Rare Genomes Project - Disease Prevalence Study

The prevalence of Cerebral Creatine Deficiency Syndromes (CCDS) is still unknown. This information is crucial for rare disease groups like ACD to advocate for treatments.

ACD has been selected to participate in a disease prevalence study led by the Rare Genomes Project (RGP) at the Broad Institute of MIT and Harvard and funded by CZI. The RGP Prevalence Team will include GAMT and SLC6A8 (CTD) genes in their study conducted in 2021-2022.

Our community, including researchers, believes that both Creatine Transporter Deficiency and GAMT Deficiency are massively underdiagnosed. **This partnership can provide the necessary evidence that there are many more patients out there that need a diagnostic and treatments.**

This is an exciting opportunity for Creatine Deficiencies to unlock crucial genetic information, and **you hold the key**. Here is how you can help:

- Join the CreatineInfo Registry at creatineinfo.iamrare.org (a step-by-step guide on how to join here)
- Take the Diagnosis Survey and upload your genetic report. Need help? Contact registry@creatineinfo.org
- Learn about **GenomeConnect,** ClinGen's data-sharing program for patients and families, and provide your consent to share the participant's genetic report and health information with ClinGen to help improve variant interpretation. Learn more about this program here.
- If you opt-in, your genetic report and health information will be collected and pseudonymized (removing identifiable information) and curated by authorized ClinGen staff working in partnership with ACD.
- The primary purpose of this curation is to collect **genetic variants** and associated information that can improve understanding of genetics for Creatine Deficiencies. Genetic variants are spelling changes in DNA coding genes among individuals or the differences between populations. There are multiple sources of genetic variation, including mutation and genetic recombination.

- De-identified genetic and health information will be shared with open centralized databases like ClinVar.

The above steps are related to the CreatineInfo Registry and are detailed in the study consent. The new partnership with RGP is not part of the registry. Still, it will benefit from the registry data that is shared with ClinGen. The more participants that upload their genetic information and opt-in to the ClinGen Data Sharing Program, the more curated genetic variations will be available in databases like ClinVar, and projects like Rare Genomes Project can access them.

How can this de-identified and curated data lead to calculating the prevalence of Cerebral Creatine Deficiency Syndromes (CCDS)?

- **Rare Genomes Project** will collect available genetic information from ClinVar, other public databases, and additional genetic information we provide as a group and will compile and curate a list of potentially pathogenic variants to **calculate an estimated carrier frequency and disease prevalence for all populations** (global, continental, and sub-continental) **available in gnomAD**.

  The Genome Aggregation Database (gnomAD) is a resource developed by an international coalition of investigators, with the goal of aggregating and harmonizing genetic data from a wide variety of large-scale sequencing projects (like ClinVar) and making summary data available for the wider scientific community.

By the end of the study (2021-2022), ACD will receive a prevalence report from the Rare Genomes Project. **This will be a powerful advocacy resource for engaging pharmaceutical companies and researchers to study Creatine Deficiencies and look for treatments and cures.**

You hold the key. Help unlock the answers.