Solid Tumour Section
Short Communication

Soft Tissues: Lipoblastoma with t(2;8)(q31;q12.1) COL3A1/PLAG1

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Abstract

Review on translocations in lipoblastoma with t(2;8)(q31;q12.1) COL3A1/PLAG1, with data on clinics, genetics and cytogenetics.

Identity

Phylum
Soft Tissue Tumors: Benign Lipomatous: Lipoblastoma

Clinics and pathology

Disease

is a rapidly growing, benign neoplasm.
It is a mesenchymal tumor of fetal white fat tissue that appears most commonly in children under three years of age and affects males three times more often than females (McVay et al., 2006).
It can present anywhere in the body, but is most commonly seen in the trunk and extremities.
Surgical excision is usually curative, with a recurrence rate of about 20% (Jimenez, 1986; Hicks et al., 2001).
Histologically, lipoblastoma shows a characteristic lobular architecture, with lobules containing lipoblasts embedded in a myxoid matrix, whereas lipoma is a tumor composed of only mature fat without lobulation (Weiss, 1996; Kuhnen et al., 2002; de Saint Aubain Somerhausen et al., 2008; Morerio et al., 2009).

Cytogenetics

Cytogenetics Morphological
t(2;8)(q31;q12.1)

Genes involved and proteins

COL3A1
Location
2q31
Note
Mutations in this gene are associated with Ehlers-Danlos syndrome types IV, and with aortic and arterial aneurysms. (Lee et al., 2008; Jeong et al., 2012)

DNA / RNA
The COL3A1 gene, located at chromosome 2q31, contains 51 exons spanning 38.43 kb of genomic distance. Two transcripts, resulting from the use of alternative polyadenylation sites, have been identified for this gene (GeneCards GCID:GC02P189803 (http://www.genecards.org/cgi-bin/carddisp.pl?gene=COL3A1), UniProt P02461-CO3A1_HUMAN (http://www.uniprot.org/uniprot/P02461)).

Protein
The gene encodes a protein of 1466 amino acids (aa) (138kDa).
The shorter isoform is missing 847-1149 aa. The protein is the pro-alphal chains of type III collagen, a fibrillar collagen that is found in extensible connective tissues such as skin, lung, uterus, intestine and the vascular system, and is frequently found in association with type I collagen. The C-terminal propeptide, also known as the COLFI domain, has crucial roles in tissue growth and repair, in which it controls both the intracellular assembly of procollagen molecules and the extracellular assembly of collagen fibrils. It binds a calcium ion which is essential for its function (GeneCards GCID:GC02P189803 (http://www.genecards.org/cgi-bin/carddisp.pl?gene=COL3A1), UniProt P02461-CO3A1_HUMAN (http://www.uniprot.org/uniprot/P02461)).

**PLAG1**

**Location**

8q12.1

**DNA / RNA**

The gene spans about 50 kb and includes 5 exons. The size of the transcript is about 7 kb. It has two alternative splicing forms (one without exon 2) (GeneCards GCID:GC08M057073 (http://www.genecards.org/cgi-bin/carddisp.pl?gene=PLAG1), UniProt Q6DJT9-PLAG1_HUMAN (http://www.uniprot.org/uniprot/Q6DJT9)).

**Protein**

The gene encodes a 500-aa zinc finger protein (74 kDa) with two putative nuclear localization signals (Cas et al., 1997). When activated, it acts as a transcription factor that up-regulates target genes, such as IGFI, leading to uncontrolled cell proliferation. When overexpressed in cultured cells, it increases the proliferation rate and transformation. Other target genes such as CRLF1, CRABP2, CRIP2, PI GF are strongly induced in cells with PLAG1 induction. PLAG1 is a proto-oncogene whose ectopic expression can trigger the development of lipoblastomas and pleomorphic adenomas of the salivary gland (Hensen et al., 2002; Voz et al., 2004; Zatkova et al., 2004) (GeneCards GCID:GC08M057073 (http://www.genecards.org/cgi-bin/carddisp.pl?gene=PLAG1), UniProt Q6DJT9-PLAG1_HUMAN (http://www.uniprot.org/uniprot/Q6DJT9)).

**Expression / Localisation**

**Hybrid Gene**

The fusion occurs as a result of a cryptic, intrachromosomal rearrangement in tumors with apparently normal karyotypes. Comparison of the fusion gene with the wild type reveals that the fusion gene is associated with the t(2;8)(q31;q12.1) translocation. The first exon of COL3A1 is fused to either exon 2 or exon 3 of PLAG1 (Yoshida et al., 2014).

**Result of the chromosomal anomaly**

**Hybrid Gene**

The fusion results in the production of a gene with altered activity, leading to the development of lipoblastomas and pleomorphic adenomas. The fusion gene is associated with the t(2;8)(q31;q12.1) translocation. The first exon of COL3A1 is fused to either exon 2 or exon 3 of PLAG1 (Yoshida et al., 2014).

**Detection**

RT-PCR using total RNA extracted from frozen tumor tissue. The COL3A1/PLAG1 fusion transcript was amplified with primers 5'-AGGGGAGCTTGGCTACCCTCC-3' (forward), and, 5'-ACGTTTCCCTGAGGAGCCTT-3' (reverse). COL3A1/PLAG1-fusion transcripts of 345 bp and 450 bp were detected (Yoshida et al., 2014).

**Fusion Protein**

**Note**

No fusion protein exist for reasons the above.

**References**


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