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UNDERSTANDING GENES & CHROMOSOMES

GenIDA

ZTTK syndrome (SON-related syndrome)

rarechromo.org

This guide is designed to help families and healthcare professionals looking after people with ZTTK syndrome (SON-related syndrome). 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 ZTTK syndrome?

ZTTK syndrome, which is short for Zhu-Tokita-Takenouchi-Kim syndrome (named after the doctors who first recognised the condition), is a rare genetic condition associated with developmental delay, intellectual disability, behavioural differences, seizures, short stature, changes in vision, changes in the structure of kidneys and the bladder, and loose (hypermobile) joints. As is common with genetic conditions, each person can be affected differently - even among affected members within the same family. Not everyone with ZTTK syndrome will have all the possible features and each person with a certain feature won't necessarily be affected by it to the same level as other people with that feature.

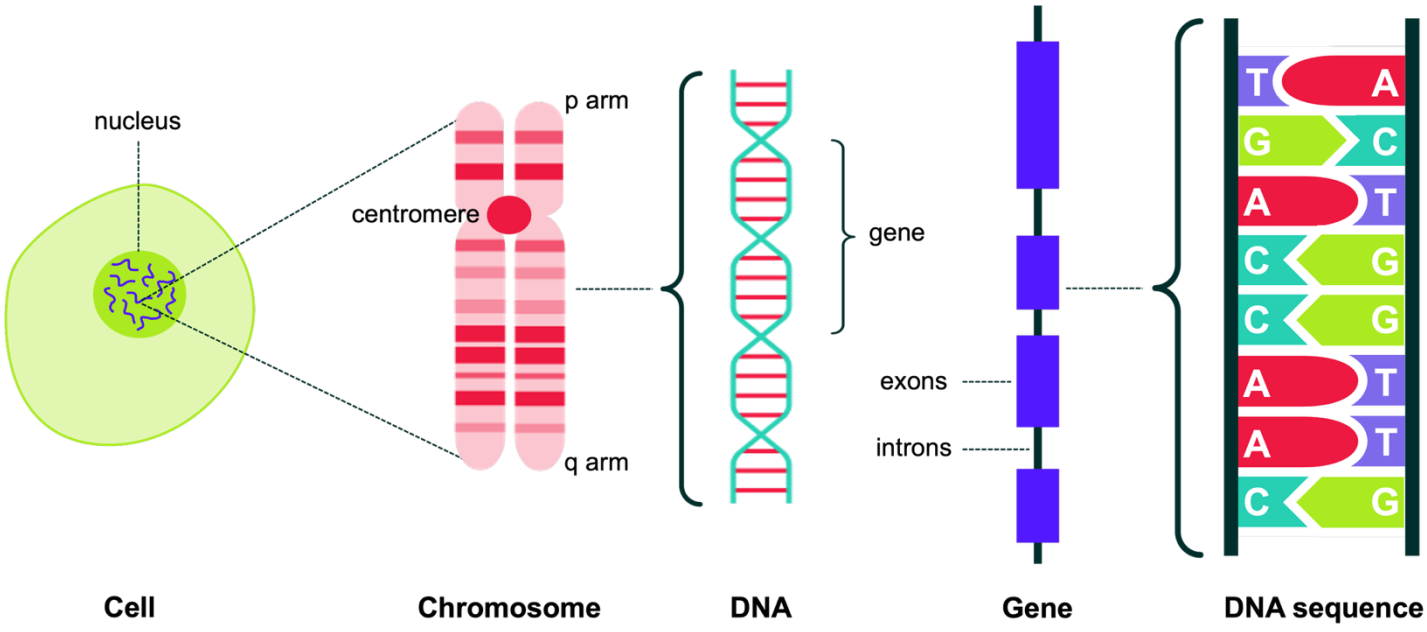
ZTTK syndrome is caused by changes (variants) in the SON gene that disrupt gene function and is also known as SON-related syndrome.

What causes ZTTK syndrome?

Genes are instructions that 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 we would expect, which can lead to changes in how their body works.

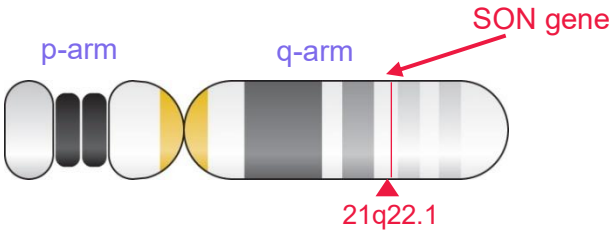
DNA is made up of building blocks called 'bases' or 'nucleotides'. There are four DNA bases which can be abbreviated to the letters A, C, G, and T. These DNA bases are paired up in the DNA structure into 'base-pairs'. The full sequence of our DNA is over three billion base-pairs long. There are changes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

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



The SON gene is located in the long 'q' arm of chromosome 21 in a region called 21q22.11 as shown in the image below.

Chromosome 21



We have two copies of chromosome 21 in our cells, so we also have two copies of the SON gene. ZTTK syndrome occurs when only one copy of the SON gene is affected; the second copy is fully functional. This is known as autosomal dominant since all numbered chromosomes are called autosomes and genetic conditions that occur when only one copy of an autosomal gene is affected are known as dominant.

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

The SON gene sequence is used to make the SON protein. The function of the protein in the body is not fully understood but it is known to interact with a number of proteins important for brain development and metabolism.

Genetic Tests

ZTTK syndrome is caused by gene sequence variants and can be identified by a type of genetic test called sequencing (e.g. whole exome sequencing (WES) or whole genome sequencing (WGS)).

Unique publishes separate guides to DNA sequencing

Genetic Test Results

The results of genetic (genomic) testing are likely to be given to you by your geneticist, a genetic counsellor or the clinician who ordered the test.

An example result of a DNA sequencing test (e.g. whole exome sequencing (WES) or whole genome sequencing (WGS)), that can identify gene variants, is shown on the next page for the SON gene.

c.1010C>T p.(Trp337Ser) (W337S): in exon 3 of the SON gene (NM_138926.3)

C>T	signifies the gene sequence change; the C nucleotide has been replaced by a T nucleotide
c.1010	signifies the base pair position of the change within the gene sequence (the position where the C nucleotide has been replaced by the T nucleotide)
p.(Trp337Ser) (W337S)	signifies the change to the protein: the amino acid Tryptophan (Trp) has been replaced by the amino acid Serine (Ser) at position 337 in the sequence of amino acids that make up the protein
exon 3	signifies which part of the gene has been altered, in this case exon 3
SON gene	signifies the gene that is affected
NM	denotes the reference sequence used

Unique publishes a separate guide to Interpreting Genetic Test Results

What features and symptoms do people with ZTTK syndrome have?

As is common with many genetic conditions, children and adults with ZTTK 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 most children with ZTTK syndrome have:

- Some degree of developmental delay, ranging from mild to profound
- Some degree of intellectual disability (ID) or learning difficulties (LD), ranging from moderate to severe
- Speech and language delay
- Behavioural differences
- Sleep disturbance
- Feeding difficulties, which usually resolve in early childhood
- Subtle distinctive facial features
- Low muscle tone (hypotonia)
- Loose joints (hypermobility)
- Movement disorders
- Growth delay
- Poor weight gain and short stature
- A small head size (microcephaly)
- Visual impairments and squint (strabismus)
- Brain anomaly
- Seizures
- Skeletal anomalies (scoliosis, joint contractures)

Other possible features include:

- Changes in the shape of the heart
- Gastrointestinal difficulties, including vomiting, reflux, and diarrhoea
- Anomalies of the kidneys and genitals (urogenital anomalies)
- Hearing loss
- Immunodeficiency leading to recurrent infections

Pregnancy and birth

While most pregnancies carrying a baby with ZTTK syndrome are unremarkable and proceed without complication, some features during a pregnancy can be detected, typically following mid-pregnancy anomaly scans.

Many babies show some signs of difficulty at birth, related to feeding. Birth weights are likely to be lower than average. Some new-born babies may be described as “unusually inactive”, a feature that may alert doctors to an underlying condition.

> ***Difficult to establish feeding and with gaining weight. Diagnosed with torticollis [when a baby's neck muscles cause their head to twist and tilt to one side] in the newborn period. Fontanelle closed prematurely.”***
>
> ***“Single umbilical artery and kidney issues.”***

Appearance

Certain facial features are found more often in children with ZTTK syndrome than in other children. These features may mean that you see unexpected similarities between your child and others with ZTTK syndrome. The facial features vary greatly, but the most noticeable features are usually around the eyes. The most common features include facial asymmetry, a prominent forehead, increased distance between the inner corners of the eyes, up- or down-slanting palpebral fissures (the openings of the eyes), unusually straight eyebrows, and a broad, flattened nasal bridge. Some also have low-set ears and a short philtrum (the groove between the nose and the upper lip).

Development

Gross and fine motor skills

Developmental delay has been reported in all children with ZTTK syndrome so far (2025). The degree of delay ranges from mild to severe, with most having moderate delay. Developmental “milestones”, including rolling, sitting, walking, playing with toys, using cutlery, using zips and buttons, and toilet training, are often delayed, although there is a wide range of eventual ability, with some children acquiring mobility and other skills around the same age as “typical” children and others showing more obvious delay. Some children have been reported to experience loss of previously acquired milestone and skills (developmental regression).

Low muscle tone (hypotonia) and loose (hypermobile) joints are common and may affect mobility. Contractures (restriction of the joints in which they cannot be fully extended), which are uncommon in ZTTK syndrome, may also affect movement. Some children may have an unusual gait when walking because of low muscle tone or balance issues (known as ataxia). A tremor and unusual movements (dystonia) have been seen in a small number of people. Many benefit from early intervention with treatments or therapies such as orthotics e.g. insoles, braces, splints and callipers; occupational therapy (OT); and physiotherapy (PT).

> ***He sat at 8 months and walked independently at 2 years. [He has] hypotonia with joint laxity. As a baby he tended to have a clenched fist and press his head to something, which he still likes. He always had a right-hand preference and tended to mirror his hand movements."***

**** "[At 5 years she] requires constant care and supervision. She is getting stronger and able to do more things everyday, but at the present moment she requires someone else to do all of her personal care, diaper changes, tube feedings, and medicines. She enjoys running, even though she falls a lot. She also really loves books and story time [and] music of all genres. [She also] loves to ride a bike and dig in the dirt."***

**** "Hypermobility of joints."***

**** "[At 3 years] he is great at parallel play with siblings. He loves to sing songs and is getting better about pronouncing the words correctly. He is able to identify objects, animals, family members, clothing pieces and vehicles."***

Unique publishes separate guides to Therapies and Toilet training and continence

Intellectual development and learning

All children with ZTTK syndrome have intellectual (learning) disability (ID) or learning difficulties. ID ranges from mild to severe but is usually in the moderate range and most children have needed additional support with their learning. Early intervention can prove particularly beneficial and formal testing to assess specific, individual needs is recommended.

> **** He is eligible for special education services as a student with a hearing impairment, in addition to a developmental delay in the areas of communication and physical development. He receives speech therapy for expressive and receptive language, occupation therapy, physical therapy, Hearing Assistant and FM Transmitter and personal care aide services."***

**** "[She] has intellectual and global developmental delays, as well as many sensory needs. She has a full IEP (Individualized Education Plan) and attends a specialized school where she receives all necessary supports, therapies, and services."***

"Moderate ID."

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

Speech and language

Children with ZTTK syndrome typically experience some degree of speech and language delay and some may find it difficult to co-ordinate movement of their lips, jaw and tongue to make the right sounds (apraxia of speech). The eventual range of achievement is broad, but a few may remain non-verbal. Those who do develop speech may achieve single words, short phrases or basic sentences and some go on to develop conversational skills and a broad vocabulary. Many parents believe that their child can understand a lot more than they can express.

An assessment by a speech therapist should be able to identify your child's specific difficulties, allowing regular therapy sessions tailored to your child's specific areas of need. Where individuals have no speech or very few words, Augmentative and Alternative Communication (AAC) methods, including pointing, pictograms, gestures, facial expression and simplified sign language and high-tech communication systems (aided communication) may help some to communicate their thoughts and needs well.

> **** He understands a lot more than he can express. He has a hearing loss on top of his syndrome, which was diagnosed late so his language articulation is behind for his age."***

"Said his first words that we could understand at 2 years."

**** "[At 5 years] she can clearly understand much more than she can express. She will respond to her name, and she can follow simple commands (when she wants too). She will use a variety of gestures, sometimes will sign, and uses a device. She can say a few words."***

**** "[At 3 years] he speaks in 4-word sentences regularly. He does extremely well with keeping his hearing aids and glasses on without the issue of taking them off."***

Unique publishes a separate guide to Communication

Feeding

Feeding issues in the new-born period are common. Low muscle tone may contribute to difficulties with swallowing, and some babies will suck weakly and may need high energy milks to encourage weight gain. Some babies also suffer from gastro-oesophageal reflux (GERD/GORD) (in which feeds return readily up the food passage), which may require treatment, including careful positioning for feeds, medication, nutritional supplements or, in some cases, insertion of a nasogastric tube (NGT) or percutaneous endoscopic gastrostomy tube (PEG/G-tube). Other issues that have been reported include aspiration (where fluid, food or saliva enters the airway or lungs). Some children have benefited from attending a feeding clinic where an assessment can be made, and advice to help treat any eating and drinking difficulties provided.

> ****Failure to thrive, tube feedings."***

Unique publishes a separate guide to Feeding

Growth and stature

Many children with ZTTK syndrome described in the medical literature so far (2025) are noted as having a small head size for age (microcephaly) and short stature. A few have been found to have growth hormone deficiency. Beyond infancy, height and weight is variable but typically remains below average.

> *[As a 12-year-old he is in the] lower 0.4th centile. He has an asymmetrical head size with relative macrocephaly [larger than expected head size for age. Hypothyroidism for a period of time. Growth hormone deficiency."*

Behaviour

Parents and clinicians often describe children with ZTTK syndrome as loving, determined and affectionate. However, this sociable nature often coexists with neurobehavioral challenges, including sleep disturbance, autism spectrum disorder (ASD), anxiety, emotional dysregulation and aggression. Challenging behaviours are not a reflection of a child's character but often stem from underlying difficulties with attention, anxiety, or sensory processing.

Understanding this complex profile is key to providing effective support. Management strategies should focus on addressing the root causes of challenging behaviours - such as providing sensory supports, using strategies to manage anxiety, and creating structured environments to help with attention - while nurturing the child's inherently friendly and sociable personality.

> *Sensitive to light and noise."*
>
> ** "Light and inconsistent sleeper."*

Unique publishes separate guides to Challenging Behaviour and Sleep

Adulthood

Experiences of adulthood are likely to vary considerably and will depend on many factors. These include the level of intellectual disability and / or learning difficulty, possible on-going medical concerns and improvements in early intervention and therapies/treatments. Adults with ZTTK syndrome have varying levels of independence.

Studies on a small number of adults known to have ZTTK syndrome have shown that they are more likely than the general population to have early-onset high blood pressure (hypertension).

Unique publishes separate guides to Puberty and Transition

Medical concerns

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

Brain

Many children have a structural brain anomaly, which can be detected by an MRI (magnetic resonance imaging) scan of their brain. The changes seen vary from person to person. The following changes are among those that have been seen in people with ZTTK syndrome:

- Underdevelopment (hypoplasia) of the white matter connecting the two halves of the brain (corpus callosum)
- A less developed part of the brain known as the cerebellum (cerebellar hypoplasia)
- Thinning of the corpus callosum
- Enlarged fluid-filled cavities in the brain (dilated ventricles)
- Changes in the folding of the brain (gyration pattern) (More rarely) atypical tissue connections of the brain (atypical white matter)

> ***MRI showed white matter volume reduction and Chiari malformation, with likely developmental supratentorial ventriculomegaly."***

