Clusterin-Associated Protein 1

Alternative Names
CLUAP1
Flagellar-Associated Protein 22, Chlamydomonas, Homolog of
FAP22
DYF3, C. Elegans, Homolog of
QILIN
KIAA0643

Record Category
Gene locus

WHO-ICD
N/A to gene loci

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

OMIM Number
616787

Mode of Inheritance
N/A to gene loci

Gene Map Locus
16p13.3

Description
The Clusterin-Associated Protein 1 (CLUAP1) gene encodes a protein involved in cilia biogenesis and Hedgehog signaling. CLUAP1 is believed to carry out its key role in ciliogenesis by associating with the multiple intraflagellar transport complex B and playing a role in the assembly and turnaround of intraflagellar particles at the base and tip of the cilium.

Studies have found that abolishing CLUAP1 expression results in a lack of ciliogenesis in both mice and zebrafish. In mice, it results in mid-gestational lethality, while in zebrafish it results in photoreceptor defects and eventually death at around 11-days post fertilization. These results help support the theory that CLUAP1 mutations in humans can have strong pathological consequences, particularly in retinal diseases such as Leber Congenital Amaurosis (LCA). So far, only one case of a CLUAP1 mutation resulting in LCA has been reported.

Molecular Genetics
The CLUAP1 gene is located on the short arm of chromosome 16. It is 38 kb long and its coding sequence consists of 15 exons. The protein encoded by the CLUAP1 gene is 48 kDa in size and made up of 413 amino acids. Alternative splicing of the gene transcript results in an additional shorter isoform made up of 247 amino acids. Both isoforms of the CLUAP1 protein contain two highly conserved regions: N-terminal calpolin homology-like domain and C terminal coiled-coil domain. While the gene is highly expressed in the testis, thyroid and trachea, both isoforms are found to be moderately expressed in the human retina.

Epidemiology in the Arab World

Saudi Arabia

Soens et al. (2016) analyzed a 5-year-old Saudi boy affected by Leber Congenital Amaurosis. His symptoms were noticed at 6-months of age and included visual dysfunction, nystagmus and an extinguished electroretinogram. Whole exome sequencing was employed to identify causal mutation/s, consequently a homozygous non-synonymous mutation, c.817C>T, was discovered in the CLUAP1 gene (c.319C>T in the short isoform). The mutation resulted in a p.L273F substitution (p.L107F in the short isoform) at a highly conserved residue within the coiled-coil domain of CLUAP1. The parents were heterozygous for the mutation and it occurred at a frequency of 1/121,086 chromosomes (0.0008%) in the ExAC database. In-silico analysis by 11 algorithms predicted the mutation to be damaging. Immunofluorescence studies in Htert-RPE1 cells showed that the mutation did not affect CLUAP1 localization while western blot analysis proved that it did not affect CLUAP1 expression. To assess the effect of the mutation on the protein's function, CLUAP-1 null zebrafish were subjected to functional rescue assays using mutant CLUAP1 that contained the proband's mutation. It was found

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that the mutation was highly hypomorphic and resulted in a CLUAP1 protein with only 5% of the activity compared to wild type.

References

Soens ZT, Li Y, Zhao L, Eblimit A, Dharmat R, Li Y, Chen Y, Naqeeb M, Fajardo N, Lopez I, Sun Z, Koenekoop RK, Chen R. Hypomorphic mutations identified in the candidate Leber congenital amaurosis gene CLUAP1. Genet Med. 2016; 18(10):1044-51. PMID: 26820066

Related CTGA Records

Leber Congenital Amaurosis 1

External Links

http://www.genecards.org/cgi-bin/carddisp.pl?gene=CLUAP1

Contributors

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