Solid Tumour Section
Short Communication

Soft Tissues: Lipoblastoma with t(8;8)(q12;q12) RAB2A/PLAG1

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Abstract
Review on translocations in lipoblastoma with t(8;8)(q12;q12) RAB2A/PLAG1, with data on clinics, genetics and cytogenetics.

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(8;8)(q12.1;q12.1)

Genes involved and proteins
RAB2A
Location
8q12.1
DNA / RNA
The RAB2A gene contains 8 exons spanning 106 kbp of genomic distance that was mapped to chromosome 8q12.1.
It has two alternative splicing forms (one without exon 2) as a result of the use of alternative polyadenylation sites (GeneCards CID:GCO8P061429 (http://www.genecards.org/cgi-bin/carddisp.pl?gene=RAB2A), UniProt P61019-RAB2A_HUMAN(http://www.uniprot.org/uniprot/P61019)).
Protein
The gene encodes a protein of 212 amino acids (23 kDa). The shorter isof orm is missing 847-1149 aa. The protein is a member of the Rab family, whose members are small molecular weight guanosine triphosphatases (GTPases) that contain highly conserved domains involved in GTP binding and hydrolysis. The Ras are membrane-bound proteins, involved in vesicular fusion and trafficking (Ali et al., 2004; Mountjoy et al., 2008).
RAB2A is a pre-Golgi intermediate and transports proteins from the endoplasmic reticulum (ER) to the Golgi complex (Tisdale EJ et al., 1996) (GeneCards CID:GC08P061429 (http://www.genecards.org/cgi-bin/carddisp.pl?gene=RAB2A), UniProt P61019-RAB2A_HUMAN(http://www.uniprot.org/uniprot/P61019)).

**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 Q6DTJ9-PLAG1_HUMAN (http://www.uniprot.org/uniprot/Q6DTJ9)).

**Protein**

The gene encodes a 500-aa zinc finger protein (74 kDa) with two putative nuclear localization signals (Kas et al., 1997).

When activated, it acts as a transcription factor that up-regulates target genes, such as IGFII, leading to uncontrolled cell proliferation. When overexpressed in cultured cells, it increases the proliferation rate and transformation.

Other target genes such as CRFL1, CRABP2, CRIP2, PIGF 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 Q6DTJ9-PLAG1_HUMAN (http://www.uniprot.org/uniprot/Q6DTJ9)).

**Result of the chromosomal anomaly**

**Hybrid Gene**

**Note**

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 t(8;8)(q12.1;q12.1) translocation. The first exon of RAB2A is fused to either exon 2 or exon 3 of PLAG1 (Yoshida et al., 2014).

**Description**

PLAG1 has a genomic fusion breakpoint in intron 1 resulting in alternative splicing of exon 2. The start codon of PLAG1 is located in exon 4 (Van Dyck et al., 2007), and the coding sequence of PLAG1 is preserved (Yoshida et al., 2014). This supports the molecular mechanism of overexpression of PLAG1 through promoter swapping: as a result of the translocation, the constitutively active promoter of the partner gene drives the ectopic expression of PLAG1 (Hibbard et al., 2000).

**Detection**

RT-PCR using total RNA extracted from frozen tumor tissue. The RAB2A/PLAG1 fusion transcript was amplified with primers 5’-CTTCCTCACAGCCCCCTCACT-3’ (forward), and, 5’-GGAACCTGCCAACCTCCACTA-3’ (reverse). RAB2A/PLAG1-fusion transcripts of 485 bp and 590 bp were detected (Yoshida et al., 2014).

**Fusion Protein**

**Note**

No fusion protein exist for reasons the above.

**Expression / Localisation**

PLAG1 protein localizes to the nucleus (Bahrami et al., 2012).

**References**


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