Leukaemia Section
Mini Review

\textbf{t(4;10)(q12;p11)}

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**Clinics and pathology**

**Disease**
Myeloproliferative syndrome with hypereosinophilia.

**Epidemiology**
Only one case to date, a 54-year old male patient.

**Evolution**
Complete remission could not be obtained with hydroxyurea. Following the identification of the PDGFRα hybrid gene, imatinib was started, and the patient entered complete cytogenetic remission (CR). The patient is still in RT-PCR CR after 18 months.

**Genes involved and proteins**

**PDGFRα**

**Location**
4q12

**Protein**
Composed of an extracellular domain, a transmembrane domain, an intracellular domain; receptor tyrosine kinase; forms homodimer, and heterodimer with PDGFRβ; dimerization induces kinase domain activation, leading to the activation of intracellular signalling pathways (Kawagishi et al., 1995).

**Somatic mutations**
Hybrid genes between various partners and PDGFRα occur in chronic myeloid leukaemia-like diseases with eosinophilia, mostly chronic eosinophilic leukemia (CEL), a clonal hypereosinophilic syndrome. PDGFRα partners known so far are: STRN (2p24) (Curtis et al., 2007), FIP1L1 (4q12) (Cools et al., 2003; Pardanani et al., 2004), CDK5RAP2 (9q33) (Walz et al., 2006), KIF5B (10p11) (Score et al., 2006), ETV6 (12p13) (Curtis et al., 2007), and BCR (22q11) (Baxter et al., 2002). Mutations of platelet-derived growth factor receptor-alpha (PDGFRα) are observed in a subset of gastrointestinal stromal tumors (GISTs) (Heinrich et al., 2003). Tumours with PDGFRα involvement are responsive to imatinib therapy (Cools et al., 2003; Debie-Rychter et al., 2004).

**KIF5B**

**Location**
10p11

**Protein**
Composed of a N-terminal globular domain that hydrolyzes ATP and binds microtubule, a central alpha-helical coiled-coil domain (dimerization domain); and a C-terminal domain that interacts with other proteins, vesicles and membranous organelles. Kif5B is involved in microtubule-based polarized vesicular transport to the apical membrane in polarized axonal transport in neurons (Nakata and Hirokawa, 2003; Jacobson et al., 2007; Jaulin and Mostov, 2007). The role of the complex of syntaxin-1-syntabulin-KIF5B in axonal transport has been established (Cai et al., 2007). Kif5B and Kifc1 interact in motility and processing of early endocytic vesicles (Nath et al., 2007). KIF5B has been shown to be essential for axonal transport of mitochondria. KIF5B associates with the kinesin-binding domain (KBD) of RanBP2 to determines mitochondria localization (Cho et al., 2007). JNK forms a complex with KIF5B and β-tubulin-III in neurites, and TNF disturbs axonal transport of mitochondria via JNK (Stagi et al., 2006).

**Result of the chromosomal anomaly**

**Hybrid gene**

**Description**
In frame fusion of KIF5B exon 23 to PDGFRα exon 12; no reciprocal PDGFRα-KIF5B product.
**Fusion protein**

**Description**
156 kDa protein of 1372 amino acids; Composed of the N-terminal globular domain and the central alpha-helical coiled-coil domain (dimerization domain) of KIF5B, fused to the kinase domain of PDGFRA. It is likely that the dimerization domain induces constitutive activation of the kinase domain.

**References**


Nath S, Bananis E, Sarkar S, Stockert RJ, Sperry AO, Murray JW, Wolkoff AW. KIF5B and KIF1 interact and are required for motility and fission of early endocytic vesicles in mouse liver. Mol Biol Cell. 2007 May;18(5):1839-49

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