CC2D1A

CC2D1A is a gene that encodes a protein involved in several crucial cellular processes, particularly in the brain. The full name of the protein is Coiled-Coil and C2 Domain-Containing Protein 1A. This protein plays an essential role in neuronal development, signaling pathways, and cellular stress responses.

Key Functions of CC2D1A: Neuronal Development and Function:

CC2D1A is involved in the development and function of neurons. It has been implicated in synaptic plasticity, which is crucial for learning and memory. The protein is also important for proper brain development during early stages of life. Signal Transduction:

CC2D1A participates in various signaling pathways within cells, particularly those involved in cellular stress responses and survival. It plays a role in regulating NF-κB signaling, a pathway that controls the expression of genes involved in inflammation, immune response, and cell survival. Cellular Stress Responses:

The CC2D1A protein is involved in cellular mechanisms that help cells cope with stress, such as oxidative stress or endoplasmic reticulum stress. It helps regulate the cell's response to these stresses to maintain cellular homeostasis and prevent damage. Clinical Significance: Intellectual Disability and Autism Spectrum Disorders:

Mutations or deletions in the CC2D1A gene are associated with autosomal recessive forms of intellectual disability. These mutations can lead to developmental delays, cognitive impairments, and in some cases, features of autism spectrum disorders. Patients with CC2D1A mutations may present with a range of symptoms, including delayed speech and motor skills, seizures, and behavioral issues. Genetic Testing and Diagnosis:

Genetic testing can identify mutations in the CC2D1A gene, helping diagnose conditions related to intellectual disabilities and providing insights into potential treatment or management strategies. Research and Potential Therapeutic Targets: Ongoing research is exploring how CC2D1A functions at a molecular level, particularly in the context of brain development and neurodevelopmental disorders. Understanding the pathways and mechanisms regulated by CC2D1A could lead to new therapeutic strategies for treating related disorders.

Intellectual and developmental disability result from abnormal nervous system development. Over a 1,000genes have been associated with intellectual and developmental disabiliy, driving continued efforts toward dissecting variant functionality to enhance our understanding of the disease mechanism.

A report from the Yale School of Medicine, New Haven, identified two novel variants in CC2D1A in a cohort of four patients from two unrelated families. They used multiple model systems for functional analysis, including Xenopus, Drosophila, and patient-derived fibroblasts. The experiments revealed that cc2d1a is expressed explicitly in a spectrum of ciliated tissues, including the left-right organizer, epidermis, pronephric duct, nephrostomes, and ventricular zone of the brain. In line with this expression pattern, loss of cc2d1a led to cardiac heterotaxy, cystic kidney disease, and abnormal CSF circulation via defective ciliogenesis. Interestingly, when we analyzed brain development, mutant

tadpoles showed abnormal CSF circulation only in the midbrain region, suggesting abnormal local CSF flow. Furthermore, the analysis of the patient-derived fibroblasts confirmed defective ciliogenesis, further supporting the observations [1].

1)

Kim AH, Sakin I, Viviano S, Tuncel G, Aguilera SM, Goles G, Jeffries L, Ji W, Lakhani SA, Kose CC, Silan F, Oner SS, Kaplan OI; MarmaRare Group; Ergoren MC, Mishra-Gorur K, Gunel M, Sag SO, Temel SG, Deniz E. CC2D1A causes ciliopathy, intellectual disability, heterotaxy, renal dysplasia, and abnormal CSF flow. Life Sci Alliance. 2024 Aug 21;7(10):e202402708. doi: 10.26508/lsa.202402708. PMID: 39168639.