Gene Section
Mini Review

PLAGL1 (pleomorphic adenoma gene-like 1)
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Identity
Hugo: PLAGL1
Other names: DKFZp781P1017; LOT1; MGC126275; MGC126276; ZAC; ZAC1
Location: 6q24.2

DNA/RNA

Description
The genome is about 64 kbp with six exons and five introns. The major mRNA transcript is about 4.7 kb in size.

Transcription
At least three splicing variants (see figure).

Protein

Description
The PLAGL1 protein is a seven C2H2-type zinc finger protein. The seven zinc finger domain is located at the amino terminal region, from the amino acid residue 1 to 210. Additional features of note are proline and glutamine rich regions at the carboxyl terminal portion (residues 220 to 444). There are two nuclear localization signals at the amino terminal region.

Expression
Ovary, breast, brain, liver, spleen, thymus, prostate, uterus, testis, intestine, colon, leukocytes.

Localisation
Nuclear.

Function
The PLAGL1 protein is a candidate tumor suppressor gene and has been shown to have transactivation and transrepression activities.
Diabetes mellitus

Disease

PLAGL1/LOT1/ZAC1 as a candidate imprinted gene

UPD 6 and normal controls, suggested

region, using DNA from TNDM patients with paternal

Analysis of the CpG islands in the TNDM critical

q24.3 between markers D6S1699 and D6S1010.

this disease within the chromosomal region 6q24.1-

formation, and neonatal lethality.

studies showed the involvement of an imprinted gene in

diseases such as breast primary tumors, ovarian

primary tumors and tumor-derived cell lines, basal cell

carcinoma, head and neck squamous cell carcinoma (HNSCC), and extraskeletal myxoid chondrosarcoma (EMC). Several mechanisms have been shown to regulate the PLAGL1 gene expression, including growth factor receptor activation, epigenetic factors, maternal imprinting, and loss of heterozygosity (LOH). Allelic deletion of 6q24-q25, the PLAGL1 locus, in the tumor tissues has been shown in the cancers of ovarian, breast, HNSCC, and pheochromocytomas (PCCs).

Carcinogenicity

Note: Alteration of the gene expression was found to be a potential genetic event silencing the PLAGL1 gene in cancers such as breast primary tumors, ovarian primary tumors and tumor-derived cell lines, basal cell carcinoma, head and neck squamous cell carcinoma (HNSCC), and extraskeletal myxoid chondrosarcoma (EMC). Several mechanisms have been shown to regulate the PLAGL1 gene expression, including growth factor receptor activation, epigenetic factors, maternal imprinting, and loss of heterozygosity (LOH). Allelic deletion of 6q24-q25, the PLAGL1 locus, in the tumor tissues has been shown in the cancers of ovarian, breast, HNSCC, and pheochromocytomas (PCCs).

Disease

Transient neonatal diabetes (TNDM)

Note: Initial reports suggested that transient neonatal diabetes mellitus (TNDM), a rare condition characterized in the patients by intrauterine growth retardation, dehydration, failure to thrive, and hyperglycemia due to a lack of normal insulin secretion, is associated with paternal uniparental disomy (UPD) of chromosome 6 (UPD 6). Later studies showed the involvement of an imprinted gene in this disease within the chromosomal region 6q24.1-q24.3 between markers D6S1699 and D6S1010. Analysis of the CpG islands in the TNDM critical region, using DNA from TNDM patients with paternal UPD 6 and normal controls, suggested PLAGL1/LOT1/ZAC1 as a candidate imprinted gene for this disease.

Disease

Diabetes mellitus

To be noted

Note: PLAGL1 has been implicated in embryonic development. The gene is variably expressed in different tissues and stages during development. Inactivation of this maternally repressed gene resulted in intrauterine growth restriction, altered bone formation, and neonatal lethality.

References


Pirks G, El Kharroubi A, Kozlov S, Escalante-Alcalde D, Hernandez L, Copeland NG, Gilbert DJ, Jenkins NA, Stewart CL. Zac1 (Lot1), a potential tumor suppressor gene, and the gene for epsilon-sarcoglycan are maternally imprinted genes:


This article should be referenced as such: