CASK-related disorders

https://pubmed.ncbi.nlm.nih.gov/37628707/

CASK

-related disorders are a form of rare X-linked neurological diseases and most of the patients are females. They are characterized by several symptoms, including microcephaly with pontine and cerebellar hypoplasia (MICPCH), epilepsy, congenital nystagmus, and neurodevelopmental disorders. Whole-genome sequencing has identified various mutations, including nonsense and missense mutations, from patients with

CASK

-related disorders, revealing correlations between specific mutations and clinical phenotypes. Notably, missense mutations associated with epilepsy and intellectual disability were found throughout the whole region of the CASK protein, while missense mutations related to microcephaly and MICPCH were restricted in certain domains. To investigate the pathophysiology of

CASK

-related disorders, research groups have employed diverse methods, including the generation of

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knockout mice and the supplementation of CASK to rescue the phenotypes. These approaches have yielded valuable insights into the identification of functional domains of the CASK protein associated with a specific phenotype. Additionally, recent advancements in the AI-based prediction of protein structure, such as AlphaFold2, and the application of genome-editing techniques to generate

CASK

mutant mice carrying missense mutations from patients with

CASK

-related disorders, allow us to understand the pathophysiology of

CASK

-related disorders in more depth and to develop novel therapeutic methods for the fundamental treatment of

CASK

-related disorders.