t(2;4)(p22;q12)

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Clinics and pathology

Disease
Myeloproliferative disease with eosinophilia

Epidemiology
Only one case to date, a 64 year old male patient.

Prognosis
The patient remained in complete remission for 24 months of treatment with imatinib, but refused any more treatment, although there was no side effect. Elevated eosinophil counts were again detected 14 months after end of treatment.

Genes involved and proteins

STRN
Location 2p22.2
Protein Composed of a caveolin-binding domain, a coiled-coil domain, a calmodulin-binding domain, and at least 6 WD-repeats. Striatin (STRN) binds many proteins, and forms multi-protein complexes. It is a scaffolding protein; striatin contains a caveolin-binding consensus motif, and binds caveolin-1, the major protein involved in caveolae and lipid rafts. Striatin is also involved in signaling and trafficking in a Ca^{2+} dependant manner, exhibiting a dual role in endocytic process and signaling.

PDGFRA
Location 4q12
Protein Composed of an extracellular domain (the immunoglobulin-like motifs), a transmembrane domain, with an inhibitory juxtamembrane WW-like domain (Irusta et al., 2002), and an intracellular domain (kinase domain); receptor tyrosine kinase; forms homodimer, and heterodimer with PDGFRB; 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 PDFRGA occur in chronic myeloid leukaemia-like diseases with eosinophilia, mostly chronic eosinophilic leukemia (CEL), a clonal hyper eosinophilic syndrome. PDGFRA partners known so far are: STRN (2p24), herein described (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 (PDGFRA) are observed in a subset of gastrointestinal stromal tumors (GISTs) (Heinrich et al., 2003).

Tumours with PDGFRA involvement are responsive to imatinib therapy (Cools et al., 2003; Debiec-Rychter et al., 2004).

Result of the chromosomal anomaly

Hybrid gene
Transcript 5' STRN-3' PDGFRA; Fusion between STRN intron 6
and a truncated PDGFRA exon 12; reciprocal product not found - in frame fusion between STRN exon 6 and PDGFRA exon 12.

**Fusion protein**

**Description**

The N-term STRN - C-term PDGFRA fusion protein retains the caveolin-binding domain, the coiled-coil domain, and the calmodulin-binding domain, but not the WD-repeats of STRN, fused to a truncated WW-like domain and the kinase domain of PDGFRA; the coiled-coil domain from STRN may act as a dimerization motif that could constitutively activate PDGFRA tyrosine kinase.

**References**


This article should be referenced as such: