**Atlas of Genetics and Cytogenetics in Oncology and Haematology**



# t(5;9)(q32;p24) KANK1/PDGFRB

## Clinics and Pathology

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|---|---|
| **Disease** | Myeloproliferative neoplasm with essential thrombocythemia |
| **Note** | No detectable BCR-ABL transcript or JAK2 V617F mutation. |
| Epidemiology | Found in one case of myeloproliferative neoplasm with severe thrombocythemia, in a 67-year-old male. |
| Clinics | Thrombocythemia (platelets, 904 x $10^9$/l) without prominent eosinophilia or neutrophilia. |
| Cytology | Increased number of polymorphic megakaryocytes without any blast cells or dysplastic features; suggestive of myeloproliferative neoplasm, most likely essential thrombocythemia. |
| Treatment | No response to hydroxyurea, complete remission with imatinib at the dose of 100 mg/day. |
| Evolution | Complete remission (FU: 3 years). |
| Prognosis | Unknown. |

## Cytogenetics

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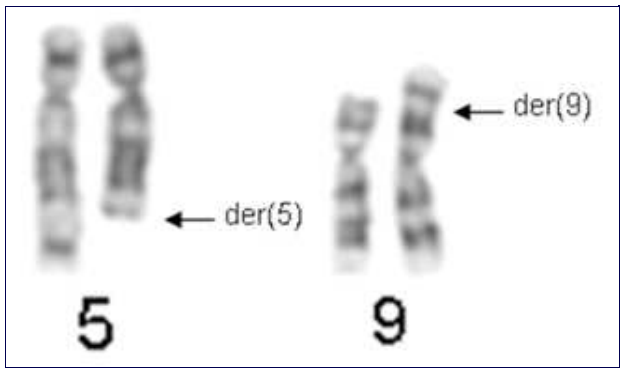
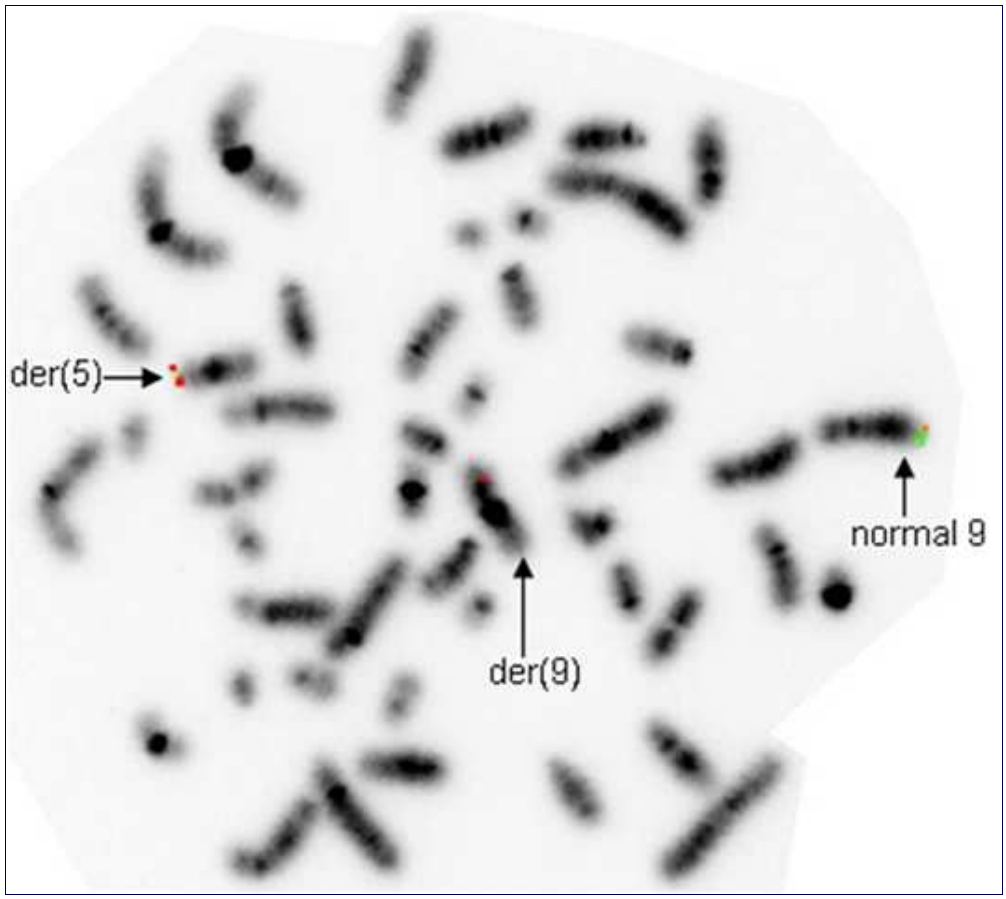
|---|---|
| Cytogenetics Morphological | 46,XY,t(5;9)(q31~32;p22~?24.3)[16]/46,XY[2]. |




| | |
|---|---|
| Cytogenetics Molecular | Disruption of PDGFRβ (5q31~32) and KANK1 (9p24.3) loci. |




FISH analysis using the RP11-130C19 and RP11-31F19 probes. RP11-130C19 is split between the der(5) and the der(9), while RP11-31F19 is translocated to the der(5).

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| Probes | RP11-130C19 and RP11-31F19. |
| Additional anomalies | No. |

## Genes involved and Proteins

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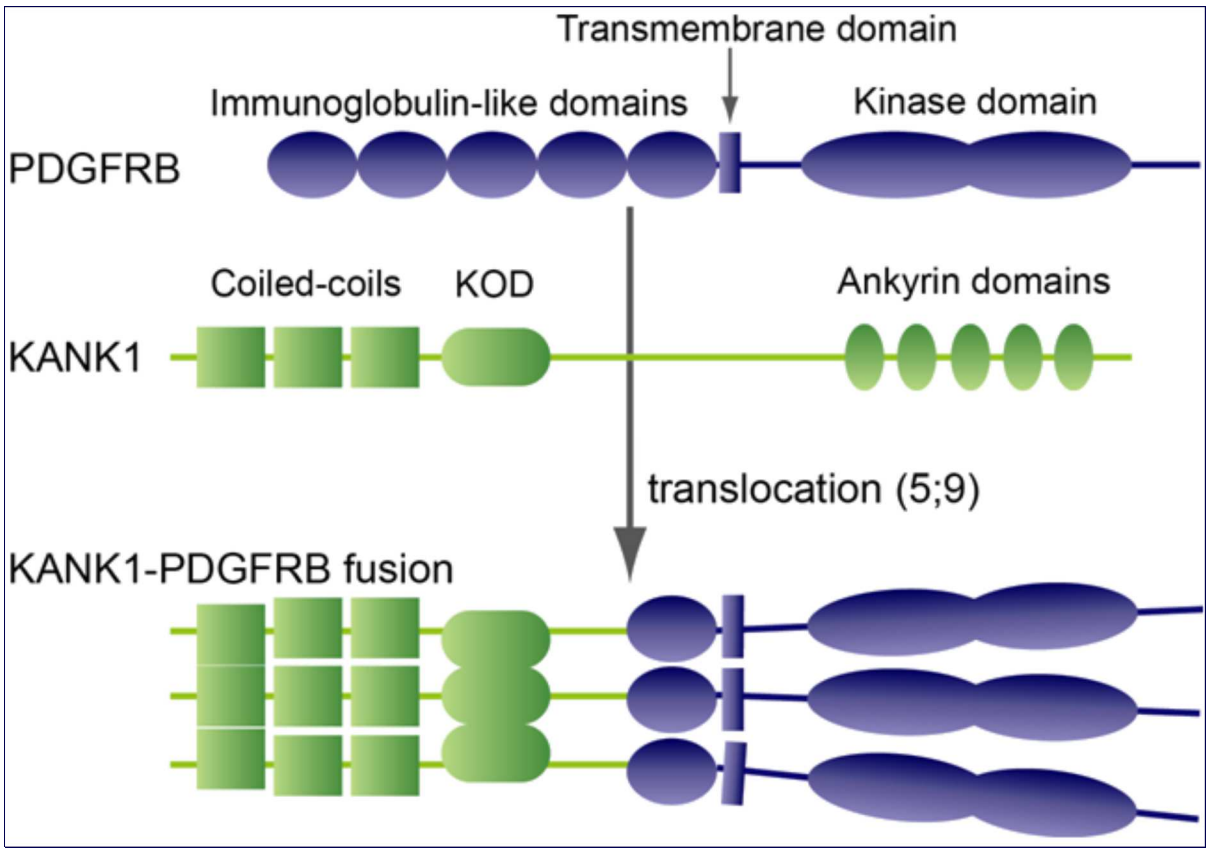
| **Gene Name** | KANK1 (KN motif and ankyrin repeat domains 1) |
| Location | 9p24.3 |
| Note | Formerly: KANK, ANKRD15, KIAA0172. |
| Protein | Two KANK1 protein isoforms are encoded by different transcripts of the same gene: a long isoform of 1352 amino-acids and a short one 1194 aa, which is predominant in hematopoietic cells (Medves et al., 2010). Both isoforms have multiple N-terminal coiled-coil domains, which are included in the fusion with PDGFRB, and C-terminal ankyrin repeat domains (Kakinuma et al., 2009). |
| **Gene Name** | PDGFRB (platelet-derived growth factor receptor, beta polypeptide) |
| Location | 5q31-33 |
| Protein | Platelet-derived growth factors (PDGF) receptor, beta isoform. This receptor belongs to the receptor tyrosine kinase family (type III). |

