

Leukaemia Section

Short Communication

ins(9;4)(q33;q12q25)

Jean-Loup Huret

Genetics, Dept Medical Information, University of Poitiers, CHU Poitiers Hospital, F-86021 Poitiers, France (JLH)

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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-PDGFR α 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.

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