UNIQUE

UNDERSTANDING GENES & CHROMOSOMES

ZNF699-related syndrome

rarechromo.org

This guide is designed to help families and healthcare professionals looking after people with ZNF699-related syndrome and to raise awareness about this very rare condition. It contains information about the cause, the ways in which it can affect people and suggestions about the help and management that can benefit people with this condition.

What is ZNF699-related syndrome?

ZNF699-related syndrome, also referred to as DEGCAGS syndrome (which is short for DEvelopmental delay with Gastrointestinal, CArdiovascular, Genitourinary and Skeletal abnormalities), is a rare genetic condition associated with developmental delay and varying degrees of learning (intellectual) disability. Anomalies affecting feeding and the intestines (gastrointestinal), the heart and blood vessels (cardiovascular), genitals and kidneys (genitourinary) and bones (skeletal) may also occur.

As is common with genetic conditions, each person can be affected differently - even among affected members within the same family. Not everyone with ZNF699-related syndrome will have all the features described in this leaflet features and each person with a certain feature won't necessarily be affected by it to the same degree as other people with that feature.

How common is ZNF699-related syndrome?

ZNF699-related syndrome is extremely rare. Currently (2026) about 30 individuals from 23 families with the syndrome have been reported in the medical literature. This group is from diverse ethnic backgrounds, including Middle Eastern, European, Asian and Hispanic descent, and the age at diagnosis ranged from one month to 21 years.

What features and symptoms do people with ZNF699-related syndrome have?

As is common with many genetic conditions, children and adults with ZNF699-related syndrome can have a range of features and symptoms. As more people are diagnosed, and information is shared, the range of features, and the likelihood of a child or adult having these features, will become clearer.

Common features

These features are listed in descending order of how commonly they have been reported, from having been reported in everyone, to having been reported in half of people described in the medical literature with ZNF699-related syndrome so far (2026):

- Distinctive facial features
- Developmental delay and/or intellectual disability
- Skeletal and dental anomalies
- Skin and hair anomalies
- Anomalies of the brain and nervous system
- Gastrointestinal anomalies
- Genitourinary anomalies
- Low muscle tone (hypotonia)
- Hearing loss
- Vision anomalies

Other possible features include:

- Weakened immune system (immunodeficiency)
- Slow growth (growth retardation)
- Low red blood cell count (anaemia)
- Deficiency of all three blood cell types (pancytopenia)
- Movement anomalies
- Underdevelopment of the voice box (laryngomalacia), windpipe (tracheomalacia) or airways in the lungs (bronchomalacia)

Pregnancy and birth

While some pregnancies are unremarkable and proceed without complication, some concerns during pregnancy have been reported. Where a cause for concern was noted, most often parents reported slow growth in the womb (intrauterine growth retardation IUGR). Other reported concerns include an excess of fluid (amniotic fluid) around the baby (polyhydramnios), a single umbilical artery (usually there are two arteries in the umbilical cord) and skeletal anomalies that may be identified during a prenatal scan.

The majority of pregnancies go to term, but some babies are born prematurely and birth weights are usually below average. A small number of babies grow very slowly in the womb and are tiny at birth. Some babies show signs of difficulty at birth related to feeding or a heart condition. Others require breathing support such as a type of gentle breathing support known as CPAP (continuous positive airway pressure) or intubation (where a tube is passed through the nose or mouth into the airways). Some new-born babies have low muscle tone (hypotonia) and have been described as “unusually inactive and placid”, a feature that may alert doctors to an underlying genetic condition.

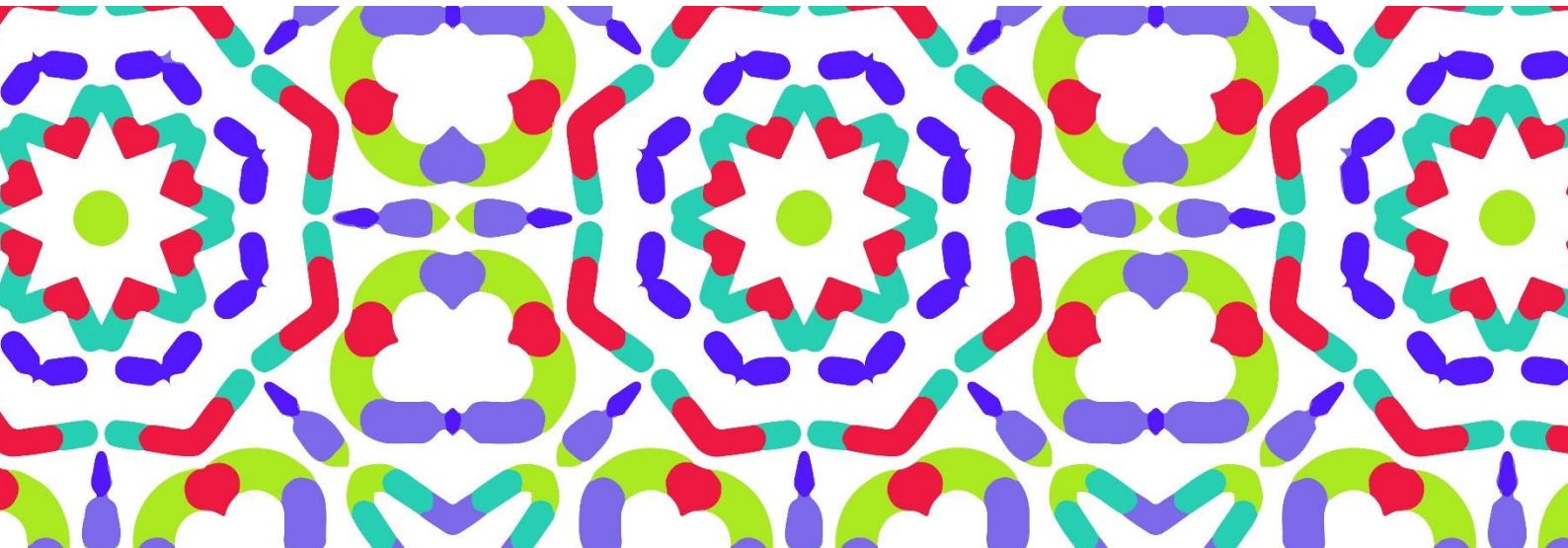
Another anomaly at birth can include a blockage in the intestines (intestinal atresia), which has been reported in nine babies so far and required surgery.

