Cyclin-Dependent Kinase Inhibitor 1C

Alternative Names
CDKN1C
p57
KIP2

Record Category
Gene locus

WHO-ICD
N.B.: Classification not applicable to gene loci.

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

OMIM Number
600856

Mode of Inheritance
N/A

Gene Map Locus
11p15.4

Description
Cyclin-Dependent Kinase Inhibitor 1C (CDKN1C) is a tumor suppressor; a protein involved in the regulation of cell division. Because it is a strong, tight inhibitor of several G1 cyclin/CDK complexes, this protein is a negative regulator of cell proliferation. One of the major functions of this protein is in controlling prenatal growth, by preventing the fetus from growing abnormally large.

Mutations in CDKN1C gene cause disorders like Beckwith Wiedemann Syndromem (BWS), a condition characterized by prenatal and postnatal overgrowth. In addition, defects in CDKN1C have also been shown to result in a condition known as Intrauterine growth restriction, Metaphyseal dysplasia, Adrenal hypoplasia congenita, and Genital anomalies (IMAGe). This condition is characterized by delayed prenatal and postnatal growth, and hormonal and genital abnormalities in males.

Molecular Genetics
The CDKN1C gene is located on the short arm of chromosome 11 at 11p15.4, where it spans a length of about 2.5 Kb. The CDKN1C protein is made up of 316 amino acid residues and has a molecular mass of 32 kDa. The protein has three structurally distinct regions; a CDK-inhibitory domain, a Pro-Ala repeat rich domain called the PAPA region, and a c-terminal conserved QT-box motif.

The CDKN1C gene is a paternally imprinted gene. This means that the maternally inherited allele is preferentially expressed over the paternal copy. This parent specific imprinting of CDKN1C is controlled by a region of DNA nearby to the gene, called the Imprinting center 2 (IC2), which preferentially methylates the maternal copy of the CDKN1C gene.

Epidemiology in the Arab World

United Arab Emirates
Bastaki et al (2016) reported a case of BWS in a 9-year old Emirati boy. The patient was born to healthy, unrelated parents. He was found to have an omphalocele which contained small bowel and a small extra liver lobe. The patient was also found to suffer from cryptorchidism. Abdominal US revealed a non-progressive abdominal cyst. PCR amplification and sequencing of exons 2 and 3 of the CDKN1C gene identified a variant (c.703C>T) in the gene. According to in silico analysis results the protein change (p.Gln235X) leads to the production of a truncated protein that completely lacked the QT box. Polyphen 2 predicted that the variant was “probably damaging”. The variant was not found in either of the parents’ DNA, marking it as a de novo mutation.

References
Bastaki F, Saif F, Al Ali MT, Hamzeh AR. Molecular and clinical characterization of a nonsense CDKN1C mutation in an Emirati patient with Beckwith-Wiedemann syndrome. Saudi Med J. 2016; 37(2):215-6. PMID: 26837408

Related CTGA Records
Beckwith Weidemann Syndrome

External Links

http://www.genecards.org/cgi-bin/carddisp.pl?gene=CDKN1C
https://ghr.nlm.nih.gov/gene/CDKN1C

Contributors

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