Leukaemia Section
Mini Review

\(t(4;5)(q21;q33)\)

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Diseases and pathology

Disease
Atypical myeloproliferative disease (a-MPD) and systemic mast cell disease (SMCD)

Epidemiology
3 cases to date, a 45-year-old female patient with a-MPD with basophilia and eosinophilia (Walz et al., 2007), a 61-year-old male patient with systemic mast cell disease (SMCD) and an associated chronic basophilic leukemia (Lahortiga et al., 2008), and a 45-year-old male patient with a SMCD with eosinophilia (Gallagher et al., 2008).

Prognosis
This translocation seems to respond well to imatinib therapy; the chromosomal anomaly disappeared with imatinib in the first patient; in the second case, the patient remained in clinical and cytogenetic remission 3 years after imatinib was initiated; the third patient was alive and well after about 4 years of therapy with imatinib.

Genes involved and proteins

Note
The patient with SMCD and an associated chronic basophilic leukemia was negative for KIT mutations (Lahortiga et al., 2008).

PRKG2
Location 4q21
Protein
762 amino acids; comprises a coiled-coil domain (leucine zipper, amino acids 23-85), cGMP binding sites (168-285 and 286-417) and a serine-threonine kinase domain (453-711); involved in signaling pathway. Belongs to the family of cyclic GMP-dependent protein kinase. PRKG2 phosphorylates CFTR. PRKG2 is an ion transport regulator (Vaandrager et al., 2005). PRKG2 regulates SOX9-mediated transcription of collagen 2 through phosphorylation (Chikuda et al., 2004). It was found that PRKG2 has an anti-proliferative effect via suppression of SOX9 expression, inhibition of Akt phosphorylation, and G1 arrest in glioma cell lines (Swartling et al., 2009).

PDGFRB
Location 5q33
Protein
Comprises an extracellular part with 5 Ig-like C2 type domains, a transmembrane domain, and an intracellular part with a tyrosine kinase domain (made of two tyrosine kinase subdomains) for transduction of the signal. Receptor tyrosine kinase; receptor for PDGF B and PDGFD (Bergsten et al., 2001); forms homodimers, or heterodimer with PDGFRA; upon dimerization, subsequent activation by autophosphorylation of the tyrosine kinase intracellular domains occurs.

Result of the chromosomal anomaly

Hybrid gene
Description
5’ PRKG2 - 3’ PDGFRB. In-frame fusion between exon 2 of PRKG2, a 5 bp insert derived from intron 2 of PRKG2, and a truncated version (last 33 bp) of exon 12 of PDGFRB in one case (Lahortiga et al., 2008), and In-frame fusion between exon 5 of PRKG2, a 17 bp
insert derived from PRKG2 intron 5, and a 41 bp truncated version exon 12 of PDGFRB in another case (Walz et al., 2007).

**Fusion protein Oncogenesis**

The coiled-coil domain from PRKG2 would favour dimerization, with subsequent constitutive activation of the PDGFRB tyrosine kinase domain.

**References**


Vaandrager AB, Hogema BM, de Jonge HR. Molecular properties and biological functions of cGMP-dependent protein kinase II. Front Biosci. 2005 Sep 1;10:2150-64


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This article should be referenced as such: