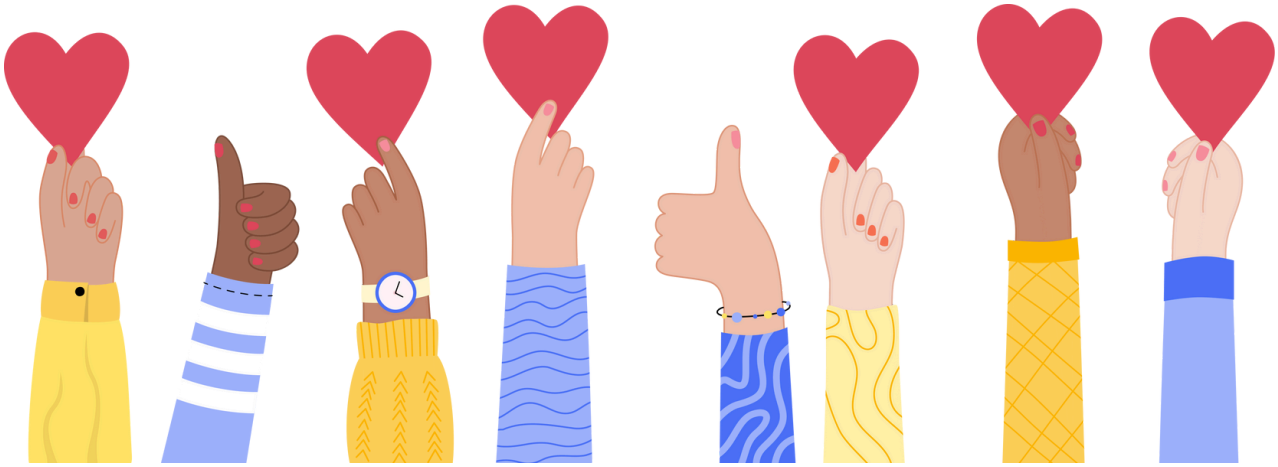
# Cure CLCN4 Welcome Pack

*Don't walk your journey alone.*



# A welcome message from Cure CLCN4

As you begin this journey with a *CLCN4*-related diagnosis, we warmly welcome you to our community. We understand the challenges and emotions that come with navigating this new terrain, and we are here to offer support, information, and connection.

In this welcome pack, you'll find a comprehensive guide to understanding the basic biology of *CLCN4*-related condition, recognising symptoms, and exploring management strategies. These resources are designed to empower and provide comfort as you take the first steps in managing this diagnosis.

In these pages, you'll also learn about Cure CLCN4—our mission, our work, and how we're making a difference. More importantly, you'll discover how to connect with our community, a group of families and experts who share experiences and provide strength to one another.

When you are ready, we invite you to engage more deeply with our efforts. Whether by participating in research, signing up for our patient registry, or contributing to fundraising initiatives, your involvement can drive crucial advancements and foster a stronger community.

Please remember, the information provided here is to support—not replace—the guidance of professional medical advisors. We urge you to discuss all health-related decisions with your genetic counselor or primary physician to ensure that your care is perfectly tailored to your needs.

You are not alone. We are here to answer your questions, help you connect with others, and support you throughout your journey with warmth and understanding.

With warmest regards,

Cure CLCN4

# Cure CLCN4:
# *Contents Page*



Make sure to check out the **glossary** for any terms or phrases you are unfamiliar with as you read through the booklet!

# Cure CLCN4: *About Us*

Cure CLCN4 is a UK registered charity aimed at providing **support**, raising **awareness** and, funding medical **research** for effective treatments for *CLCN4*-related condition. Cure CLCN4 was founded by Peter Trill and Gina Tan, the parents of Daphne, a little girl with *CLCN4*-related condition.

Click here to read our story

> ***Cure CLCN4 was set up with the goal of advancing the much-needed basic science and translational research in this condition. It is built on the foundation of hope and commitment, that one day there would be a cure for Daphne and children like her.***

## *Our Mission*

Our mission is to enhance the understanding and treatment of *CLCN4*-related condition through research, in addition to supporting affected individuals and their families, and driving awareness initiatives. We are committed to fostering collaboration among scientists, healthcare professionals, and communities to discover effective treatments and improve the lives of those impacted by *CLCN4*-related condition.

## *Our Vision*

Our vision is a world where a diagnosis of a *CLCN4*-related condition comes with hope and support, not uncertainty. We aim to transform the landscape of *CLCN4* research, ensuring that every family has access to precise, comprehensive information, effective *CLCN4*-specific therapies, and a supportive community. By connecting families with each other and with leading experts, we aim to build a strong network of advocacy and support, empowering individuals and their loved ones to face this challenge with knowledge and collective strength.

# Your Checklist

As you navigate this new chapter, we have put together a list of initial steps you can take to become more informed, supported and involved. Each action will help you connect with others, access valuable resources, and contribute to our joint understanding of *CLCN4*-related condition.

## Visit our website and follow us on social media

Our platforms provide information on *CLCN4*, research updates, community stories, and much more. Click on the icons to keep up with the latest news!

## Join the *CLCN4* Families Facebook Group

You can link up with other families living with *CLCN4*-related condition through a private Facebook support group so that you can share stories, and learn what has helped others.

Join now

## Sign up to our newsletter

Stay up to date with all the latest information by signing up for our newsletter. It's a great way to get regular updates directly to your inbox.


Sign up

## Sign up to the *CLCN4* Patient Registry

Contribute to *CLCN4* research by joining our Patient Registry. Your participation helps researchers gain a deeper understanding of the condition, and also gives you important updates on what we know about *CLCN4*-related condition.

Learn more

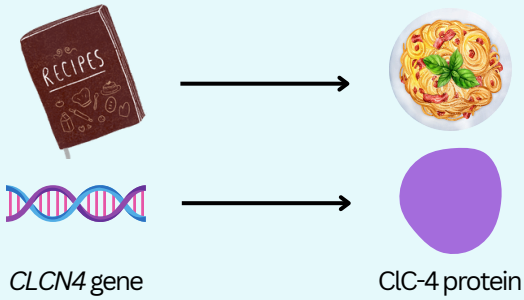
# *CLCN4*-related Condition: *Biology*

## *What is CLCN4-related condition?*

*CLCN4*-related condition is a rare genetic neurodevelopmental condition that can cause differences in learning, neurodiversity and health.

## *What is CLCN4?*

- ***CLCN4*** is a **gene** that codes for (gives instructions) the **production of the ClC-4 protein**.
- We are not sure what the **exact function** of ClC-4 is yet, but we know that it is important in helping our **brain develop and work**.




*Just like recipe books contain instructions to make a specific meal, DNA contains genes, which provide instructions for the production of a specific protein, a small molecule with a special job (function) in the body.*

## *What causes CLCN4-related condition?*

- *CLCN4*-related condition is caused by **changes** (also known as pathogenic variants) in the ***CLCN4* gene.**
- These changes affect the **function** of the ClC-4 protein, causing *CLCN4*-related condition.
- Changes in the *CLCN4* gene can be found by **genetic testing**.


## *Does CLCN4-related condition affect everyone the same?*

**No two individuals with *CLCN4*-related condition are the same**. The type and severity of symptoms depends on many factors including sex and the type of variant; even family members with the same genetic *CLCN4* change can experience a **different range and severity of symptoms**. It is important to know that although progress has been made in the last few years, we are **still learning about this condition**.

## *Does CLCN4-related condition affect both females and males?*

### *What do you need to know?*

- In humans, biological sex is determined by sex chromosomes. Females have two X chromosomes (XX), and males have one X chromosome and one Y chromosome (XY).
- The *CLCN4* gene is located on the X chromosome.
- This means that variations in the *CLCN4* gene can affect males and females differently, as females have two copies of the *CLCN4* gene, while males only have one copy.

- **Females and males can both be affected** by *CLCN4*-related condition, but the range and severity of symptoms can vary depending on their biological sex.

- Because males only have one X chromosome, meaning they only have one copy of the *CLCN4* gene – they have no 'back up' copy if they have a pathogenic variant in the *CLCN4* gene which affects the function of ClC-4. **Males with a pathogenic *CLCN4* gene change**, either inherited from their mother or due to a *de novo* (new) change, **will have symptoms of *CLCN4*-related condition** – but these can range widely in severity and frequency.

- For females, it is more complicated. The **impact on females often varies** depending on whether they are the first person in the family to have the *CLCN4* genetic change (*de novo*), or if they inherited the genetic change from a parent.

### *In summary...*

- Males with a pathogenic *CLCN4* variant always have symptoms.
- Females with a pathogenic *CLCN4* variant could be completely unaffected, have mild symptoms or more severe symptoms.
- Females are more likely to be affected if the gene change happened *de novo* (when they were conceived) rather than being inherited from a parent. We still have a lot to learn to understand this complexity better.

In most (but not all) females who are significantly affected the change in the *CLCN4* gene is *de novo* (meaning it has not been inherited and they are the first person in the family to have the genetic change).

Females who have an X chromosome with a *CLCN4* gene change (whether inherited or *de novo*) are often called 'carriers'. Female carriers may have no symptoms at all, or may have some symptoms of *CLCN4*-related condition, usually (but not always) on the mild end of the spectrum. Some female carriers may, for example, have mild learning or speech problems or an increased chance of mental health conditions (anxiety and/ or depression).

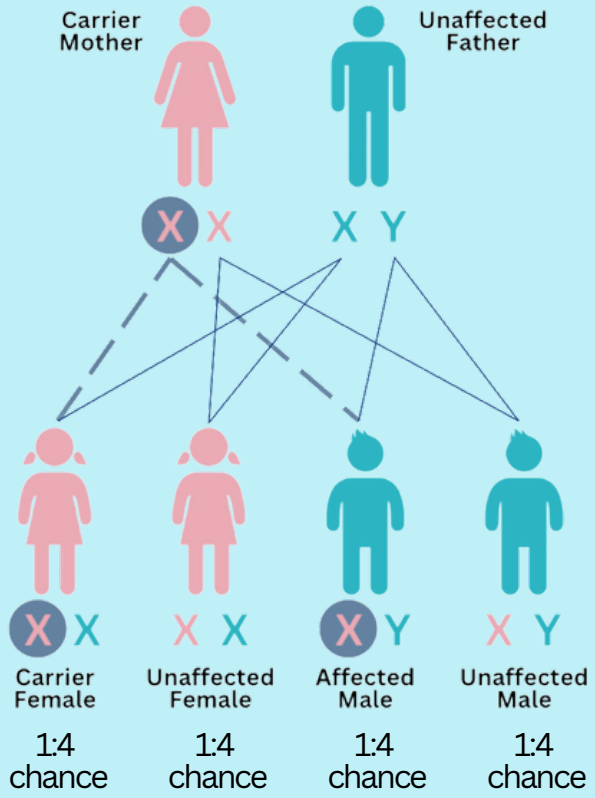
## What are the chances of a female carrier having a child with *CLCN4* related condition?

People with *CLCN4* or who are a carrier of *CLCN4* have choices when planning children and these options can be discussed further with a **clinical geneticist or genetic counsellor**.

When a female carrier is having children, for each pregnancy, there is a 50% chance of passing on the X chromosome with the working *CLCN4* gene and a 50% chance of passing on the X chromosome with the *CLCN4* gene change (see diagram below).

This means, for each pregnancy a female carrier of *CLCN4* would have:

- 1 in 4 (25%) chance of an affected boy.
- 1 in 4 (25%) chance of a female who is a carrier (may be completely unaffected or mildly affected).
- 1 in 2 (50%) chance of a child who is not affected by *CLCN4* and can not pass on *CLCN4*-related condition to their children.



# *CLCN4*-related Condition: *Diagnosis*

## *How is CLCN4-related condition diagnosed?*

*CLCN4*-related condition is **diagnosed via genetic testing**. A commonly used test is called 'whole exome sequencing', which reads an individual's DNA, and identifies changes or variants which may explain a clinical phenotype (symptom or set of symptoms).