**** "MRI revealed partial agenesis of the corpus callosum, polymicrogyria, periventricular leukomalacia, white matter loss, thin pituitary gland, thin optic nerves and asymmetrical ventricles."***

Seizures

About half of all children with ZTTK syndrome experience some form of seizure (a sudden and unexpected change in the electrical activity in the brain). Depending on the part(s) of the brain affected, symptoms vary, but include temporary confusion, uncontrollable jerking movements and loss of consciousness or awareness. Age of onset can vary considerably, while seizures may be isolated to a single incident or occur more regularly. More than one type of seizure may be present in the same individual. Electroencephalograph (EEG) and video telemetry (video EEG) are medical tests that can be used to measure and record the electrical activity of the brain and are tools that, when used alongside other tests, can help diagnose the type of seizure experienced.

Seizures can cause a lot of worry for families and can be frightening to observe, but in the majority of cases they self-resolve or resolve with medical treatment. There have been no studies on what anti-seizure medication works best for ZTTK syndrome, but successful seizure control in ZTTK syndrome has been achieved with levetiracetam, carbamazepine, and clobazam.

If your child has a seizure for the first time, it is important to remove nearby hazards so they can't hurt themselves and contact a medical professional.

Many types of seizures have been seen in ZTTK syndrome. Febrile seizures are the most common, but there is otherwise no predominant seizure type. Seizure types include:

Febrile seizure Episodes only occur when the child has a high temperature.

Absence seizure A change in behaviour as if the child 'switches off', sometimes with staring, eyelid flickering or lip smacking. Absences are very brief often lasting less than half a minute.

Infantile spasm Type of seizure usually occurring in clusters in babies between 3-10 months. Seen most often when a baby wakes and may be obvious or subtle.

Generalised tonic clonic At the onset of a seizure, the abnormal electrical activity involves both sides of the brain. The seizure involves a phase of stiffening followed by jerking.

Myoclonic generalised seizure Involving jerky or shock-like contraction of different muscles anywhere in the body but usually the arms or legs. Each myoclonic seizure lasts for a fraction of a second or a second at most.

Myotonic Seizure involving stiffening of the muscles.

Myoclonic-atonic Seizure involving jerky or shock-like contraction of muscles, followed by a loss of tone so someone standing up falls to the ground.

Heart

Changes in the shape of the heart conditions have been found in some people reported so far with ZTTK syndrome, which are present at birth (congenital). In children for whom heart problems are suspected, these can be diagnosed using tests like an echocardiogram (ultrasound scan of the heart). Most often these 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))
- Failure of closure of the tube that carries blood between the aorta and the pulmonary artery during the foetal period (persistent ductus arteriosus (PDA))

Bicuspid aortic valve, murmur at left sternal border."

Constipation

Constipation and other gastrointestinal difficulties are common among children with ZTTK syndrome and can be related to low muscle tone, little exercise, a low-bulk diet and small fluid intake, among other reasons that are not fully understood. It is important that possible causes are discussed with a health visitor or doctor, who may recommend adapting diet or giving stool softeners or laxatives. Some children have benefitted from enemas when symptoms were particularly severe.

Eyes and sight

Problems with eyes and vision are common in children with ZTTK syndrome. A wide range of conditions have been reported, and an individual may have more than one vision or eye-related concern. This is most commonly long-sightedness (hypermetropia), which can usually be corrected by glasses; a squint (strabismus), where one eye or both turns inward, outward, up or down, which may be treated with patching, glasses, exercises or surgical correction; or a change in part of the brain which processes visual signals leading to vision loss (cortical visual impairment).

He has left anisometropia [when there is a significant difference in vision between the eyes] with small exophoria [where one or both eyes drift outward when focusing, for instance when using a screen]. He has had glasses since he was 2 years old."

Spine and bones

A few babies are born with or develop a spinal curvature, either a sideways curve of the spine (scoliosis), a rounding of the upper back (kyphosis) or kyphoscoliosis (a combination of kyphosis and scoliosis). The curvature can be treated with physiotherapy and exercises, or a support brace or surgery may be needed.

A few babies with ZTTK syndrome have been born with a change in a vertebra (the bones of the spine), in which only one half of the bone forms (hemivertebra). This may exacerbate scoliosis, but is otherwise usually not harmful.

Sometimes, other changes in the skeleton can be seen, such as abnormalities of the limbs, hands, feet and ribs.

> *Vertebral abnormalities."*

Joints

Joint anomalies are a known feature of ZTTK syndrome. These include extremely loose (hyper-mobile) joints (elbows, wrists, knees, hips), which mean babies and children can move their limbs into positions others find impossible. While this may cause no problems, hyper-mobility is sometimes associated with pain and stiffness in the joints and muscles, joints that dislocate (come out of position) easily, and injuries including sprains. Children with very loose joints may need physiotherapy, massage or additional braces (supports, splints) before they are able to walk. In a few cases, joints are unusually tight and may require surgery and tendon lengthening to extend their range of movement.

Palate

Rarely, anomalies of the roof of the mouth (palate), ranging from those that may be invisible to the casual onlooker such as a high or arched palate to more obvious conditions such as a cleft palate, have been reported. Anomalies of the palate, particularly clefting, can cause difficulties in feeding, hearing, teething and speech production. Surgical repair eases these problems and may even eliminate them altogether.

Kidney and urinary tract

Some babies are born with anomalies of the kidneys or urinary tract. Reported anomalies include horse-shoe kidney, where the bottom points of the two usually separate kidneys are joined, creating a U (horseshoe) shape; absence or small size of one kidney; and other structural changes in one or both kidneys. These can usually be identified on an ultrasound scan of the kidneys.

Urinary tract infections (UTIs) are relatively common and may need to be treated with antibiotics. Repeated urinary infections may require preventive treatment with antibiotics. Kidney (urethral) reflux, where urine flows upwards from the bladder back up to the kidney, potentially damaging the kidneys and leading to frequent UTIs, has also been recorded.

> *Bilateral vesicoureteral reflux (VUR)."*
>
> * *"Right kidney is slightly smaller than left."*

Hearing

A few children experience hearing loss. It may be possible to manage hearing loss using hearing aids. A few children experience "glue ear", where fluid builds up behind the ear drum, which may be made worse by unusually narrow external ear canals and excess wax in the ear canal. Glue ear is a type of conductive hearing loss and is typically treated by inserting aeration tubes (grommets) into the eardrum. 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

How common is ZTTK syndrome?

ZTTK syndrome is extremely rare. Currently [2025], about 80 individuals with a SON gene variant have been reported in the medical literature, but more are known to have been diagnosed (the ZTTK SON-Shine Foundation estimates that 450-500 affected individuals have been diagnosed worldwide (2025)).

It is expected that more people will be diagnosed with this condition as awareness increases and genetic testing becomes more routine.

Why did this happen?

When children are conceived, their parents' genetic material (DNA) is copied in the egg and sperm that makes a new child. The biological copying method is not perfect, and random changes occur in the genetic code of all children, that are not seen in the DNA of their parents. This happens naturally and is not due to the parents' diet, environment or lifestyle. Most of these DNA changes have no obvious effect. But in rare instances these random DNA changes can lead to health issues or affect development. When such a random change disrupts the function of the SON gene then a child will have ZTTK syndrome. In almost all people identified so far [2025] with ZTTK syndrome, the genetic change was a random (or "de novo") change, meaning the change occurred for the first time in that family in the affected individual.

Can it happen again?

The possibility of having another child affected by a rare gene disorder depends on the genetic code of the parents. Almost every reported case of ZTTK syndrome so far [2025] is de novo, or new, meaning it was NOT inherited from the parents. For individuals with de novo variants neither parent was found to have the same SON gene change as their child and therefore the chance of having another child with ZTTK syndrome is usually less than 1%.

In families where the SON variant has been inherited from a parent, the possibility of having another child - either a girl or a boy - with ZTTK syndrome rises to 50% (1 in 2) in each pregnancy. However, the effect on the child's development, health and behaviour cannot be reliably predicted. Your genetics centre should be able to offer counselling before you have another pregnancy.

If your child with a SON variant goes on to have children of their own, the chances of passing on the variant to their child are 50% in each pregnancy. Your child's ability to look after their own child is very likely to be closely related to their own learning ability and behaviour.

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

Can ZTTK syndrome be cured?

There is no current cure for ZTTK syndrome since the effects of the genetic change took place during a baby's formation and development. However, knowing the diagnosis means that appropriate monitoring and interventions can be put in place.

Management

No clinical practice guidelines for ZTTK syndrome have been published (2025). The following suggestions have been provided by clinicians, who have personal experience of managing/treating individuals with a ZTTK syndrome, to improve quality of life and reduce complications.

Children and adults with ZTTK 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 physiotherapy, occupational therapy, speech therapy and, if needed, behavioural therapy. Individuals may have evaluations with neurology, endocrinology, cardiology, ophthalmology, gastroenterology, urology and nephrology, depending on their features (see Supportive care).

Immediately following diagnosis

When not carried out as part of the diagnostic process, an evaluation of the features of ZTTK syndrome that are present in the child or adult who has been diagnosed with this genetic condition is recommended. These are likely to include developmental, neurologic, neuropsychiatric, ophthalmologic, audiologic and endocrine evaluations. An ultrasound scan of the heart (echocardiogram), kidneys and urinary tract is recommended. This can determine which of the features of ZTTK syndrome are present and how severe they are.

Supportive care

Children with ZTTK syndrome are likely to be under the care of a multidisciplinary team. The team should include a community or hospital paediatrician who can oversee care; monitor growth, development and behaviour; and link in with affiliated services. How a person with ZTTK syndrome is supported is likely to require co-ordinated care by a team of specialists, which may include:

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

Geneticist – a doctor who specialises in genetic conditions.

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

Cardiologist – a doctor who specialises in heart conditions.

Endocrinologist – a doctor who specialises in hormones and their effect on the body, as well as growth.

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

Nephrologist – a doctor who specialises in conditions affecting the kidneys.

Ophthalmologist – a doctor who specialises in conditions affecting the eyes.

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

Physiotherapist (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.

Specialist nurses and/or other healthcare professionals may need to systematically and comprehensively plan a child or adult's treatment.

Treatments and therapies

Early intervention can prove particularly 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 ZTTK syndrome but may include:

Physiotherapy for low muscle tone, which may include certain strengthening exercises and aid development of motor skills.

Occupational therapy for physical supports, such as splints, which may help with daily activities.

Speech therapy to aid speech development.

Feeding therapy to help improve coordination or sensory-related feeding issues.

Behavioural therapy for features of autism, ADHD, and anxiety, which can include structured therapies like Applied Behaviour Analysis (ABA) for/to help manage challenging behaviours, improve social skills, and develop coping strategies.

Medications may be prescribed depending on specific symptoms, such as gastrointestinal problems or seizures.

Diet, such as a high-fibre diet or stool softeners and/or laxatives may be recommended to help relieve constipation. Some benefit from enemas when symptoms are particularly severe.

Surgery and treatment for health concerns such as skeletal anomalies, heart conditions and kidney and urinary tract anomalies. The placement of a gastrostomy tube (G-tube) for severe, long-term feeding difficulties may be necessary to ensure adequate nutrition. Procedures to correct a squint (strabismus) and improve vision may be considered. Hearing aids may be helpful for some.

Surveillance

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

- Regular developmental and educational reviews
- Neurologic review for low muscle tone and movement disorders, as well as for seizures if these are present
- Regular ophthalmology review for visual changes
- Monitor hearing annually or as needed
- Consider an annual cardiac review if congenital heart disease is identified
- Consider an abdominal ultrasound and review for kidney and urinary tract abnormalities as needed
- Monitor growth. Consider a gastroenterology review if feeding is challenging, or if issues such as reflux or constipation become frequent
- Assessment of the need for social support, such as respite care and home nursing care, or genetic counselling and family planning advice

Research into new treatments for ZTTK syndrome

The genetic changes causing ZTTK syndrome affect development of the brain and other parts of the body even before birth. Although the brain continues to develop to some degree after birth, the extent to which ZTTK syndrome could be treated later in life, once a diagnosis is made, is not clear.

Research into improved treatments and management for various features of ZTTK syndrome, like low muscle tone, is ongoing. In addition, although ZTTK syndrome is a relatively rare condition, the SON gene is the subject of ongoing research. Furthermore, research into treatments such as gene therapies that could possibly correct the variants causing ZTTK syndrome, may help individuals with ZTTK syndrome in the future.

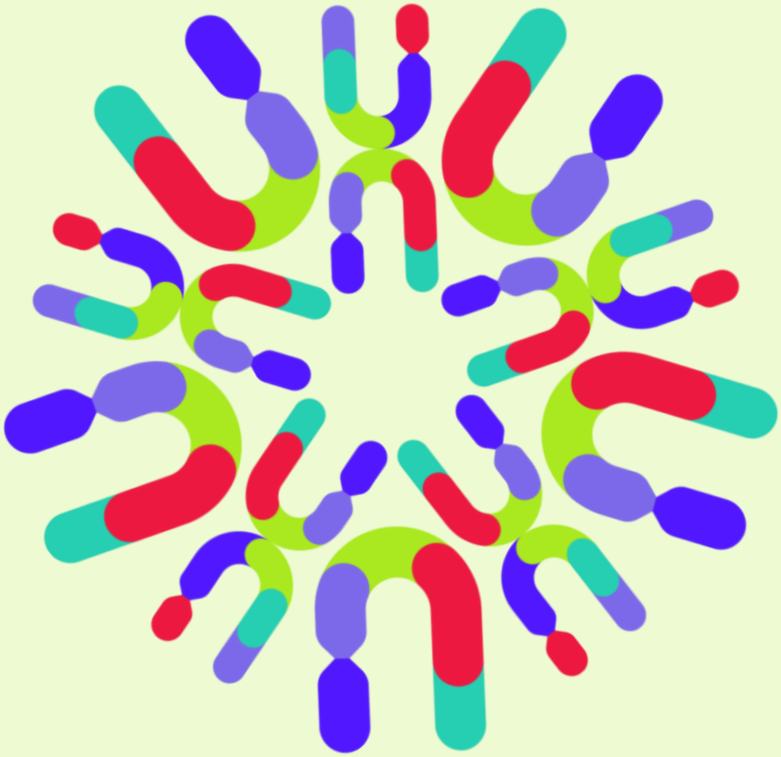
Details of clinical trials related to a particular condition or gene can be found at **ClinicalTrials.gov** and **EU Clinical Trials Register**.

Families say ...

"He is very loving, caring and he can be very funny too. He loves to cuddle, and he is friendly to everyone."

** "He has the motivation and determination to learn. He shows and is aware of his emotions, especially love. He has a contagious smile and laugh. He is a fighter and shows the world that having this disorder will not deter him."*

** "She is very clever and motivated. She is funny and loves to laugh. She also likes to make others laugh. She loves her family and her big brother, and she and her brother are very close. She is very joyful, and she is at her happiest when she is home with her family, on the swings or slides at the park, or eating ice cream. She brings abundant joy to our lives."*



Sources

The information in this booklet is drawn from the published medical literature and information from Unique members. In 2025, Unique had 11 members with ZTK syndrome. 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

Mori et al. (2025). Zhu-Tokita-Takenouchi-Kim Syndrome. GeneReviews® [Internet] Seattle (WA): 2025 Sep 25. **Link to article**

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Note: an asterisk indicates articles which are “open access” and available to everyone at **pubmed.ncbi.nlm.nih.gov**

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

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This guide was produced in collaboration with **GenIDA**

Facebook groups and other links:

- **ZTTK SON-Shine Foundation**
- **ZTTK SON-Shine Foundation Facebook group**
- **Simons Searchlight | SON**
- **Simons Searchlight SON Facebook group**

This information 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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Version 1.1.1 (CA) [2026]

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