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 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 kidneys, 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.