Following testing, a detailed **genetic report** is provided, outlining the findings. It is **crucial** that this report is **reviewed and discussed** with an **experienced healthcare professional**, such as a genetic counsellor or clinical geneticist, who can help interpret the results, provide guidance on potential implications, and discuss possible next steps in management and care. They will also be able to help you with questions around inheritance of the condition and family planning.

## *Receiving the news*

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.

It can be overwhelming to understand your genetic report. That's why we're including an '**Understanding Your Genetic Report**' section in our upcoming Cure CLCN4 Deep Dive pack (December 2024). This will help you grasp the essentials of your report, but for detailed insights, consult a genetic counselor or experienced healthcare professional.

# *CLCN4*-related Condition: *Symptoms*

As you learn more about *CLCN4*-related condition, it's important to **familiarise yourself with its potential symptoms**. Here, we provide a list of previously observed symptoms. Remember, however, that their presence and severity can vary widely. Not every patient will experience all listed symptoms, and symptoms can vary widely, even in the same family. This information is intended to serve as a guide, helping you to be aware of possible symptoms so that appropriate care and preparations can be made. **By understanding what might occur, you can better advocate for and support your child's health needs**.

## Intellectual disability

Most males and most females with a *de novo CLCN4* change will have intellectual disability, that can range from borderline to severe. In females with an inherited *CLCN4* variant only about 25% will have an intellectual disability.

## Speech and language difficulties

Males: >95%
Females (*de novo*): 95%
Females (inherited): 15%

## Epilepsy

Males: 60%
Females (*de novo*): 25%
Females (inherited): 5%

## Microcephaly

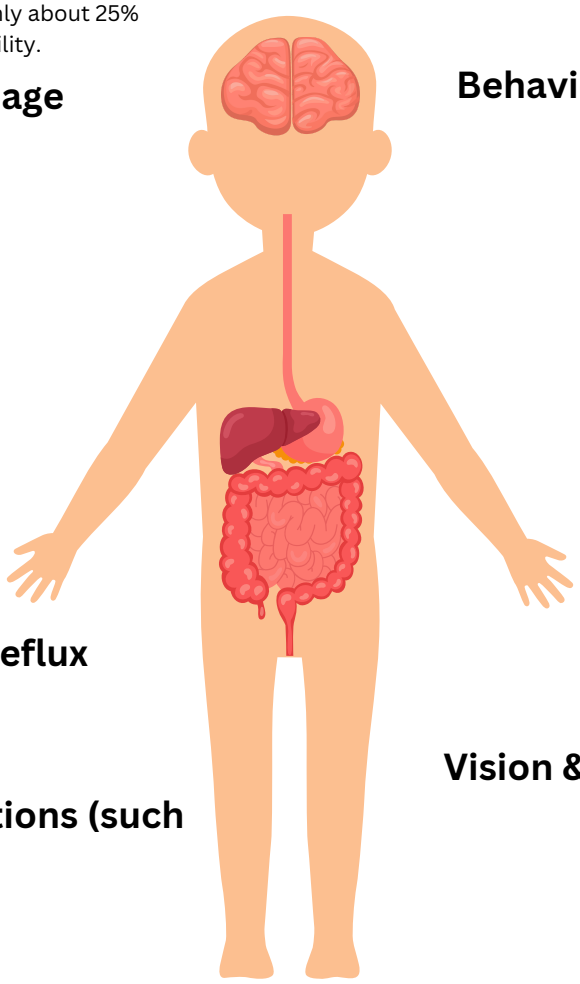
**(*smaller head size)**
Males: 20%
Females (*de novo*): 70%
Females (inherited): <5%

## Gastrointestinal reflux

Males: 15%
Females (*de novo*): 25%
Females (inherited): <5%

## Movement conditions (such as ataxia)

Broad observations across individuals: 10%



## Mental health conditions (e.g. Anxiety)

Males: 30%
Females (*de novo*): 45%
Females (inherited): 10%

## Behavioural conditions (e.g. Autism)

Males: 55%
Females (*de novo*): 40%
Females (inherited): 15%

## Feeding difficulties

Males: 20%
Females (*de novo*): 55%
Females (inherited): 10%

## Short stature

Males: 15%
Females (*de novo*): 30%
Females (inherited): <5%

## Constipation

Males: 15%
Females (*de novo*): 35%
Females (inherited): <5%

## Vision & Hearing Impairment

Males: 10%
Females (*de novo*): 15%
Females (inherited): <5%

## Sleep Issues

Males: <5%
Females (*de novo*): 25%
Females (inherited): <5%

***Percentages last updated February 2023 (Palmer et al., 2023)**

# *CLCN4*-related Condition: *Care*

*Your family's specific care team will depend on what the main symptoms of CLCN4-related condition are in your family and how they change over time. CLCN4-related condition can vary widely between individuals, so regular appointments with a paediatrician will help to identify any symptoms which may need* ***early intervention*** *and* ***specialist care*** *and help you get coordinated and proactive* ***care and support****.*

**Neurologist**

for seizures/epilepsy and uncoordinated movement (ataxia)

**Speech therapist**

for speech delay and language development

**Paediatrician**

for general care

## Who might make up your care team?

**Psychiatrist**

for mental health conditions (such as anxiety, depression, or bipolar disorder). Ideally experienced with neurodevelopmental conditions.

**Sleep physician**

for issues with falling or staying asleep

**Physiotherapist**

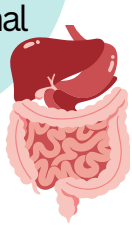
for low muscle tone (hypotonia)

**Opthalmologist**

for visual (eyesight) problems

**Neurogastro-eneterologist**

for digestive issues (e.g. constipation and gastrointestinal reflux)



**Endocrinologist**

for slow growth / growth delay

*It is very important to know that although we don't have a cure for CLCN4-related* condition *right now,* ***there is professional support available which will make a huge difference to your child's future health, development and wellbeing***.

Therapies are available for many of the complications that might develop in someone with *CLCN4*-related condition. Early intervention will help with your child's learning and social development and so it is important that these therapies are started as soon as possible.

There are three areas of particular importance for a good quality of life:

**Seizure control**
(if seizures are present)

**Mental health support**


**Sleep**

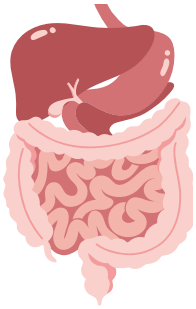
## *Resources - to share with your clinician*

- The *CLCN4* Gene Review - an excellent resource to share with your doctor and healthcare professionals! This publication contains up to date information about *CLCN4*-related neurodevelopmental condition including diagnosis, clinical characteristics, management and resources.

- A link to the Human Disease Gene Webseries site, where they can directly connect with our clinical and scientific specialists, Dr Emma Palmer and Dr Vera Kalscheuer.

# *CLCN4*-related Condition: *Frequently Asked Questions*

## Symptoms of *CLCN4*-related condition



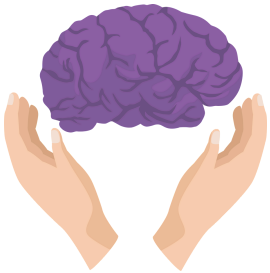
### Are there any feeding or gut issues related to *CLCN4*-related condition?

Gut problems are not uncommon, including gastrointestinal reflux and constipation as well as feeding difficulties. This is likely because *CLCN4* is important for the nervous system function, not just in the brain but also in the gut's nervous system. A gut that is slow or not working can lead to pain and discomfort, and it can be harder to sleep, eat and learn. If you have concerns ask for referral to a gastroenterologist (gut specialist).

### My child has very bad constipation. What can I do?

If your child has issues with opening their bowels on a regular basis, it is important that you visit a gastroenterologist. Although using laxatives can usually help with this issue there are other things that can be done to help your child open their bowels. It is important that this happens every second day or ideally every day, as constipation can cause other symptoms such as acid reflux or abdominal pain.

### Can seizures start at any age?



Approximately a third of individuals (see page 9 for further detail) with *CLCN4*-related condition develop seizures, which are usually well-controlled with standard anti-seizure medication. Seizures most commonly appear in the first 3 years of life, although there have been some cases with later onset (in adolescence).

### I am worried that my child will develop seizures. What can I do?

Be prepared. Learn what a seizure can look like and talk to your child's paediatrician about what to do if you see an unusual movement or pattern of behaviour. If you do see unusual movement/behaviour, record it on your phone so you can show your doctor. It is also helpful to stay up to date with first-aid courses.

## What do developmental milestones such as toilet training, speech, motor skills, etc look like in individuals with *CLCN4*-related condition?

People with *CLCN4*-related condition progress at their own pace, and no two individuals are exactly alike. This variation is observed even among siblings with the condition within the same family.

Importantly, and even more so with the availability of modern therapies, we generally see individuals continue to gain skills over time rather than losing them. The rate at which they develop these skills typically follows their previous developmental patterns. Therefore, we expect each child to continue advancing at their own unique pace.



## What steps should be taken to ensure that a child with *CLCN4*-related condition receives appropriate developmental support?

To ensure optimal development, it's crucial for the child to undergo a comprehensive developmental assessment. Based on this assessment, appropriate therapies should be accessed, including speech therapy, physiotherapy, and occupational therapy.

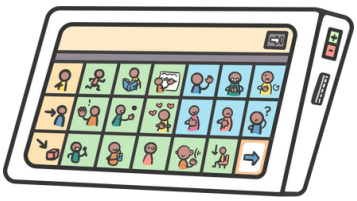


## Are speech & language usually affected in *CLCN4*-related condition?

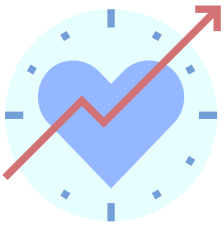
Research has shown that 100% of males with *CLCN4*-related condition and 95% of females with *de novo* variants* have speech & language difficulties. Affected individuals may be slower to learn to speak, may struggle to articulate or speak clearly and fluently and may need specialised support from a speech pathologist (*<15% of females with inherited variants have these difficulties).

## What can be done to help communication in individuals with *CLCN4*-related condition?

Even though many individuals with *CLCN4*-related condition may not be able to use words to communicate, they can still express themselves in other ways. It's crucial to consult a speech and language specialist who can evaluate your child and explore all potential communication methods. Augmentative and Alternative Communication (AAC) tools, such as iPads equipped with communication apps and devices that utilise pictograms for example, can be really helpful.



## Does *CLCN4*-related condition affect life expectancy?



Adults with *CLCN4*-related condition can have a long and full life. *CLCN4*-related condition affects the nervous system. It has not been found to affect vital organs (heart, liver, lungs) or life expectancy. For a good quality of life, three elements are key: mental health support, sleep and, if seizures are present, seizure control.

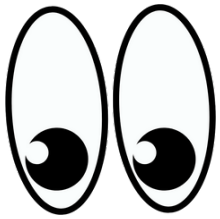
## Are hormone -related problems a feature of *CLCN4*-related condition?

*CLCN4*-related condition has not been found to be associated with hormone-related problems. However it is of course possible for someone with *CLCN4*-related condition to also have an unrelated hormone condition (such as thyroid problems). In such cases, there is no evidence that such hormone-related issues should be treated any differently in someone with *CLCN4*-related condition.

## Is growth affected in individuals with *CLCN4*-related condition?

Although growth is not affected in the majority of individuals with *CLCN4*-related condition we have found that a small subgroup of individuals, specifically females with a certain type of *CLCN4* variant tend to have a small head size and short stature. However we do not yet understand the reason behind this.

## Are vision and hearing affected in individuals with *CLCN4*-related condition?



Yes, vision and hearing can both can be affected, especially vision, so it is really important that they are screened for. They should be checked upon diagnosis of *CLCN4*-related condition, regularly during childhood, when entering adulthood, or if there are any reasons that make you believe your child can't see or hear properly.

# Genetics & biology of *CLCN4*-related condition

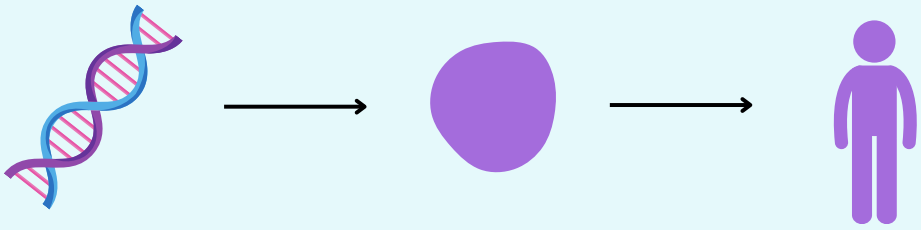
## How many people are there with *CLCN4*-related condition?

We don't know the real number of individuals with *CLCN4*-related condition. As of July 2024, 127 families have been published in the literature and we know of at least another 20 families that are currently unpublished. However due to factors such as the complexity of the condition and the lack of access to genetic testing in some parts of the world, the real number is likely in the hundreds, or even thousands.

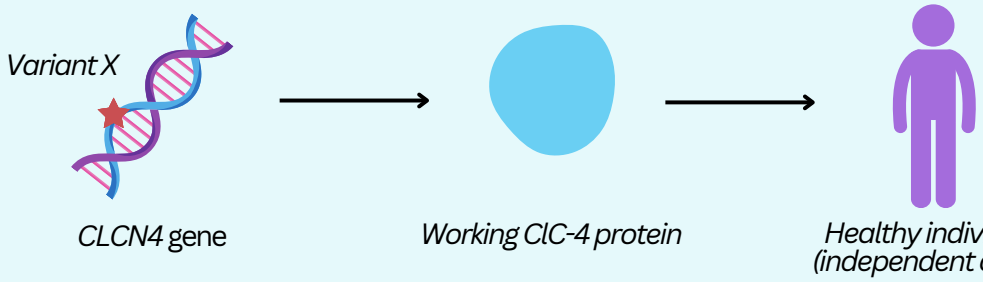
## Are all *CLCN4* variants pathogenic (do all *CLCN4* variants cause *CLCN4*-related condition)?

No. Not all *CLCN4*-variants are pathogenic. We know from population databases, which contain sequencing results from healthy individuals that the *CLCN4* gene can have benign changes which most likely do not affect protein function. We also know that in a small number of females a deletion of partial deletion of *CLCN4* does not lead to symptoms. Overall, whether a *CLCN4* gene change causes *CLCN4*-related condition depends on whether that specific gene change affects the function of the ClC-4 protein. Below are three scenarios to help you understand this:

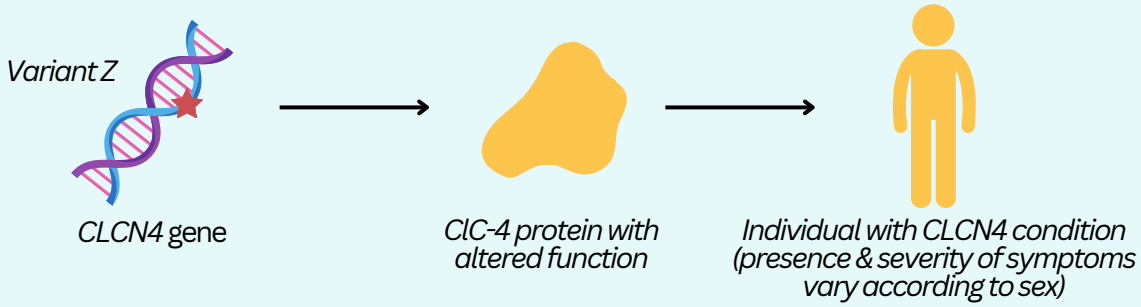
**(A) No changes/variants in the *CLCN4* gene**




**(B) Change/variant in the *CLCN4* gene with no effect on the ClC-4 protein (we call these non-pathogenic or benign variants)**




**(C) Change/variant in the *CLCN4* gene affecting the ClC-4 protein (we call these changes 'pathogenic variants')**



## My child has a variant of unknown significance, is this likely to change or is information too limited at the moment?

With more and more people being diagnosed with *CLCN4*-related condition, there is a low chance that we find the same variant in another child or family (known as recurrent). However, researchers are working to carry out studies on new *CLCN4* variants to understand whether variants of uncertain clinical significance affect the function of the ClC-4 protein, and therefore help understand whether the variant causes *CLCN4*-related condition or not. In addition, genetic testing of informative family members and clinical evaluations can provide further insights into the significance of the variant, aiding in more accurate diagnoses.

**Do you or a family member have a variant of unknown significance?**

Email us at info@cureclcn4.org ,and we will connect you with the research team investigating these variants.

## Is gene therapy a potential approach for *CLCN4*-related condition?

Gene therapy could be a potential approach for treating *CLCN4*-related condition. However, while promising, it's important to note that this would likely be a long-term possibility as the development and availability of gene therapy for *CLCN4* would require further scientific advancements on the basic biology of the condition as well as clinical trials to ensure safety and efficacy.


***Have more questions?***

Get in touch with us by emailing us at info@cureclcn4.org

# Living with *CLCN4*-related condition: *Teegan*

Teegan, born in 1986, defied expectations despite a diagnosis of *CLCN4*-related condition. Her journey, marked by challenges and victories, offers hope to others facing similar paths. Initially, her delays in speech and development raised concerns, but with early intervention, she began to communicate. Teegan thrived in a supportive special school environment, gaining confidence and skills. At 14, she embarked on work experience, becoming a trailblazer for inclusivity in the workplace. Later, she pursued further education, immersing herself in a self-sufficient community. Now aged 38, Teegan lives independently with her beloved three-legged dog, Fudge, enjoying hobbies like photography and baking. Despite complexities, her story is one of resilience, friendship, and determination, offering solace and inspiration to families navigating similar journeys. Teegan's aspiration to support others underscores her altruistic nature, epitomising the power of hope and community in overcoming challenges.

*"Teegan is on an incredible journey! From a little girl who didn't vocalise and barely communicated, to a young woman who is able to show deeper understanding than anyone ever thought possible!"*

**Click here to read Teegan's story**

# Living with *CLCN4*-related condition: *Ashley-Jai*

*"The diagnosis of CLCN4 did, of course, not redefine who Ashley-Jai is, a loving little boy with a love for numbers and the outdoors, but it provided his parents with an understanding as to why Ashley-Jai had certain behaviours and needs."*

Ashley-Jai, a gentle and inquisitive 9-year-old from southwest England, was diagnosed with a *CLCN4* gene variant in May 2020, discovered through the 100,000 Genomes Project. This diagnosis brought relief to his family, as it explained his symptoms like speech delay, autism, and sleep issues, providing insight into his behaviours and needs. Despite the diagnosis, Ashley-Jai remains a loving boy who enjoys numbers and outdoor play, especially spending time on his swing and watching Thomas The Tank Engine.

Ashley-Jai's vibrant personality shines through despite his challenges. He finds joy in simple pleasures like counting and exploring the outdoors. His love for Thomas The Tank Engine reflects his curious and imaginative nature. Ashley-Jai's family cherishes his gentle spirit and unwavering curiosity, seeing him as a beacon of love and resilience in their lives.

His mum, Dawn, navigates the complexities of caring for a child with *CLCN4*-related condition, advocating for increased awareness and support. She envisions a future where Ashley-Jai's condition is widely understood, eliminating the need for constant explanations and ensuring he receives the care and understanding he deserves. Ashley-Jai's journey highlights the importance of embracing individuality and fostering a supportive community for children like him.

**Click here to read Ashley-Jai's story**

# Living with *CLCN4*-related condition: *Gabrysia*

Gabrysia, a vibrant 5 year-old with blond hair and blue eyes, was born healthy in January 2019. However, concerns arose as she showed reluctance to lie on her tummy and had a slightly crooked foot. After consultations and physiotherapy, her developmental milestones were significantly delayed. At nine months, speech therapy was added to her regimen. Further worries prompted tests for spinal muscular atrophy (SMA), which came back negative, leading to genetic testing. Six months later, a diagnosis of a de novo *CLCN4* variant was confirmed, a rare condition with limited scientific understanding. Gabrysia's parents embraced various therapies, including psychological, sensory, physical, and speech therapy.

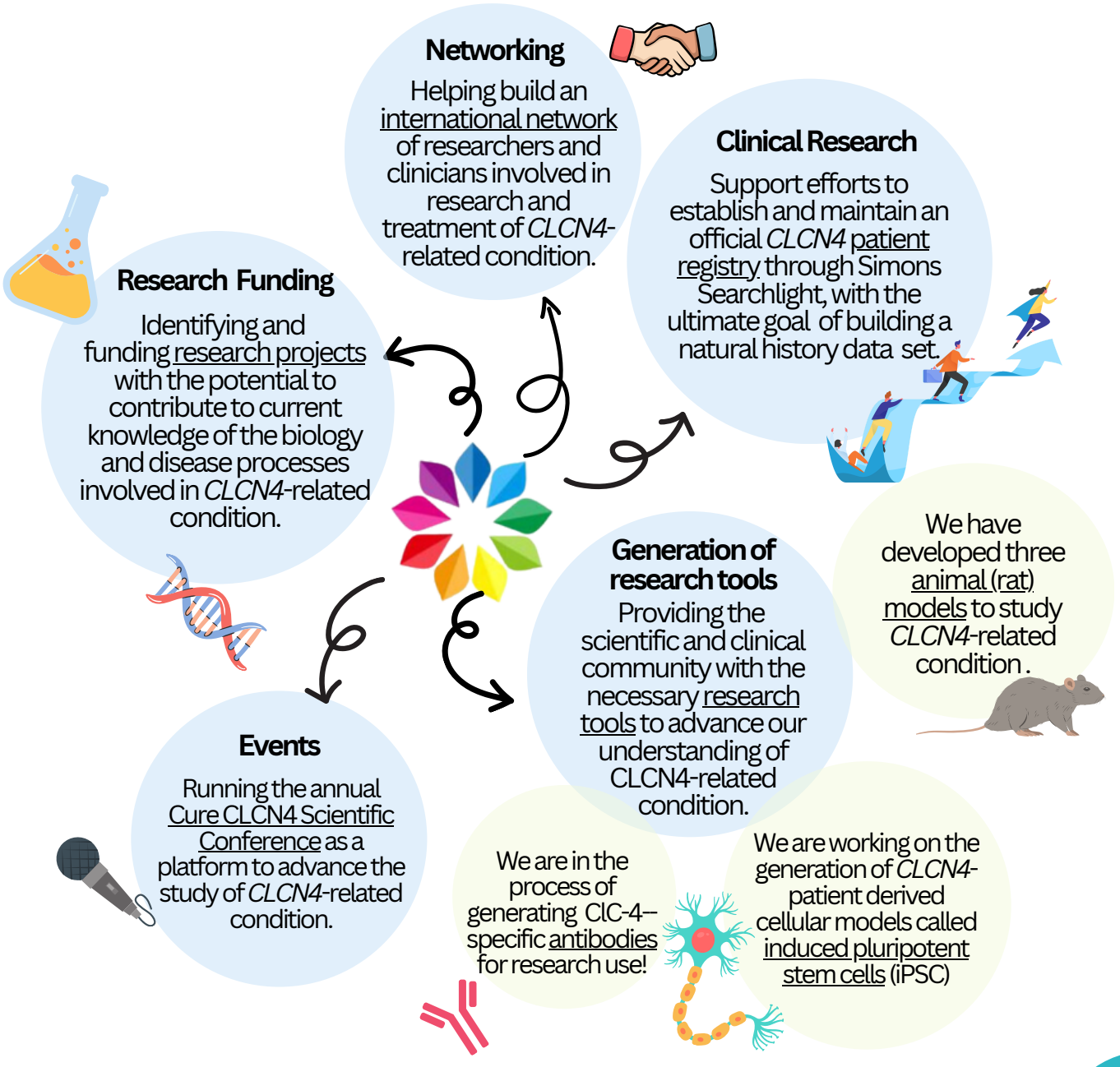
Despite the challenges, Gabrysia has made remarkable progress. She walks, communicates using words and gestures, imitates animals, and engages in activities like drawing and playing doctor. However, she struggles with concentration and balance. Despite uncertainties about her future, Gabrysia's family remains hopeful and dedicated to her well-being, emphasising the need for research to aid children like her with *CLCN4*-related condition. Gabrysia is described as sweet, empathetic, and curious, bringing joy despite the challenges she faces.