Appearance

Certain facial features are found more often in children with ZNF699-related syndrome than in other children. These features may mean that you see unexpected similarities between your child and others with ZNF699-related syndrome.

Key facial features may include narrow opening of the eyes, a pear-shaped nose with a bulbous tip, thick lips and an open-mouth appearance.

A distinctive feature is an increased quantity of hair that may include a low hairline, excessive hair growth (hypertrichosis), eyebrows that meet in the middle (synophrys) and long eyelashes. Also, early white hair and/or eyebrows that can be visible during childhood can occur.



Development

Intellectual development and learning

All children with ZNF699-related syndrome reported so far (2026) have learning (intellectual) disability (LD/ID) or learning difficulties. LD/ID ranges from mild to profound but is usually in the severe range. In at least one child, developmental regression (a loss of previously acquired skills) has been reported (Bertoli-Avella 2021). Most children will require significant additional support with their learning throughout their education.

Unique publishes separate guides to Education and Further education, training and work

Feeding

Gastrointestinal anomalies are an important feature of this condition. Feeding issues in the new-born period have been reported in 4 of 14 individuals (29%) in one study (Biela 2022). Specific difficulties can include problems with swallowing (oral-pharyngeal dysphagia) and a poor suck or choking episodes. A few babies also suffer from gastro-oesophageal reflux (GERD/GORD), in which feeds return readily up the food passage. The feeding and gastrointestinal issues can have a significant impact on growth, leading to poor weight gain (failure to thrive).

Structural gastrointestinal anomalies are also common and can be severe. These can include a blockage in the intestines (intestinal atresia), including complete blockage of the upper small intestine in newborns (jejunal atresia), which was seen in nine individuals in one report (Biela 2022). Other reported structural anomalies include a narrowing of the opening between the stomach and the small intestine (pyloric stenosis) and the upper part of the stomach bulging into the chest cavity through an opening in the diaphragm (hiatus hernia). Sadly, in some cases, these structural anomalies have been the reason that some infants have passed away.

Unique publishes a separate guide to Feeding

Growth and stature

Most children with ZNF699-related syndrome described in the medical literature are noted as having growth delay. Growth delay can begin before birth, with intrauterine growth retardation (IUGR) being reported in 5 out of 14 babies in one study (Biela 2022). Beyond infancy, height and weight remains below average, with some individuals experiencing failure to thrive and decreased body weight.

Behaviour

Children with genetic conditions typically tend to have behaviour in keeping with their overall degree of developmental delay and often have a happy disposition. Understanding a behaviour profile is key to providing effective support and management strategies should focus on addressing the root causes of each behaviour. Efforts to take into account and introduce strategies to tackle communication and other difficulties can also be beneficial.

Unique publishes a separate guide to Challenging Behaviour

Puberty

There is limited information available about puberty in children with ZNF699-related syndrome. Some families of children with genetic disorders and behavioural difficulties or learning disability can be particularly concerned at their daughter's ability to cope with menstruation, and for some discussing menstrual regulation options with a paediatrician may be beneficial.

Unique publishes a separate guide to Puberty

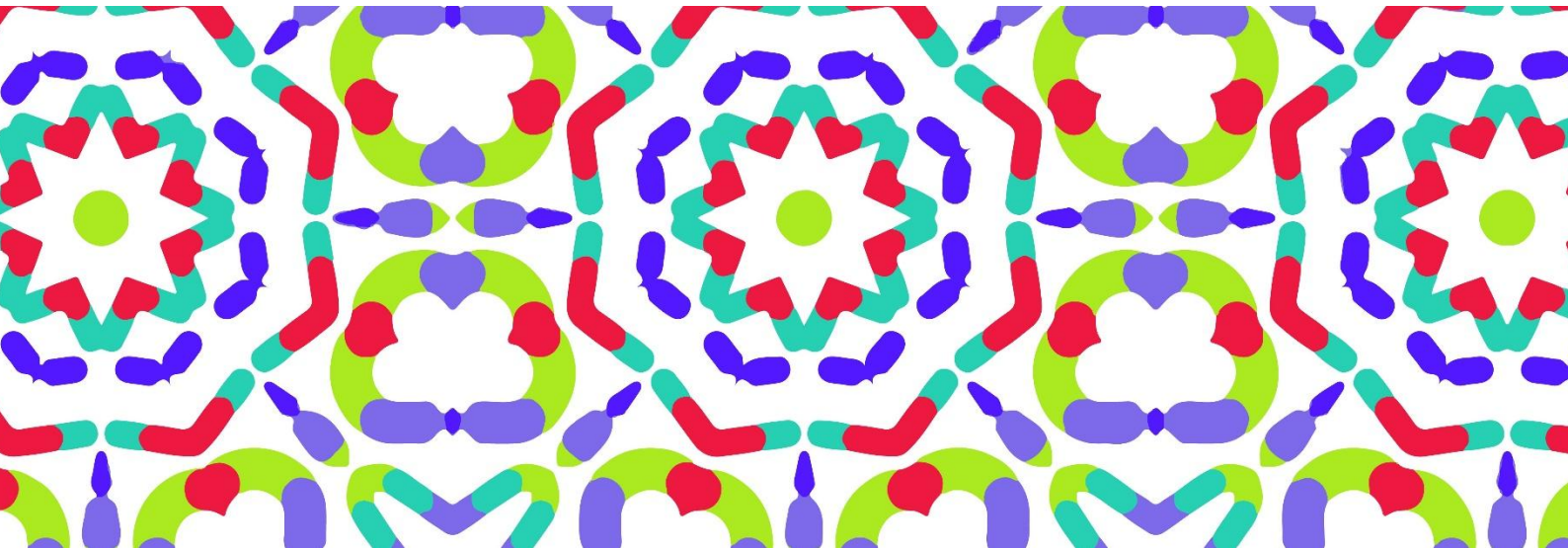
Simons Searchlight publishes a guides to Navigating Menstruation

Adulthood

There is limited information available about adults with ZNF699-related syndrome. Experiences of adulthood are likely to vary considerably and will depend on many factors. These include the level of any LD/ID, possible on-going medical concerns and improvements in early intervention and therapies/treatments.

Adults with ZNF699-related syndrome will likely have varying levels of independence. Some may go on to have families of their own and manage to run their own households and work. Others will likely continue to live with their parents or in supported settings such as a group/residential care home, with caregivers who can provide support. Some may live independently but require some support from family or friends with certain tasks. Levels of employment and the nature of employment will vary but some may undertake some form of paid or unpaid employment.

Unique publishes a separate guide to Transition



Medical concerns

The following medical concerns have been found in children with ZNF699-related syndrome. They are not found in all children so not all children with the syndrome will be affected.

Heart and circulation

A heart condition(s) has been found in many individuals reported so far with ZNF699-relatedsyndrome, which can be present at birth (congenital). The type of heart condition(s) is variable but includes anomalies affecting the size and structure of the heart muscle and valves. In addition to structural anomalies, other circulatory issues such as a fast heart rate (tachycardia) have also been noted. Many of these conditions are relatively minor; in a study of 14 people, none required an intervention for their heart condition (Biela 2022).

Heart anomalies can include:

- A hole between the top two chambers of the heart (atrial septal defect (ASD)) or a hole between the bottom two chambers of the heart (ventricular septal defect (VSD))
- Narrowing of the vessel carrying blood from the heart to the lungs (pulmonary stenosis)
- A change in one of the heart valves (e.g. a dysplastic pulmonary valve)
- An underdeveloped (hypoplastic) heart (e.g. a hypoplastic left ventricle)
- A complex heart anomaly where both the aorta and the pulmonary artery connect to the right ventricle (double outlet right ventricle)
- Narrowing of the main artery of the body (coarctation of the aorta)

Brain

A number of children reported so far, 17 out of 26 (65%) in one report (Karimi 2024), have been found to have a structural brain anomaly, which can be detected by MRI (magnetic resonance imaging) or a CT (computerised tomography) scan of their brain. The specific anomalies can vary significantly, even between siblings with the same genetic change. The changes seen vary but include:

- Underdevelopment (hypoplasia) or partial/complete absence (agenesis) of the white matter connecting the two halves of the brain (corpus callosum)
- Enlarged fluid-filled cavities (ventricles) in the brain (ventriculomegaly)
- A small head size (microcephaly)
- Atypical development of the protective covering (myelin sheath) around nerve fibres in the brain (abnormal myelination)
- Early fusing of the bones of the skull (craniosynostosis)
- A flattened appearance to the head (plagiocephaly)

Ears and Hearing

A few individuals with ZNF699-related syndrome have a hearing impairment. This is mostly a sensorineural type of hearing loss which is caused by problems with the inner ear, sometimes with the cochlea or auditory nerve (the nerve that sends signals to the brain about sound).

Many types of hearing loss can be managed by using hearing aids. As children are at risk of speech delay, parental concerns should be acted on early and home- or school-based therapy provided.

Unique publishes a separate guide to Hearing

Eyes and sight

Eye and sight-related symptoms are a feature of ZNF699-related syndrome. Problems with the sharpness of vision (refractive errors) such as short-sightedness (myopia) or long-sightedness (hypermetropia) are common, affecting 14 out of 26 individuals (54%) in one report (Karimi 2024).

Other eye and sight-related symptoms that have been seen in a single individual include:

- Unusually small eyes (microphthalmia)
- Bulging eyes (proptosis)
- Drooping of the upper eyelid (ptosis)
- Involuntary, repetitive eye movements (nystagmus)
- An unusual result on a test that measures the electrical response of the light-sensing cells in the eye (abnormal electroretinogram)

Anemia

While unusual blood test results (hematologic findings) in people with ZNF699-related syndrome have not been well described, there are a number of observations of low blood cell counts because the bone marrow is not working properly to produce new cells. In very rare cases, a few people with low blood counts experience a sudden, temporary spike in new red blood cells - especially when they get an infection. While they seem to recover at first, their bone marrow then suddenly stops working completely.

Breathing

Children with ZNF699-related syndrome may be prone to allergies and asthma, sometimes triggered by respiratory infections. In one person with a co-occurring immunodeficiency, specific conditions included pneumonia, asthma and rhinitis (irritation/inflammation of the nasal membrane). Other issues may include structural anomalies of the airway that cause noisy breathing (tracheomalacia or laryngomalacia) and airway collapse during breathing (chronic bronchomalacia). Recurrent respiratory infections are a significant concern (reported in five individuals, two of whom had a confirmed immunodeficiency); chronic lung disease and elevated diaphragm (diaphragmatic eventration) have also been noted.

Bones

Various bone and skeletal anomalies have been identified in a few children with ZNF699-related syndrome. These include:

- Shortening of long bones
- A hand that bends towards the forearm due to an anomaly of the radius bone or bones of the hand (radial ray abnormality)
- Delayed bone age
- Anomalies of developing cartilage and bone ends, mainly in the hip joints (epiphyseal dysplasia)
- Curvature of the spine (lordosis)

Anomalies of the hands and feet have also reported as described on the following page.

Hands and feet

Children with ZNF699-related syndrome often have characteristic anomalies of the hands and feet. Most common among these are:

- Fingers or toes that are unusually short (brachydactyly) or fused (syndactyly), which was reported in 7 out of 14 individuals in one study (Biela 2022). Short thumbs and fusion of the 2nd and 3rd toes is specifically noted
- Club foot (talipes), with the foot turned inwards and the soles pointing towards each other
- Extra fingers or toes (polydactyly), was reported in 2 out of 14 individuals in the same study
- Short or absent thumbs

Some children are only mildly affected, and treatment is not required. Others may benefit from massage, orthotics and physiotherapy. Treatment is tailored to the individual child and in some cases surgical correction may be needed.

Teeth

Dental concerns are very common in children with ZNF699-related syndrome, with dental anomalies observed in 22 out of 26 (85%) individuals in one study (Karimi 2024). A number of issues have been described including unusual dental development (such as abnormal dentine – the part of the tooth that lies immediately below the protective covering of enamel); an unusual size of the jaw, leading to overcrowding or widely-spaced teeth; and unusually thin, weak enamel (abnormal tooth enamel).

Unique publishes separate guides to Looking after your child's teeth and Teeth: common concerns

Kidney and urinary tract

Some babies are born with minor anomalies of the kidneys and/or urinary tract. Urinary tract infections (UTIs) are relatively common and may need to be treated with antibiotics. This susceptibility to infections may be linked to an underlying immune system problem in some individuals. Repeated urinary infections may require preventive treatment with antibiotics.

Other conditions that have been described include babies born with:

- Under-sized kidneys (renal hypoplasia)
- Disorganised development of the kidneys (bilateral renal dysplasia)
- Anomalies in the structure of the inner and outer layers of the kidneys (abnormal morphology of the renal cortex and medulla)

Long-term (chronic) kidney disease has also been reported in a couple of individuals (Biela 2022).

Genitals

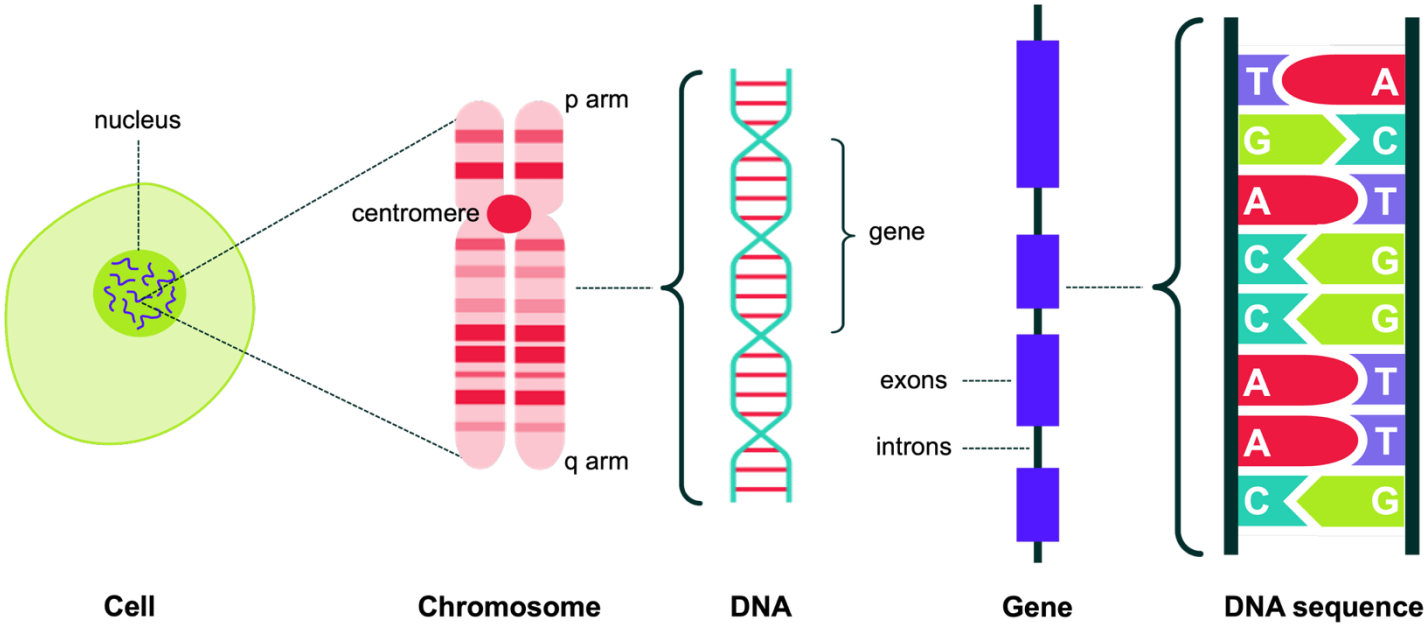
Minor anomalies of the genitals in boys have been reported. Most common among these are ambiguous genitalia, where the genitals do not have the standard appearance of either a boy or a girl; hypospadias, where the hole normally found at the end of the penis lies on the underside; a curved penis (chordee); and undescended testes (cryptorchidism). Many of these anomalies can also be seen in children without ZNF699-related syndrome and are not of major concern. If necessary, most can be corrected with surgery. Girls are much less likely to be affected.

This section includes some more complicated scientific terms and concepts - don't worry if it's a lot to take in, you can always come back to this section later if you want to.

Genes and chromosomes

Genes are instructions which have important roles in our growth and development. They are made of DNA and are incorporated into organised structures called chromosomes. Chromosomes therefore contain our genetic information. Chromosomes are located inside our cells, the building blocks of our bodies. In people with genetic conditions, one or more of their genes don't instruct the body as expected, which can lead to changes in how their body works.

DNA is made up of building blocks called 'bases' or 'nucleotides'. There are four DNA bases which can be abbreviated to the letters A, C, G, and T. These DNA bases are paired up in the DNA structure into 'base-pairs'. The full sequence of our DNA is over three billion base-pairs long. There are changes in the DNA sequence (variants) present in everyone's genes. It is variants in our genes that make each one of us unique individuals.

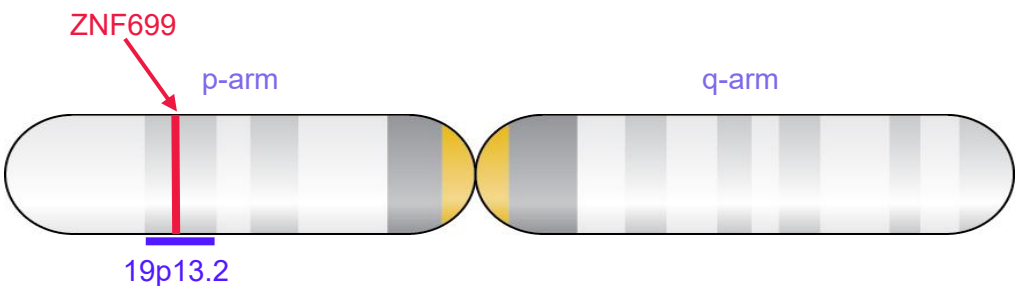


What causes ZNF699-related syndrome?

The syndrome is caused by specific changes (known as pathogenic variants) to the DNA sequence of a gene called ZNF699.

The *ZNF699* gene is located in the short 'p' arm of chromosome 19 in a region called 19p13.2 as shown in the image below.

