Leucyl-tRNA Synthetase 2

Alternative Names
LARS2
Leucyl-tRNA Synthetase, Mitochondrial
Mitochondrial Leurs

Record Category
Gene locus

WHO-ICD
N/A to gene loci

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

OMIM Number
604544

Mode of Inheritance
N/A to gene loci

Gene Map Locus
3p21.31

Description
The LARS2 gene encodes mitochondrial leucyl-tRNA synthetase, an enzyme that belongs to the class I aminoacyl-tRNA synthetase group of proteins. During mitochondrial protein translation, leucyl-tRNA synthetase is responsible for attaching the amino acid leucine to the appropriate tRNA. As a mitochondrial enzyme, LARS2 is believed to play an important role in mitochondrial energy production.

The gene has been linked to Perrault Syndrome 4, an autosomal recessive disorder characterized by hearing loss and ovarian failure. The gene is also associated with Hydrops, Lactic Acidosis, and Sideroblastic Anemia (HLASA), a fatal multisystem disorder defined by cardiovascular, neurologic, hepatic, respiratory and metabolic irregularities.

Molecular Genetics
The LARS2 gene is located on the short arm of chromosome 3. It spans a length of 160.9 kb and is coding sequence is spread across 23 exons. The protein encoded by the LARS2 gene is made up of 903 amino acids and has a molecular mass of 01.9 kDa. While the gene is ubiquitously expressed in the body, highest expression is seen in tissues with high metabolic rates, such as the heart, skeletal muscle and kidney. Variants in the LARS2 gene associated with Perrault Syndrome 4 and HLASA are generally homozygous and compound heterozygous missense mutations that reduce or eliminate LARS2 enzyme activity.

Epidemiology in the Arab World
Saudi Arabia
Anazi et al. (2016) conducted a study to compare the diagnostic yield of genomic tools with standard clinical evaluations in Intellectual Disability (ID) cases. 337 patients with ID were recruited and subjected to molecular karyotyping, exome sequencing and sequencing by a multi-gene panel comprised of neurologically associated genes. Genomic tools were found to have a higher diagnostic yield than standard clinical evaluations (58% vs 16%). In one patient, the genomic approach uncovered a homozygous c.457A>C (p.Asn153His) mutation in the LARS2 gene. Although the gene is associated with Perrault syndrome 4, the patient showed atypical features such as ID, short stature, T1DM, cirrhosis, thrombocytopenia, leukopenia, seizures, psoriasis, absent ovaries and uterus, vitiligo and osteoporosis.

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

Perrault Syndrome 4 (OMIM 615300)

External Links

http://www.genecards.org/cgi-bin/carddisp.pl?gene=LARS2

Contributors

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