FACTS ABOUT HEALTH CONDITIONS
CAUSED BY CHANGES IN THE *ANKRD11* GENE

This fact sheet contains information about the possible impact of a change (variant) in the *ANKRD11* 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 *ANKRD11* gene. These changes were identified by a genomic (DNA) test. This fact sheet does not relate to cancers that are due to acquired variants in the *ANKRD11* gene (changes that occur after a person is born).

Key points

- Changes (variants) in the *ANKRD11* gene are one of the most common genetic causes of intellectual disability. Variants in the *ANKRD11* gene are seen in about 1 in 100 children (1%) who receive a genetic diagnosis of developmental delay/intellectual disability
- Developmental delay/intellectual disability can range from mild to severe
- Variants in the *ANKRD11* gene cause a condition called KBG syndrome
- Features of KBG syndrome include large front teeth, distinctive facial features, and behavioural differences
- Variants in the *ANKRD11* gene that cause health problems often occur as a new (*'de novo'*) change in a child. The variant may also be inherited from a parent, so future children may also carry the same genetic change. 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 *ANKRD11* gene. Support is available from a number of different organisations and services

Other names this condition may be referred to as

- KBG syndrome
- Chromosome 16q24.3 microdeletion syndrome

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 *ANKRD11* gene

Genes contain instructions that tell our body how to grow, develop and function. *ANKRD11* is a gene that tells the body to produce a protein called ankyrin repeat domain-containing protein 11 (ANKRD11). ANKRD11 helps to control genes involved in brain cell development. Changes (variants) in the *ANKRD11* gene can affect many parts of the body.

The *ANKRD11* gene is found on chromosome 16. *ANKRD11*-related conditions may be caused by a single spelling variation in the gene, which means the message is not read or received properly. In some individuals, a section of the chromosome that includes the *ANKRD11* gene (called 16q24.3) is missing. This is called a deletion. Children who have a larger 16q24.3 deletion usually have more severe symptoms.

In two-thirds (two out of three) individuals with *ANKRD11*-related conditions, the change in the gene occurred when the baby was conceived (a new or *'de novo'* variant) and is not seen in the parents. In one-third of individuals, the variant was passed to the child from a parent.

ANKRD11-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. *ANKRD11*-related conditions are rare. It is likely that many people with a variant in the *ANKRD11* gene have not been diagnosed because of the variety of symptoms seen.

What could a change in the *ANKRD11* gene mean for my child?

A change in the *ANKRD11* gene can affect children in different ways. Some are more severely affected than others. There may be a range of signs and symptoms in children with the same genetic variant and even within the same family. Variants in the *ANKRD11* gene are the only known genetic cause of KBG syndrome.

Children with *ANKRD11*-related conditions may be slower to reach their physical milestones (sitting, crawling, walking, running), and have problems with learning. Most will have problems with their speech. The most common sign is having very large adult front teeth (macrodontia).

Most children have a triangular face, eyebrows that meet in the middle (synophrys), prominent nasal bridge, upturned nose and a thin upper lip. A significant proportion of children have bone-related differences such as small hands and feet, or a curved spine (scoliosis). A small number of children have seizures (epilepsy).

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 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%)	• 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
Challenging behaviours (20%)	• Diagnosis and management by paediatrician as appropriate
Attention-deficit/hyperactivity disorder (ADD/ADHD) (15%)	• Diagnosis and management by paediatrician as appropriate
Autism spectrum disorder (ASD) (10%)	• Diagnosis and management by paediatrician as appropriate
Feeding difficulties (20%)	• Investigation for swallowing difficulties or reflux where appropriate
Dental problems such as when the surface of the tooth is very thin (enamel hypoplasia) and losing teeth (dental loss) (90%)	• Yearly dental check for signs of tooth decay (dental caries) and tooth loss
Rib and spine abnormalities (e.g. scoliosis) (75%)	• Initial review by paediatrician. X-rays or other imaging may be helpful for diagnosis and management if skeletal differences are considered a possibility
Short stature (40–70%)	• Growth hormone deficiency is common and may respond to therapy. Consultation with an endocrinologist may be required
Differences in pubertal development (uncertain)	• Assess for early puberty
Differences in heart structure (cardiac malformations) (10–25%)	• Consultation with a cardiologist including a baseline ultrasound (echocardiogram) of the heart
Palate (mouth) abnormalities (10–25%)	• Paediatrician review for presence of cleft palate, bifid uvula, velopharyngeal insufficiency, and referral as required
Undescended testes (25% of males)	• If the testicles cannot be felt (palpated), a surgical consultation is required
Seizures (epilepsy) (20–40%)	• Standard investigations and treatments, including EEG and anti-epileptic medications. Consultation with a paediatric neurologist if seizures are difficult to control
Brain structural abnormalities (uncommon)	• Most structural differences do not require any specific investigation
Hearing loss (25–30%)	• Hearing assessment at birth and repeated as needed. 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
Visual (eyesight) problems (15%)	• Initial review by ophthalmologist for assessment of vision and squint (strabismus) • Yearly eye review by ophthalmologist • A squint (strabismus) may require patching or glasses • Short-sightedness (refractive error) may require glasses

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 *ANKRD11*-related condition. You can make these connections through:

- Social media (e.g. closed Facebook groups such as the **KBG Patient Group**)
- Umbrella groups (e.g. **Genetic Alliance Australia** and **Rare Voices Australia**)
- Condition-specific groups (e.g. the **KBG Foundation**)
- 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 *ANKRD11*-related conditions

You can find further information about *ANKRD11*-related conditions by following the links below.

- Unique: **ANKRD11 and KBG Syndrome**
- MedlinePlus: **ANKRD11 gene** and **KBG syndrome**
- National Organization for Rare Disorders (NORD): **KBG Syndrome**
- Genetic and Rare Disease Information Centre (GARD): **KBG 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 KBG Syndrome Foundation has an online **Contact Registry**, which is collecting information from families.

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 'ANKRD11'.

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