Leukaemia Section
Short Communication

**ins(9;4)(q33;q12q25)**

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**Clinics and pathology**

**Disease**
Chronic eosinophilic leukemia

**Epidemiology**
One case to date, a 71-year-old female patient with chronic eosinophilic leukemia in accelerated phase (Walz et al., 2006).

**Prognosis**
Remission was obtained with imatinib, but the patient relapsed with imatinib-resistant acute myeloid leukemia that was characterized by a normal karyotype, absence of detectable CDK5RAP2-PDGFRA mRNA, and a newly acquired G12D NRAS mutation.

**Genes involved and proteins**

**PDGFRA**

- **Location**: 4q25
- **Protein**: Receptor tyrosine kinase. Gain-of-function mutations of PDGFRA are implicated in a subset of gastrointestinal stromal tumors (Heinrich et al., 2003). PDGFRA has also been involved in translocations, making hybrid genes with STRN (2p22), FIP1L1 (4q12), KIF5B (10p11), ETV6 (12p13) and BCR (22q11).

**CDK5RAP2**

- **Location**: 9q33
- **Protein**: Centrosomal protein; regulates CDK5; binds EB1. The CDK5RAP2-EB1 complex stimulates microtubule assembly (Fong et al., 2009); critical for centrosomal localization of dynein throughout the cell cycle (Lee and Rhee, 2010). CDK5RAP2-knockdown cells have increased resistance to paclitaxel and doxorubicin (Zhang et al., 2009). Homozygous mutations in CDK5RAP2 can cause microcephaly (Bond et al., 2005).

**Result of the chromosomal anomaly**

**Hybrid gene**

**Description**
In-frame fusion between exon 13 of the CDK5RAP2, a 40 bp insert from an inverted sequence of PDGFRA intron 9, and a truncated PDGFRA exon 12. No reciprocal PDGFRA-CDK5RAP2 transcript.

**Fusion protein**

**Description**
N-term CDK5RAP2 - C-term PDGFRA; 1003 amino acids; contains 494 amino acids, including several potential dimerization domains, of CDK5RAP2 and 509 amino acids from PDGFRA tyrosine kinase domains.

**Oncogenesis**
Constitutive tyrosine kinase activity is likely.

**References**


Gotlib J, Cools J. Five years since the discovery of FIP1L1-PDGFRα: what we have learned about the fusion and other molecularly defined eosinophilias. Leukemia. 2008 Nov;22(11):1999-2010

Fong KW, Hau SY, Kho YS, Jia Y, He L, Qi RZ. Interaction of CDK5RAP2 with EB1 to track growing microtubule tips and to regulate microtubule dynamics. Mol Biol Cell. 2009 Aug;20(16):3660-70


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