Coiled-Coil and C2 Domains-Containing Protein 2A

Alternative Names
CC2D2A
KIAA1345

Record Category
Gene locus

WHO-ICD
N/A to gene loci

Incidence per 100,000 Live Births
N/A to gene loci

OMIM Number
612013

Mode of Inheritance
N/A to gene loci

Gene Map Locus
4p15.32

Description
The CC2D2A gene encodes a protein that forms a part of the tectonic complex. This complex is localized at the ciliary transition zone and prevents the diffusion of transmembrane proteins between the cilia and plasma membranes. Based on studies in lower species, the protein is believed to be involved in a number of biological processes, including primary cilium assembly, determination of left/right symmetry and embryonic brain development.

The CC2D2A gene is associated with Joubert Syndrome 9 (JBTS9), a rare ciliopathy characterized by cerebellar ataxia, oculomotor apraxia, hypotonia, breathing difficulties, abnormal eye and tongue movements, intellectual disability, and brain anomalies. Mutations in the gene have also been linked to Meckel Syndrome 6 (MKS6), a ciliopathy with a more severe phenotype compared to JBTS. The autosomal recessive disorder is characterized by occipital encephalocele, large cystic kidneys, fibrotic changes in the liver and polydactyly. COACH syndrome is another disorder that is related to the CC2D2A gene. The disease, which has overlapping features with JBTS and MKS, is characterized by cerebellar vermis hypo/aplasia, oligophrenia, ataxia, ocular coloboma, and hepatic fibrosis.

Molecular Genetics
The 132 kb long CC2D2A gene is located on the short arm of chromosome 4. Its coding sequence is made up of 40 exons. The protein encoded by this gene is approximately 186 kDa and made up of 1620 amino acids. Multiple transcript variants exist due to alternative splicing. Mutations in the gene associated with MKS6, JBTS9 and COACH syndrome usually include homozygous and compound heterozygous transitions.

Epidemiology in the Arab World

Saudi Arabia

Shaheen et al. (2013) analyzed the genome of 18 MKS affected Saudi families to determine the underlying genetic defects. Members of these families were diagnosed with MKS based on the presence of occipital encephalocele as well as any combination of liver fibrosis, cleft palate, dysplastic kidneys, polydactyly and early lethality. DNA from both affected and healthy members was obtained. Due to the consanguineous nature of the families, an autozygome guided approach was considered. Known MKS genes within these autozygous regions were screened for mutations. In this manner, CC2D2A mutations were uncovered in six of the families. The mutation c.3084delG resulting in p.Lys1029Argfs3 was found in four of these families. In the remaining two, a novel mutation, c.4531T>C (p.Trp1511Arg) was found. In-silico analysis by PolyPhen categorized this variant as ‘probably damaging’ while SIFT predicted it to affect protein function.

References
Shaheen R, Faqeih E, Alshammari MJ, Swaid A, Al-Gazali L, Mardawi E, Ansari S, Sogaty S, Seidahmed MZ, AlMotairi MI, Farra C, Kurdi W, Al-Rasheed S, Alkuraya FS. Genomic analysis of Meckel-Gruber syndrome in Arabs reveals marked

genetic heterogeneity and novel candidate genes. Eur J Hum Genet. 2013; 21(7):762-8. PMID: 23169490

Related CTGA Records

Meckel Syndrome, Type 1

External Links

https://www.genecards.org/cgi-bin/carddisp.pl?gene=CC2D2A

Contributors

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