignancies in *ARID1B*-RD. So, there is no recommended screening.

Development

- **Physical development** physical development is delayed in most children with a *ARID1B*–RD but the vast majority of children learn to walk without support. On average children learn to walk around 30 months, but this can range between 15 months and 5 years. Physiotherapy is recommended.
- **Learning** children with *ARID1B*–RD usually need learning support. Most are reported to have moderate intellectual disability, but some have a low-normal IQ, and others are more severely affected (2023). Some children with *ARID1B–RD* are able to read and write and most are able to use tablets or computers for various activities. An ID assessment is needed and measures put in place to help each child reach their full potential.
- **Speech** most children with *ARID1B*–RD do develop speech. The age at which this occurs is variable, but around half speak some words before their fourth birthday (2014). Because it appears that expressive speech is particularly affected, it may help to offer alternative forms of communication such as sign language and picture-based systems. Speech therapy is recommended.
- **Behaviour** children with *ARID1B*-RD are often considered very friendly, but like most children, they can become frustrated, especially if they have difficulty communicating. 31% of children with *ARID1B*-RD diagnosed to date (2023) have autistic features and 13% have an ASD (autistic spectrum disorder) diagnosis; 20% are hyperactive and 14% have an ADHD (attention deficit hyperactivity disorder) diagnosis. Some children find social interactions difficult and other diagnoses have been given (e.g. anxiety, impulsivity, short attention span, aggressive behaviour, OCD (obsessive compulsive disorder). A neurodevelopmental assessment is recommended.

Managing ARID1B syndrome

At Diagnosis

- Heart and kidney ultrasound scans
- Hearing and eyesight tests if needed
- EEG (test of the brain's electrical activity) if seizures are suspected
- Feeding management and dietary advice if needed

After Diagnosis

- Yearly evaluation by a developmental paediatrician
- Early intervention with speech and/or physical therapy where needed
- Regular eyesight and hearing tests
- ID and neurodevelopmental assessment