*"We hope for the best for her future. We pray for the strength as a family, to face the challenges that will be ahead of us. Only through research can my daughter and other children like her with CLCN4 be helped."*

**Click here to read Gabrysia's story**

# Cure CLCN4: *Making a Difference through Research*

*From animal and cell models to a patient registry and networking opportunities, our aim is to equip scientists with the resources to drive the research on CLCN4-related condition forward.*



# Join the Patient Registry

Without the **involvement of families** living with *CLCN4*-related condition, many of our **aims** would **not be possible**. One of the key ways you can **participate and drive research** is to **join the *CLCN4* patient registry!**

### *Need to know*

A patient registry is like a big filing cabinet that keeps **organised information** about people with a **certain health condition**. It includes details like medical history, family health, medications, and any changes over time.

## *Why are patient registries important?*

By looking at information from many people, researchers can spot patterns in how the condition behaves, how severe it can get, and which treatments work best. This **helps them understand the condition better** and make smarter choices in research. Essentially, patient registries are key tools for advancing medical studies in ways that really matter to patients and their families.

## *How does participating in the registry benefit me?*

Joining our patient registry directly benefits you as you will receive **quarterly reports** showing you the **latest information** on *CLCN4*-related condition, its symptoms, where in the world participants are & how your child or loved one compares to others in the ***CLCN4* community**!

**Click here to see the latest report**

## *How do I participate in the registry?*

Click here to join our patient registry!

The ***CLCN4* patient registry** is hosted by our trusted partner & collaborator **Simons Searchlight**.

**Participation** is very easy and **straightforward**. All you need to do is start the sign up process!

SIMONS SEARCHLIGHT
Driven by science. United by hope.


## *Other benefits of participating in the patient registry:*

### Amplify patient voices

The registry will ask you to give your **point of view** on **important matters** about your child. For example, asking for your view on which symptoms are most important to find treatments for, or which existing treatments you wish there was better information on. Sharing your point of view is **extremely powerful**, because it helps researchers learn how to best meet your needs.

### Improving patient care

As we learn more about *CLCN4*-related condition, we can provide **better information** and **treatments** to those **newly diagnosed**, especially since individual clinicians rarely see many cases. With each family that shares their experience and knowledge, more information will be added to the **knowledge bank, improving patient care**.

### Improving the chances of drug development

Drug development is hard, time-consuming and expensive. Drug companies are much more **attracted to develop new therapies** for rare disorder communities that already have **patient registries with useful data**. This saves them much time and expense, and allows for **greater chances of success** with regulatory approval.

# **Get involved:** *Other ways you can help!*

## Donate and fundraise

Donating and fundraising is a great way to **support us**, as it provides the **necessary financial resources** for us to achieve our aims of funding **scientific research** into *CLCN4*-related condition.

There are **many ways** in which you can help us fundraise, such as setting up a Facebook fundraisers to sponsor a run, hosting a bake sale or bingo night. **Click here** to explore more fundraising ideas!

## Raising awareness

Raising awareness about *CLCN4*-related condition is **crucial for our charity** and can be part of your mission too! You can help by following and sharing our social media posts, or by contributing your story to **our Community page**.

If you're ready to do more, consider giving a talk about *CLCN4* at your school, workplace, or a scientific meeting. We'll support you with presentation slides, the Cure CLCN4 logo, and other useful resources. Send us an email (info@cureclcn4.org) to find out more!


## Donate your time & skills

As a small charity, we are always incredibly grateful for **any time or skills families can donate**! For example, if you can speak multiple languages, then you can help by translating our website content and other resources.

# Available Resources

*In addition to the information provided in this document, here is a list of **other useful resources** available to you:*

## Learn more about *CLCN4*-related condition

**Cure CLCN4 website (www.cureclcn4.org)**

- Visit our website to understand more about *CLCN4*-related condition, Cure CLCN4's key aims, and much more!

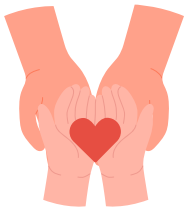
***CLCN4*-related Condition Factsheet**

- This factsheet provided by the Center for Genetics Education (Australia) for families affected by *CLCN4*, contains key information about the condition (genetics, symptoms, management), and much more!

## Connect with other families

**CLCN4 Families Facebook Group**

- A private group for the those living with *CLCN4*-related condition and their families. Join for an opportunity to connect with the rest of the *CLCN4* community. This group is not linked to or managed by Cure CLCN4.



## Resources to share with your doctor

**GeneReviews**

- An excellent resource to share with your doctor and healthcare professionals! This GeneReview publication contains information about *CLCN4*-related neurodevelopmental disorder including diagnosis, clinical characteristics, management and resources.