Chromosome 19



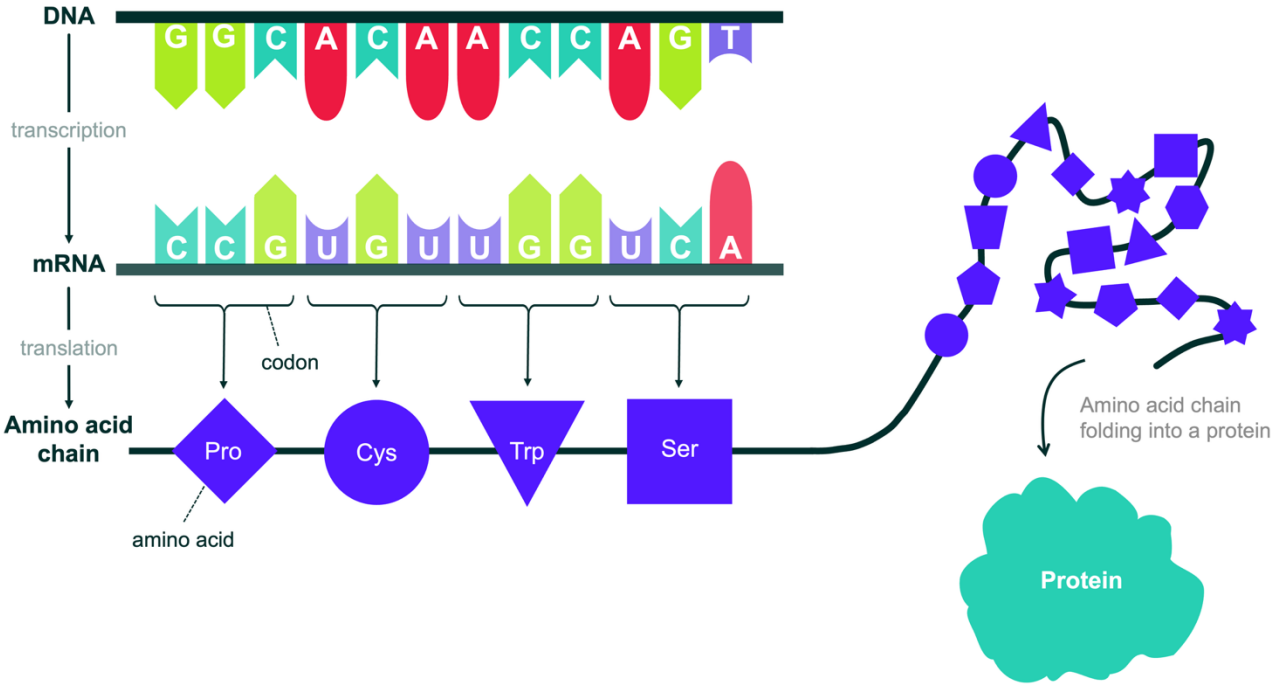
We have two copies of chromosome 19 in our cells, so we also have two copies of the *ZNF699* gene. The ZNF699-related syndrome occurs when both copies of the *ZNF699* gene are affected. This is known as an autosomal recessive syndrome since all numbered chromosomes are called autosomes and genetic conditions that occur when both copies of an autosomal gene are affected are known as recessive. Affected individuals can have two identical variants (homozygous) or two different variants (compound heterozygous).

Unique publishes a separate guide to single gene disorders – autosomal recessive inheritance

Most genetic conditions are caused by changes to genes that provide instructions for making proteins; these are called protein-coding genes. *ZNF699* is one of thousands of these protein-coding genes. The *ZNF699* gene encodes a type of protein called a 'nuclear zinc finger' (hence ZNF) protein that regulates other genes by binding to DNA (known as a transcription factor).

Genes and proteins

Proteins are molecules that are made up of long chains of chemicals called amino acids and play critical roles in the body. This is because proteins are essential for lots of processes such as breaking down food, moving our muscles, and growing the body's organs and making sure they function properly. To make these amino acids a copy of the DNA sequence is created, called messenger RNA (mRNA). mRNA uses the same A, C and G bases as DNA, but the 'T' bases are swapped to 'U' bases. Within a gene, each three-letter sequence (codon) of mRNA bases provides the instructions for one amino acid. Changes to the amino acid sequence can affect the function of the protein.



The role of the KRAB-zinc finger (KZNF) protein

The *ZNF699* gene sequence is 'read' to make the ZNF699 protein. This protein is important because its main role is to regulate the activity of other genes. It does this by binding to the DNA sequence of other genes and interacting with other proteins.

A crucial function of the ZNF699 protein is also to regulate the epigenome, this involves modifying the genome but not changing DNA or protein sequences. This modification is called methylation, which is the addition of a chemical group called a methyl group to DNA or the proteins attached to it.

The absence of ZNF699 changes the epigenome by disrupting the addition of methyl groups. There are tests that can be carried out to look at changes to the addition of methyl groups (methylation patterns). The absence of ZNF699 has been found to cause a unique and distinct DNA methylation pattern. This pattern is known as an "episignature". In ZNF699-related syndrome, the episignature shows that methylation is increased for most affected genes (hypermethylation) which means these genes will be less active or inactive.

Different types of genetic changes

People with ZNF699 syndrome are more commonly found to have a gene sequence variant, that produces a shortened, non-functional ZNF699 protein. These variants are known as loss of function variants, or LOF for short.

Gene sequence variants, loss of function (LOF)

Such variants include:

- Nonsense variants: Where the amino acid change results in a premature ‘stop’ signal, stopping protein production too early, leading to a shorter, unfinished (truncated) protein
- Frameshift variants: Where the DNA coding sequence is shifted by the addition or deletion of individual DNA bases which means the incorrect amino acid sequence is used to produce the protein or a premature ‘stop’ signal is introduced
- Splice-site variants: Where a change affects how the gene's instructions are put together, which can disrupt typical protein production
- Missense variants: Where one amino acid is replaced by another, producing an altered protein

Genetic Tests

ZNF699-related syndrome can be identified by a type of genetic test called sequencing, such as whole exome sequencing (WES) or whole genome sequencing (WGS).

Unique publishes a separate guide to DNA sequencing

Genetic Test Results

The results of genetic (genomic) testing are likely to be provided by a geneticist, a genetic counsellor or the healthcare professional who ordered the test. Depending on the test that was carried out, someone with ZNF699-related syndrome might have results that look like the following example on the following page.

An example result of a DNA sequencing test (e.g. WES or WGS), that can identify gene variants, is shown below for the ZNF699 gene:

p.Cys113TrpfsTer11 (A>-): c.339del ZNF699 (NM _198535.3)

p.Cys113Trp	signifies the change to the protein: the amino acid cysteine (Cys) has been replaced by the amino acid tryptophan (Trp) at position 113 in the sequence of amino acids that make up the protein
Fs	Fs signifies this is a frame shift variant
Ter11	Ter signifies the frame shift has introduced a stop codon and protein assembly is stopped 11 amino acids later
A>-	signifies the gene sequence change: the A nucleotide has been deleted
c.1672	signifies the base pair position of the change within the gene sequence (the position where the A nucleotide has been deleted)
ZNF699	signifies the gene that is affected
NM_198535.3	this is the specific 'reference sequence' or blueprint of the gene that scientists use to identify the location of the variant

Unique publishes a separate guide to Interpreting Genetic Test Results

Why did this happen?