## Result of the chromosomal anomaly

### Hybrid gene

| | |
|---|---|
| Description | Exon 2 of KANK1 (ENST00000382293, Ensembl database, up to nucleotide 3020) is fused to exon 9 of PDGFRB (ENST00000261799, from nucleotide 1714). |

**Fusion Protein**




Structure of PDGFRB, KANK1 and the KANK1-PDGFRB fusion. See text for details. KOD, KANK1 oligomerization domain. Adapted from Demoulin et al., 2012 and Medves et al., 2012.

Description The fusion protein contains the first 741 residues of KANK1 fused to the last 692 residues of PDGFRB (Medves et al., 2010). This includes several coiled-coil domains of KANK1 and the fifth immunoglobulin-like domain, the transmembrane domain and the kinase domain of PDGFRB. The deletion of the immunoglobulin-like domain does not affect the oncogenic activity of the fusion (Medves et al., 2010). By contrast, deletion of the coiled-coil domains prevents cell transformation and signaling via STAT5 and MAP kinases (Medves et al., 2011). Our data suggest that KANK1-PDGFRB adopts a trimeric and multimeric conformation (Medves et al., 2011).

Oncogenesis This fusion protein induces the proliferation of Ba/F3 cells (Medves et al., 2010) and CD34+ human progenitors (Medves et al., 2011).
The fusion was identified in thrombocythemia, which is associated with JAK2 mutations or indirect activation of JAK2 by mutated thrombopoietin receptors (c-MPL). In the present case, no JAK2 activation was detected in cells expressing KANK1-PDGFRB and these cells are not sensitive to JAK inhibitors (Medves et al., 2011). Instead, they are highly sensitive to imatinib.

## External links

Other database t(5;9)(q32;p24) KANK1/PDGFRB Mitelman database (CGAP - NCBI)

## To be noted

Additional cases are needed to delineate the epidemiology of this rare entity:
**you are welcome to submit a paper to our new Case Report section**.

## Bibliography

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## Contributor(s)

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