Phosphoglycerate Dehydrogenase

Alternative Names
PHGDH
3-Phosphoglycerate Dehydrogenase
3PGDH

Record Category
Gene locus

WHO-ICD
N/A to gene loci

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

OMIM Number
606879

Mode of Inheritance
N/A to gene loci

Gene Map Locus
1p12

Description
The PHGDH gene encodes an enzyme that is essential for the synthesis of the L-serine amino acid. Using NAD+/NADH as a cofactor, PHGDH forms a homotetramer and catalyzes the first step in the serine biosynthesis pathway, the transition of 3-phosphoglycerate into 3-phosphohydroxypyruvate. As serine is essential for protein synthesis and is a precursor to compounds such as sphingomyelin, glycine, and cysteine, PHGDH deficiency can have strong pathological consequences.

Mutations in the PHGDH gene result in Neu-Laxova Syndrome 1 (NLS1), a severe and usually fatal disorder characterized by ichthyosis, microcephaly, intra-uterine growth retardation, nervous system abnormalities, limb deformities, edema, and facial dysmorphia. The gene is also associated with Phosphoglycerate Dehydrogenase Deficiency (PHGDHD), a less severe phenotype characterized by congenital microcephaly, psychomotor retardation, and seizures.

Molecular Genetics
Located on the short arm of chromosome 1, the PHGDH gene is 84.4 kb long and made up of 16 exons. The protein encoded by this gene has a molecular mass of 56 kDa and consists of 533 amino acids. While alternative splicing results in multiple isoforms of this protein, the full length nature of most of them are yet to be elucidated. Mutations in this gene that are associated with NLS1 include homozygous transitions and transversions, whereas mutations resulting in phosphoglycerate dehydrogenase deficiency include homozygous as well as compound heterozygous defects.

Epidemiology in the Arab World

Saudi Arabia
El-Hattab analyzed two subjects diagnosed with NLS1 disorder. Subject 1 was stillborn at 36-weeks to healthy Saudi Arabian parents. He suffered from microcephaly, IUGR, syndactyly with puffy hands and feet, edematous skin, and facial dysmorphia. Autozygome analysis identified PHGDH as a candidate gene and Sanger sequencing uncovered a homozygous c.418G>A (p.Gly140Arg) mutation. Subject 2 was a 2-month-old male infant born to healthy Emirati parents. He suffered from microcephaly, ichthyotic skin, brain anomalies, anemia, hypertonia, facial dysmorphia and low plasma and CSF levels of serine and glycine. The patient was treated with L-serine therapy. Genetic analysis of known NLS genes (PHGDH, PSAT1 and PSPH) revealed a novel homozygous c.1286G>T (p.Gly429Val) mutation in the PHGDH gene. The mutation affected a moderately conserved amino acid and was predicted by in-situ analysis to be probably damaging.

UAE
See Saudi Arabia > [El-Hattab et al., 2016]

References
El-Hattab AW, Shaheen R, Hertecant J, Galadari HI, Albaqawi BS, Nabil A, Alkuraya FS. On the phenotypic spectrum of serine biosynthesis defects. J Inherit Metab Dis. 2016; 39(3):373-81. PMID: 26960553.

Related CTGA Records

Neu-Laxova Syndrome 1

External Links

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

Contributors

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