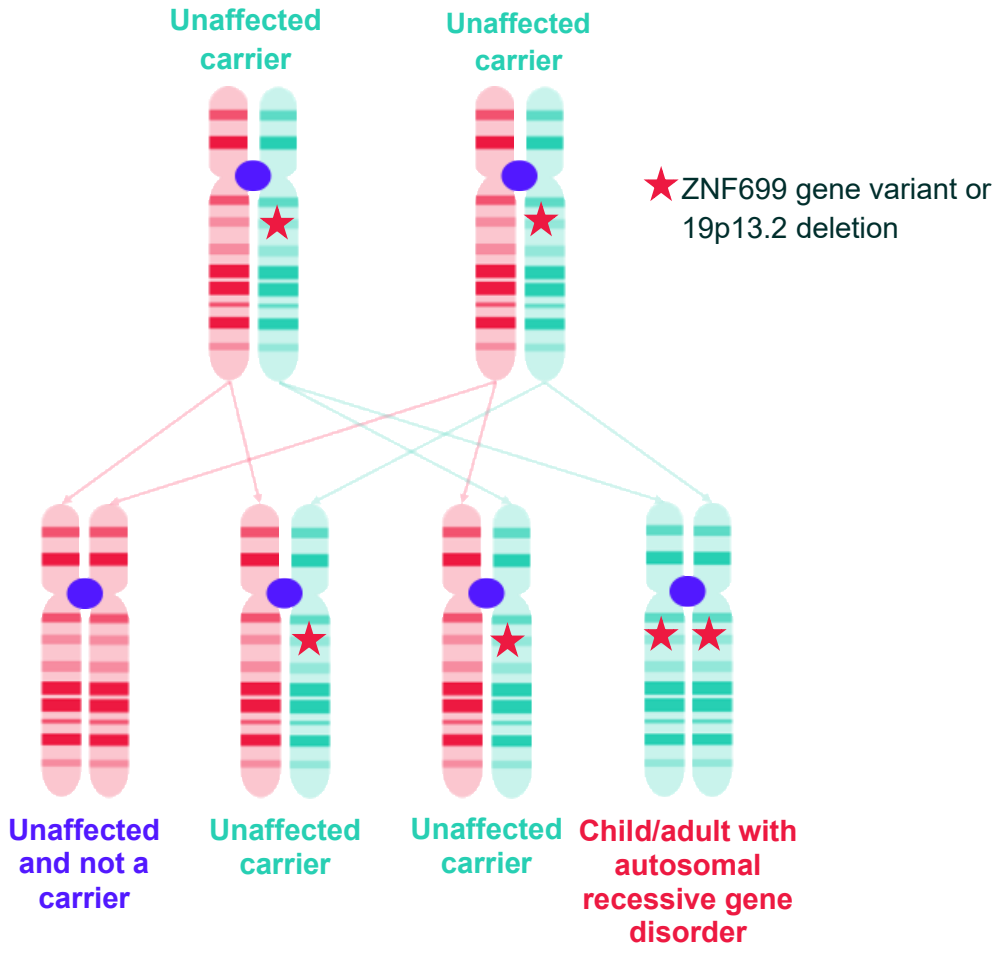
In almost all people identified so far (2026) with ZNF699-related syndrome, both parents passed on a copy of the *ZNF699* pathogenic gene variant to their child with ZNF699-related syndrome, so one variant was inherited from the biological mother and one from the biological father. There is nothing that happened before or during the pregnancy that caused this to happen. We all have small changes in our genes, and it is by chance that two parents have alterations in the same gene, or because the parents share a common ancestor. It is important to recognize that no one should be blamed for variants in their DNA and no parent is at fault when DNA changes are present in their child.

For many genes, including the *ZNF699* gene, having only one copy of the fully functional gene is enough for the body's healthy functioning. Therefore, when parents have only one copy of the *ZNF699* gene with a pathogenic variant they are typically unaffected and do not know they are carriers of the pathogenic variant. ZNF699-related syndrome only occurs if both copies of the *ZNF699* gene contain a pathogenic variant and/or are deleted.

Very rarely individuals are identified as having a variant in both copies of a particular gene, but the genetic changes are different, this is known as compound heterozygosity. For example, in a study of 30 individuals with this condition, two had two different pathogenic variants in the ZNF699 gene (Karimi 2024). Some individuals may carry a gene variant in one copy of a gene and the other copy may be affected in a different way, such as there being a deletion of part of the chromosome that includes this gene.
In some conditions, when parents are related by blood, e.g. first cousins (consanguinity), genomic testing may show runs of homozygosity, where both parents share common ancestry and pass down identical regions of DNA. This is the most common cause of ZNF699-related syndrome. In one study of 30 affected individuals (Karimi 2024), 28 had inherited two identical copies of a pathogenic variant due to consanguinity.

Can it happen again?

The possibility of having another child affected by a rare autosomal recessive gene disorder depends on the genetic code of the parents. If both parents are known to carry a pathogenic variant (also known as a mutation) in the *ZNF699* gene, theoretically there is a one in four (25%) chance their child would have ZNF699-related syndrome, a one in two (50%) chance their child would be an unaffected carrier (like their parents) and a one in four (25%) chance of their child being unaffected and not a carrier, as shown in the image below. This chance resets for each pregnancy.



Once an affected person has received the genetic confirmation of ZNF699-related syndrome, genetic testing can be carried out on their parents to establish carrier status, particularly if they are planning more children.

A clinical geneticist or genetic counsellor can provide specific advice for each family about the chance of having further children with ZNF699-related syndrome.

Can ZNF699 syndrome be cured?

There is no cure for ZNF699 syndrome since most of the effects of the genetic change took place before or during a baby's formation and development. Although there may also be later onset features, such as an inward curve of the lower back (lumbar lordosis), joint contractures and a wide-based standing posture or anaemia. Knowing the diagnosis means that appropriate monitoring and interventions can be put in place. As a cure is not available, treatment is symptomatic, focusing on managing the specific health issues and providing supportive care to improve an individual's quality of life.

Management

No clinical practice guidelines for ZNF699-related syndrome have been published (2026). The following suggestions have been provided by clinicians, who have personal experience of managing/treating individuals with the syndrome, to improve quality of life and reduce complications.

Children and adults with ZNF699 syndrome should be under the care of a multidisciplinary team. The team should include a geneticist and paediatrician (for children) who can oversee care so that development and behaviour can be monitored, and the best help given in the form of different therapies. Individuals may also have evaluations with various specialist doctors.

Immediately following diagnosis

When not carried out as part of the diagnostic process, an evaluation of the features of ZNF699 syndrome that are present in the child or adult who has been diagnosed with this genetic condition is recommended. This can determine which of the features of ZNF699 syndrome are present and how severe they are.

The following assessments are recommended:

- A developmental and physical examination to look for developmental delay, low muscle tone (hypotonia), skeletal anomalies (such as shortened long bones, radial ray anomalies and syndactyly) and facial features associated with the condition
- A neurologic assessment to determine whether conditions such as learning (intellectual) disability are present. Brain magnetic resonance imaging (MRI), a technique that can be used to visualise the brain, should be carried out as structural and myelination anomalies (changes to the white matter) of the brain are a known feature of ZNF699 syndrome
- A gastrointestinal and nutritional assessment to check for gastrointestinal anomalies, such as intestinal atresia, and to monitor growth
- A cardiac assessment, including an echocardiogram, to look for congenital heart defects
- A genitourinary assessment, including a renal and bladder ultrasound, to check for kidney and urinary tract anomalies
- A hearing (audiological) assessment to determine the severity of hearing loss and ensure early intervention
- An eye (ophthalmology) evaluation to test for vision problems such as myopia or hypermetropia
- A haematology and immunology assessment, including a complete blood count (CBC) to screen for anaemia and pancytopenia. An immunology workup is also recommended if there is a history of frequent or severe infections
- A respiratory assessment if there are breathing difficulties, to check for conditions such as laryngomalacia, tracheomalacia and bronchomalacia
- A dental and dermatological (skin) examinations to assess for dental and skin anomalies

Genetic counselling for affected individuals and their families should also be offered together with the provision of signposting to family support and resources.

Supportive care

How a person with ZNF699 syndrome is cared for is likely to require co-ordinated care by a multidisciplinary team of specialists, which may include a/an:

Audiologist – a health care professional who diagnoses, treats and helps manage a condition that involves hearing or balance

Cardiologist – a doctor who specialises in heart conditions

Dermatologist – a doctor who specialises in skin conditions

Developmental paediatrician – a doctor who oversees a child's overall health and development

Dentist/Orthodontist – manages dental anomalies

Gastroenterologist – a doctor who specialises in the digestive system

Haematologist – a doctor who specialises in blood-related conditions

Immunologist – a doctor who investigates and treats issues with the immune system

Nephrologist – a doctor who specialises in conditions affecting the kidneys

Neurologist – a doctor who specialises in conditions of the brain, spinal cord and nervous system

Occupational therapist (OT) – a health care professional who uses activities to aid self-management of a condition and can provide equipment

Ophthalmologist – a doctor who specialises in conditions affecting the eyes

Orthopaedic surgeon – a doctor who monitors and treats skeletal anomalies

Otolaryngologist (ENT) – a doctor who specialises in conditions of the ear, nose and throat

Paediatrician – a doctor who specialises in the physical, mental and social health of children from birth to young adulthood

Physiotherapist/physical therapist (PT) – a health care professional who uses exercise, movement, manual therapy, education and advice to help with the body's strength and mobility

Speech and language therapist (SALT) – a health care professional who helps with speech, language communication and sometimes feeding/swallowing difficulties

Surgeon – a doctor who is specially trained to perform medical operations

Urologist – a doctor who specialises in diagnosing and treating conditions affecting the urinary system

Specialist nurses and/or other healthcare professionals may need to systematically and comprehensively plan a child or adult's treatment. This approach involves an initial comprehensive evaluation to establish a baseline, the development of an individualised care plan, regular follow-ups to monitor growth and development, and a plan for transitioning from paediatric to adult care.

Treatments and therapies

Early intervention can be beneficial and formal testing to assess specific, individual needs is recommended. An education, health and care plan (EHCP) in the UK, individualized education plan (IEP) in the US, or equivalent document in other countries, may be issued after a child has undergone an assessment, to help ensure that the educational, health and social provisions deemed necessary to support the child's needs are delivered.

Treatment will depend on the specific features and symptoms experienced by the person with ZNF699 syndrome but may include:

Physiotherapy for low muscle tone (hypotonia) which usually includes exercises to build core strength, improve balance, and enhance coordination to help children achieve motor milestones like sitting, crawling, and walking, and to improve overall mobility

Occupational therapy for fine motor skill delays, which can include activities to improve hand strength and coordination for daily tasks (e.g. feeding and dressing), and to develop visual-perceptual skills and cognitive abilities to promote independence

Speech therapy for a range of speech and language delays or difficulties and feeding/swallowing difficulties. For children with moderate to severe difficulties, this can include regular sessions focusing on Augmentative and Alternative Communication (AAC) methods (e.g. sign language, picture exchange systems and high-tech communication devices) and provides a functional means of communication for individuals who are non-verbal or have very limited speech

Feeding therapy and nutritional support to manage feeding difficulties and failure to thrive, which may include nasogastric tube feeding to ensure adequate caloric intake

Surgery, such as procedures to correct intestinal atresia (a blockage in the intestines), congenital heart defects or skeletal anomalies

Surveillance

It is recommended that the following evaluations are carried out/considered to monitor an individual's existing symptoms, how they respond to care and treatment and whether any new symptoms emerge over time:

- Monitor for growth and adequate nutritional intake to manage failure to thrive
- Neuropsychiatric and learning assessments every few years to optimise the EHCP/IEP and to monitor neurodevelopmental progress
- Physical and occupational therapy evaluations to manage low muscle tone (muscular hypotonia)
- Gastrointestinal review, including post-operative monitoring and functional evaluation following surgery for intestinal atresia
- Consider an annual cardiac review to monitor for congenital heart defects
- Pulmonology consultation for laryngeal, tracheal or bronchial anomalies (laryngomalacia, tracheomalacia, bronchomalacia)
- Regular blood tests to monitor for haematological issues, such as low red blood cells (anaemia) and low levels of all types of blood cells (pancytopenia)
- Immunological evaluation for those with frequent infections
- Consider annual audiologic assessments
- Consider a neurology review (including MRI and EEG, if indicated by seizures)
- Consider a skeletal review for anomalies such as synbrachydactyly, an accentuated lordotic curve, reduced vertebral body height or insufficient vertebral arch closure
- Assessment of the need for genetic counselling and family planning advice to help families understand the inheritance pattern, prognosis and potential risks for future pregnancies

Research into a possible treatment for ZNF699-related syndrome

The genetic change causing ZNF699-related syndrome affects the development of the brain and other parts of the body before birth. Therefore, a complete cure is unlikely, even in the future, since the brain has already formed by the time a diagnosis is made. In addition, although ZNF699-related syndrome is a relatively rare condition, the *ZNF699* gene is the subject of research. As of early 2026, there are no specific curative treatments or targeted therapies in clinical development. Instead, research is in the early stages and is focused on understanding the gene's function, outlining the full range of clinical features, and characterising

the biological mechanisms that cause the condition. All current foundational work is a necessary first step to identifying targets for future drug or gene-based therapies.

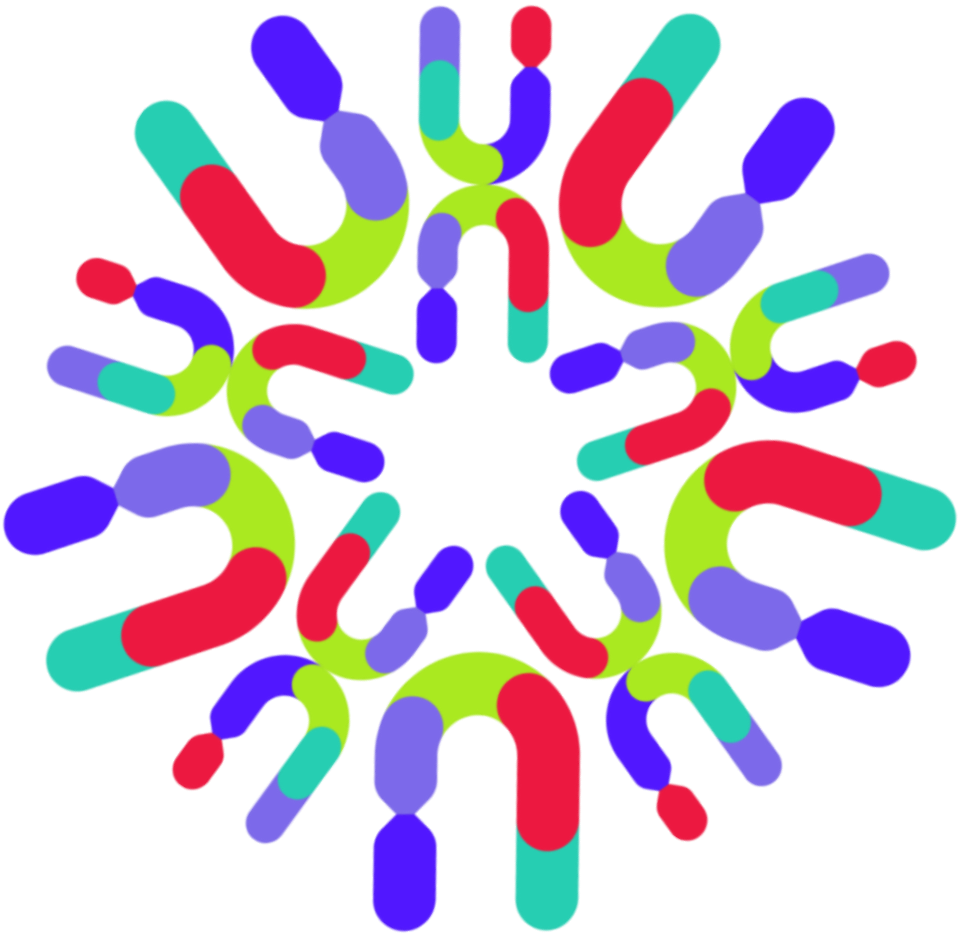
Details of clinical trials related to a particular condition or gene can be found at **ClinicalTrials.gov** and **EU Clinical Trials Register**.

Sources

The information in this booklet is drawn from the published medical literature and information from Unique members. The first-named author and publication date for articles in the medical literature are given to allow you to look for the abstracts or original articles on the internet in PubMed (**pubmed.ncbi.nlm.nih.gov/**).

References

- Bertolli-Avella AM (2021). Combining exome/genome sequencing with data repository analysis reveals novel gene-disease associations for a wide range of genetic disorders. Genet Med, 23(8): 1551-1568. PMID 33875846. **Link to article**
- Biela M (2022). Further Delineation of Developmental Delay with Gastrointestinal, Cardiovascular, Genitourinary, and Skeletal Abnormalities Caused by ZNF699 Gene Mutation. Genes, 13(2). PMID 35205213. **Link to article**
- Karimi K (2024). Epigenomic and phenotypic characterization of DEGCAGS syndrome. European Journal of Human Genetics, 32(12): 1574-1582. PMID 39424669. **Link to article**



Inform Network Support

Rare Chromosome Disorder Support Group
The Stables, Station Road West, Oxted, Surrey, RH8, 9EE, UK
Tel: +44(0)1883 723356
help@rarechromo.org I rarechromo.org

Join Unique for family links, information and support:

Become a member

Please help us to help you!

Unique is a charity without government funding, existing entirely on donations and grants. If you can, please make a donation:

Donate via our website

Websites, Facebook groups and other links:

There are currently no know support groups for ZNF-related syndrome (2026)

This guide was reviewed by Dr. Sofia Douzgou Houge MD, PhD, FRCP, Senior Consultant in Medical Genetics at Department of Medical Genetics, Haukeland University Hospital, Bergen, and Frambu and Brain Disorders unit, Norwegian National Centre for Rare Diagnoses, Oslo, Norway.

This guide was produced as part of a collaborative project between the Manchester Rare Condition Centre, Shorthills AI and Unique (AP/CA). We thank the North West Genome Medicine Service Alliance for supporting the project.

Version 1 (AP/CA) [2026]

unique

UNDERSTANDING GENES
& CHROMOSOMES

rarechromo.org