# Research Strategy

**Our mission**

CASK Research Foundation is primarily a scientific research organisation focused on delivering treatments and an eventual cure for CASK gene related disorders (CASK gene disorders relate to the two conditions 'MICPCH' and 'XL-ID with or without nystagmus'). Its secondary purpose is to support families in the UK living with the effects of CASK gene mutations.

**Our Vision**

Our vision is a world where CASK gene related disorders are much better understood, the effects on the body as a whole are understood and clinicians are able to access greater and more accurate information about prognoses, progression and treatments. We envisage ultimately that there will be drugs that treat the symptoms more effectively and drugs that target the mechanisms of the disease, providing relief, allowing greater cognitive development and perhaps, one day, even curing the disease.

**What are CASK Gene related disorders?**

CASK gene related disorders are any neurological conditions caused by a mutation in the CASK gene. Currently there are two rare genetic conditions of the brain associated with this (MICPCH and XL-ID with or without nystagmus). Patients normally present with microcephaly, a small cerebellum and learning difficulties. Most CASK patients are non-verbal, struggle to learn to walk, and many cannot feed themselves or learn basic life skills. Some suffer severe and frequent seizures that are not responsive to medical therapies. The majority of males with CASK mutations die within infancy whilst females are often less severely affected although there is a very broad spectrum of phenotypes and some females are life-limited. There is no treatment beyond supportive and often ineffective measures such as feeding tubes, orthopaedic surgeries and medications for seizures. Due to the disorders being ultra rare and poorly diagnosed on an international level there is little research into the gene and its related conditions.

**What is the CASK gene?**

The CASK gene is found on the X chromosome and codes for the CASK protein which plays an important role in the brain, allowing brain cells to work properly. It also interacts with a large number of other proteins, making its role wide-ranging and important. Research has also shown that the protein is involved in metabolic pathways and that some of the symptoms of CASK gene mutation may be a result of metabolic stress on the body. Latest research indicates that loss of CASK function results in death of neurones in the brain.

**Our Principles**

- EQUALITY

All patients with CASK gene related disorders regardless of age, gender and severity of their condition should have access to emerging treatments and cures.

● COMPASSION

Beyond treatments and a cure, many patients with CASK gene related disorders are likely to require some level of holistic medical management, the extent of which will be based on whether they have been able to access and/or benefit from the treatments/cure or not and the age they were and condition they were in when this became available.

● COLLABORATION

We believe in collaboration. Delivering treatments and a cure for CASK gene related disorders is a big job and it needs all of us to bring about real change everywhere.

● DIVERSITY

We value diversity. We want to ensure that no one is marginalised as we move together towards our common goal.

● SCIENCE

We are aware that, although science holds the answers, it is important that we follow strict rules in terms of ethics and fairness.

CASK Research Foundation exists to deliver treatments and a cure for CASK gene related disorders. We aim to fund international CASK research by working together with the CASK Gene Foundation (Cask Gene Foundation Inc, USA) and the Angelina CASK neurological research foundation Ltd (Australia). We work to ensure that as treatments become viable, they are accessible to patients in the UK.

**What we aim to do:**

● We will advocate for and fund improved clinical treatment for children and adults with CASK gene related disorders.

● We will fund laboratory and clinical research projects focused on understanding the functions of the CASK gene and improving lives.

● We hope to facilitate the implementation of UK and European clinical trials.

● We will collate relevant up to date health and research-based best practice information and make it accessible for anyone supporting someone with CASK gene related disorders.

● We collaborate with other like-minded CASK Gene and rare disease organisations around the world.

**<u>International laboratory research funding</u>**

CASK Research Foundation works in collaboration with the French based Association Enfants CASK France and the Australian based Angelina CASK Neurological Research Foundation (ACNRF) to push a global effort to increase understanding, create treatments and investigate possible cures for CASK Gene related disorders. Projects which are financially supported by CASK Research Foundation via their collaborative partners are not peer reviewed by CASK Research Foundation because they are peer reviewed and monitored through the lead partner's peer review process.

## UK Clinical research funding

All new applications include the question, 'do you use animals in your research?'

New projects will be assessed against our project selection criteria to ensure we focus on activities that make the best use of our funds. All new projects must fall within the scope of our purpose and must pass an internal triage before progressing through the stages listed below. We follow the recommendations of the AMRC (Association of Medical Research Charities).

## Project selection criteria

**Stage 1: An RFA is followed by internal assessments/triage**

**level 1 - the project must be able to meet at least one of the following criteria:**

- Improve the scientific community's understanding of how the CASK gene works.
- Animal model development.
- Targeted drug development to alleviate symptoms associated with CASK mutations.
- Investigate the epilepsy associated with CASK mutations.
- Clinical study of a CASK population.
- Development of a gene therapy to benefit people with CASK-related disorders.
- Identify biomarkers that will help accelerate and facilitate a the path to clinical trials

**Level 2**

1. What is the specific unmet clinical need being targeted?

2. How does the project fulfil this need?

3. Is the research underpinned by scientific excellence?

**level 3**

1. How will the research help CASK patients?

2. Has the right team been identified?

3. Why is this research needed now?

**Stage 2: Successful applicants will be invited to submit full proposals. Peer reviews will commence.**

Experts from around the world provide written comments on the research application. A minimum of three written reviews will be sought. Completed peer reviews will be sent to applicants whom will have the opportunity to respond.

**Stage 3: Scientific Advisory Board Review**

Members of the SAB will meet to discuss each application and the written peer review comments. They will make an independent and impartial funding recommendation to the charity.

Note: There is a conflict of interest policy for RRC members and those with a conflict are not in a position to influence funding decisions.

**Stage 4: Trustees**

Trustees make the final decision on whether the charity should award funding to the research application. Sometimes this decision making is delegated back to other groups but trustees are kept informed of the research review committee's activity.