## Connect with us

**Follow us on social media**

**info@cureclcn4.org**


**Newsletter sign-up**

# Glossary

| Term | Explanation |
|---|---|
| Amino acid | Amino acids are small molecules which act as the building blocks of proteins, and are essential for the growth and repair of tissues in the body. |
| Animal model | An animal model is a living, non-human animal which is used by scientists to help them understand and find ways to treat diseases. |
| Antibody | An antibody can be used as a scientific tool to help scientists find and study particular proteins they're interested in, such as finding a lost toy (protein) in a big room (cell). |
| Anxiety | Anxiety involves experiencing excessive and persistent worry, fear, or nervousness that can interfere with daily activities and well-being. |
| Ataxia | As a symptom, ataxia presents as difficulty coordinating movements, often leading to unsteady walking, clumsiness, and problems with fine motor skills like writing or buttoning clothes. |
| Autism | Autism is a neurological condition that influences the way individuals interact, communicate, and experience the world, often leading to unique strengths and challenges in social behavior and communication. |
| Behavioural condition | Behavioural conditions are disorders that affect the way people act, making it challenging for them to control their actions or relate to others in typical ways. |
| Bipolar disorder | Bipolar affective disorder, or bipolar disorder, is characterised by extreme mood swings, involving periods of elevated energy and euphoria (mania) followed by episodes of deep sadness and low energy (depression). |
| Cell | A cell is like a building block of your body: a tiny, incredibly busy unit that performs all sorts of tasks to keep you alive and functioning. |
| Cell line / Cell model | A cell line is like a group of identical, well-behaved cells with a specific gene variant that scientists can keep in the lab and study to learn more about how diseases work or to test new medicines. |

# Glossary

| Term | Explanation |
|---|---|
| *CLCN4* | The *CLCN4* gene, made of DNA, acts as a recipe for making the CIC-4 protein, where the gene contains the instructions and the protein is the end product that carries out specific tasks in the body. |
| ClC-4 | ClC-4 is the protein made from the *CLCN4* gene, which acts as a transporter through which different substances can travel in and out of the cell. |
| *De novo* variant | *De novo* variants are new, spontaneous changes that occur in a germ cell (sperm or egg), or in the fertilised egg early during embryonic development, and are not inherited from their parents. |
| Depression | Depression involves persistent feelings of sadness, hopelessness, and a lack of interest or pleasure in activities, often accompanied by physical symptoms like changes in sleep and appetite. |
| DNA | DNA is like a biological instruction manual that contains all the information needed to build and operate your body. |
| DNA variant | A DNA variant is a change or 'glitch' in your body's instruction manual (DNA) - sometimes it has no effect at all, other times it can change the way we look or affect our health! |
| Epilepsy / Seizures | Epilepsy is a condition or symptom where the brain sometimes has sudden bursts of unusual electrical activity, causing a person to have seizures that can affect their body movements or awareness. |
| Exons | An exon is a part of a gene that contains the instructions for building proteins in the body. |
| Gene | A gene is like a recipe in your body's instruction book (DNA) that tells it how to make a specific protein, which does important jobs in your body. |

# Glossary

| Term | Explanation |
|---|---|
| Gender | Gender refers to the social, cultural, and psychological traits and behaviors that a society associates with men, women, and other gender identities. Unlike biological sex, which is determined by physical characteristics, gender encompasses a range of identities that do not necessarily align with binary notions of male and female. Gender identity is deeply personal and is about how individuals perceive themselves and what they call themselves. |
| Genome | A genome is all of a living creature's genetic material, like a blueprint containing instructions for how it grows and functions. |
| Hemizygous | Hemizygous refers to having only one copy of a particular gene e.g. genes located on the X chromosomes in males are hemizygous, as there is only one copy. |
| Heterozygous | Heterozygous means having two different versions of the same gene (alleles) at a particular genetic location. In a heterozygous genotype, each gene may have a different change or one of the genes may be mutated and the other one is normal. |
| Homozygous | Homozygous means having identical versions of the same gene (alleles) at a particular genetic location. |
| Inherited variant | Inherited variants are changes in genes that are passed down from parents to their children. |
| iPSC | An induced pluripotent stem cell (iPSC) is a type of stem cell that is artificially obtained from adult cells, like blood cells, and reprogrammed to a stem cell-like state. iPSCs can then develop into any type of cell in the body. To find out more, click here to see an infographic posted on our Instagram! |
| Mental health | Mental health refers to a person's emotional and psychological well-being, encompassing thoughts, feelings, and behaviours that contribute to a balanced and fulfilling life. |

# Glossary

| Term | Explanation |
|---|---|
| Microcephaly | Microcephaly is a condition where a person's head is smaller than expected for their age and gender, often indicating that the brain hasn't developed properly, or has stopped growing. |
| Movement condition | A group of neurological conditions that affect a person's ability to move smoothly, involving problems with speed, fluency, and coordination of voluntary movements. |
| Neurodevel-opmental condition | A neurodevelopmental condition is a condition that influences how the brain develops and functions, and can impact things like learning, behaviour, and communication. |
| Nucleotide | A nucleotide is a basic building block of DNA, consisting of a sugar molecule, a phosphate group, and a nitrogenous base, similar to a bead on a string forming the structure of DNA. |
| Pathogenic | Pathogenic means something that can cause a health condition or illness. |
| Pathogenic variant | A pathogenic variant is a change in a person's DNA that can cause or increase the risk of developing a health condition. |
| Patient registry | A patient registry is a helpful tool that stores information about people with a particular health condition, so that we can better understand it and find ways to treat it. |
| Phenotype | A phenotype is how a living creature looks and acts, determined by both its genes and environmental factors. |
| Protein | Proteins are like tiny workers in your body. Different proteins perform different tasks, like building, repairing, and transporting things, and controlling chemical reactions to keep your body functioning properly. |

# Glossary

| Term | Explanation |
|---|---|
| Stem cell | A stem cell is a special, all-purpose type of cell that can turn into different types of specialised cells (like a skin or brain cell for example). |
| Sex (Biological) | Biological sex refers to the physical characteristics, such as chromosomes, hormones, and reproductive organs, that typically classify individuals as male or female, while gender refers to the social and cultural roles, behaviors, and identities that people identify with. |
| Stereotypies | Stereotypies are repetitive movements seen in some people, often without an apparent reason, and are linked to conditions like autism or certain neurological disorders. |
| Variant | A variant is a change or difference in a person's DNA that can affect how genes work and may or may not have an impact on health. |
| Whole exome sequencing | Whole exome sequencing is a technique that reads and analyses a subset of DNA that encodes the protein coding parts (exons), to identify potential genetic causes of diseases or conditions. |

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