Bone: Aneurysmal bone cyst with t(5;17)(q33;p13) RABEP1/PDGFRB

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Published in Atlas Database: July 2015
Online updated version: http://AtlasGeneticsOncology.org/Tumors/t0517q33p13BoneCystID6977.html
Printable original version: http://documents.irevues.inist.fr/bitstream/handle/2042/66068/07-2015-t0517q33p13BoneCystID6977.pdf
DOI: 10.4267/2042/66068

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Abstract

The t(5;17)(q33;p13) rearrangement has been observed as sole cytogenetic abnormality in one case of chronic myelomonocytic leukemia, a soft-tissue aneurysmal bone cyst, and a case of myeloid and lymphoid neoplasms (MLNs) with eosinophilia. The t(5;17)(q33;p13) generates a fusion gene, located on the rearranged chromosome 5, comprised of the 5' portion of RABEP1 (encoding the coiled-coil domain) and the 3' portion of PDGFRB (encoding the intracellular kinase domain). Expression of the resulting fusion protein has been demonstrated to cause myeloproliferative disease in mice.

Disease
Aneurysmal bone cyst (primary)

Note
t(5;17)(q33;p13) RABEP1/PDGFRB in hematological malignancies has also been described.

Epidemiology
One case of aneurysmal bone cyst with t(5;17)(q33;p13) to date: a white female patient who was 10 years old at diagnosis (Ellison et al., 2007).

Clinics
Patient developed limp and contracture after a fall down stairs. MRI revealed a cystic mass soft-tissue mass in posterior medial aspect of the left thigh (Ellison et al., 2007).

Cytology
Fibrous tissue and multinucleated giant cells observed on frozen section (Ellison et al., 2007).

Pathology
Mass of fibrous tissue with areas of bone rimmed with bony trabeculae (Ellison et al., 2007).

Treatment
Resection
**Cytogenetics**

**Cytogenetics Morphological**
Cytogenetic analysis has revealed t(5;17)(q33;p13) as a sole abnormality.

**Cytogenetics Molecular**
Metaphase FISH analysis with PDGFRB break apart probe reveals rearrangement of 5q33, interphase FISH with probe encompassing RABEP1 locus reveals rearrangement of 17p13.

**Probes**

**Additional anomalies**
Reported only as a sole anomaly.

### Genes involved and proteins

**PDGFRB**
- **Location** 5q33.1; chr5:150,113,839-150,155,859 (hg38)
- **DNA / RNA**
  Gene is 42 kb and contains 26 exons. Transcription occurs in telomere to centromere orientation. 5 transcripts are reported.
- **Protein**
  PDGFRB encodes a tyrosine kinase receptor that is located on the plasma membrane and is activated by binding of members of the platelet-derived growth factor family of proteins. The product of the largest transcript is 1106 amino acids. Composed from NH2 to COOH of: Ig-like extracellular domains, a transmembrane domain, and a cytosolic tyrosine kinase domain.

**RABEP1**
- **Location** 17p13.2; chr17: 5,282,263-5,385,812 (hg38)
- **DNA / RNA**
  Gene is 103 kb and contains 20 exons. Transcription occurs in centromere to telomere orientation. 6 transcripts are reported.
- **Protein**
  RABEP1 encodes a protein involved in endocytic membrane fusion and the trafficking of recycling endosomes. The product of the largest transcript is 826 amino acids and contains coiled-coil domains, a NH2-terminal RAB4 binding site, and a COOH-terminal RAB5 binding site.

### Result of the chromosomol anomaly

**Hybrid Gene**
5' RABEP1-3' PDGFRB; no reciprocal transcript.

**Fusion Protein**
- **Description** 1318 amino acid fusion protein, including the first 739 aa of RABEP1 fused to the transmembrane and cytosolic tyrosine kinase domains of PDGFRB.

**Oncogenesis**
Expression of the fusion protein via infection with a MSCV-based retroviral plasmid was sufficient to transform Ba/F3 cells such that they grew independent of IL-3 (Magnusson et al., 2001). Expression of the fusion gene in murine bone marrow cells transplanted into lethally irradiated mice caused development of fatal myeloproliferative disorder (Magnusson et al., 2001).
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A schematic of the fusion transcript generated by the t(5;17)(q33;p13) rearrangement. Modified from Magnusson et al., 2001.

References


This article should be referenced as such: