KIAA0196 Gene

Alternative Names
KIAA0196

Record Category
Gene locus

WHO-ICD
N/A to gene loci

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

OMIM Number
610657

Mode of Inheritance
N/A to gene loci

Gene Map Locus
8q24.13

Description
The KIAA0196 gene encodes the strumpellin protein. The protein, found in the cytosol and endoplasmic reticulum, forms a part of the WASH core complex along with F-actin-capping protein subunits alpha and beta, WASH1, FAM21, KIAA1033 and CCDC53. The WASH complex localizes at the surface of endosomes and is believed to be involved in the process of recruiting and activating the Arp2/3 complex to induce actin polymerization. Based on ortholog studies, the strumpellin protein is also predicted to be involved in oocyte maturation, meiotic spindle assembly and polar body extrusion after meiotic divisions. Interestingly, Kiaa0196 knockdown studies in zebrafish have been shown to result in severe cardiac contractile dysfunction, tail curvature, and impaired motility.

The gene is associated with Spastic Paraplegia 8, Autosomal Dominant (SPG8) and Ritscher-Schinzel Syndrome 1 (RTSC1). SPG8 is an adult-onset neurologic disorder characterized by progressive lower limb spasticity and urinary incontinence. RTSC1 is a rare multisystem disorder characterized by cerebellar brain abnormalities (Dandy-Walker malformation and cerebellar vermis hypoplasia), congenital heart deformities (septal defects and aortic stenosis) and craniofacial dysmorphia (prominent occiput and forehead, low-set ears, down-slanting palpebral fissures, depressed nasal bridge and micrognathia).

Molecular Genetics
The KIAA0196 gene, located on the long arm of chromosome 8, spans a length of 67 kb. Its coding sequence consists of 31 exons and it encodes a 134 kDa protein product made up of 1159 amino acids. While the gene is ubiquitously expressed in the human body, it is found to be overexpressed in skeletal muscles. Heterozygous missense mutations in the KIAA0196 gene are associated with Spastic Paraplegia 8, the most common being Val626Phe caused by a 1956G-T transversion; while a homozygous splice site mutation in the gene has been linked to Ritscher-Schinzel Syndrome 1.

Epidemiology in the Arab World
Saudi Arabia
Anazi et al. (2016) carried out a study to determine the diagnostic yield of genetic analysis tools compared to standard clinical evaluations. By analyzing a cohort of 337 Intellectual Disability (ID) patients, it was found that the genomic approach is a better first-tier test in diagnosing ID cases. To identify gene mutations, the authors used molecular karyotyping, exome sequencing and a multi-gene panel comprised of genes associated with neuro-genetic diseases. The genetic tests helped uncover a de-novo mutation (c.1669G>A, p.Ala557Thr) in the KIAA0196 gene of one patient, suggesting a diagnosis of spastic paraplegia 8. Apart from ID, it was noted that the subject exhibited other atypical features such as an infantile onset and a lack of spasticity.

References
Anazi S, Maddirevula S, Faqeih E, Alsedairy H, Alzahrani F, Shamseldin HE, Patel N, Hashem M, Ibrahim N, Abdulwahab F, Ewida N, Alsaif HS, Al Sharif H, Alamoudi W, Kentab A, Bashiri FA, Alnaser M, AlWadei AH, Alfadhel M, Eyaid W, Hashem A, Al Asmari A, Saleh MM, AlSaman A,

Alhasan KA, Alsughayir M, Al Shammari M, Mahmoud A, Al-Hassnan ZN, Al-Husain M, Osama Khalil R, Abd El Meguid N, Masri A, Ali R, Ben-Omran T, El Fishway P, Hashish A, Ercan Sencicek A, State M, Alazami AM, Salih MA, Altassan N, Arold ST, Abouelhoda M, Wakil SM, Monies D, Shaheen R, Alkuraya FS. Clinical genomics expands the morbid genome of intellectual disability and offers a high diagnostic yield. Mol Psychiatry. 2016 Jul 19. PMID: 27431290.

Related CTGA Records

Spastic Paraplegia 8, Autosomal Dominant (OMIM 603563)

External Links

http://www.genecards.org/cgi-bin/carddisp.pl?gene=KIAA0196

Contributors

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