Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section

Mini Review

KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog)

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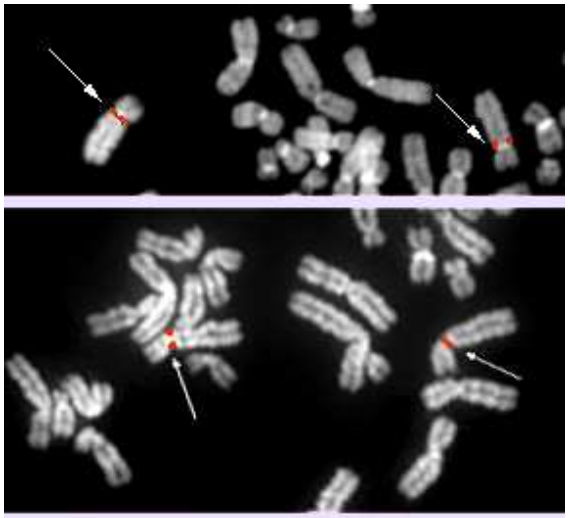
Identity

Other names: SCFR (Stem cell factor receptor); CD117

Location: 4q12

Local order: Centromere-PDGFRA-KIT-KDR-telomere.



bA74L18 (top) and bA586A2 (bottom)

KIT (4q12) - Courtesy Mariano Rocchi.

DNA/RNA

Description

Spans over 70 kb; 21 exons; size of intron 1: >30 kb.

Transcription

5,23 kb mRNA; alternative splicing of exon 9 gives rise to two isoforms, KITA and KIT, that differ by the presence or absence of four amino acids.

Protein

Description

976 aa; 145 kDa; type III receptor tyrosine kinase; contains an extracellular domains with 5 Ig-like loops, a highly hydrophobic transmembrane domain (23 aa), and an intracellular domain with tyrosine kinase activity split in an ATP-binding region and in the phosphotransferase domain by a kinase insert (KI).

Expression

Hematopoietic stem cells, mast cells, melanocytes, germ-cell lineages and ICCs (interstitial cells of Cajal).

Localisation

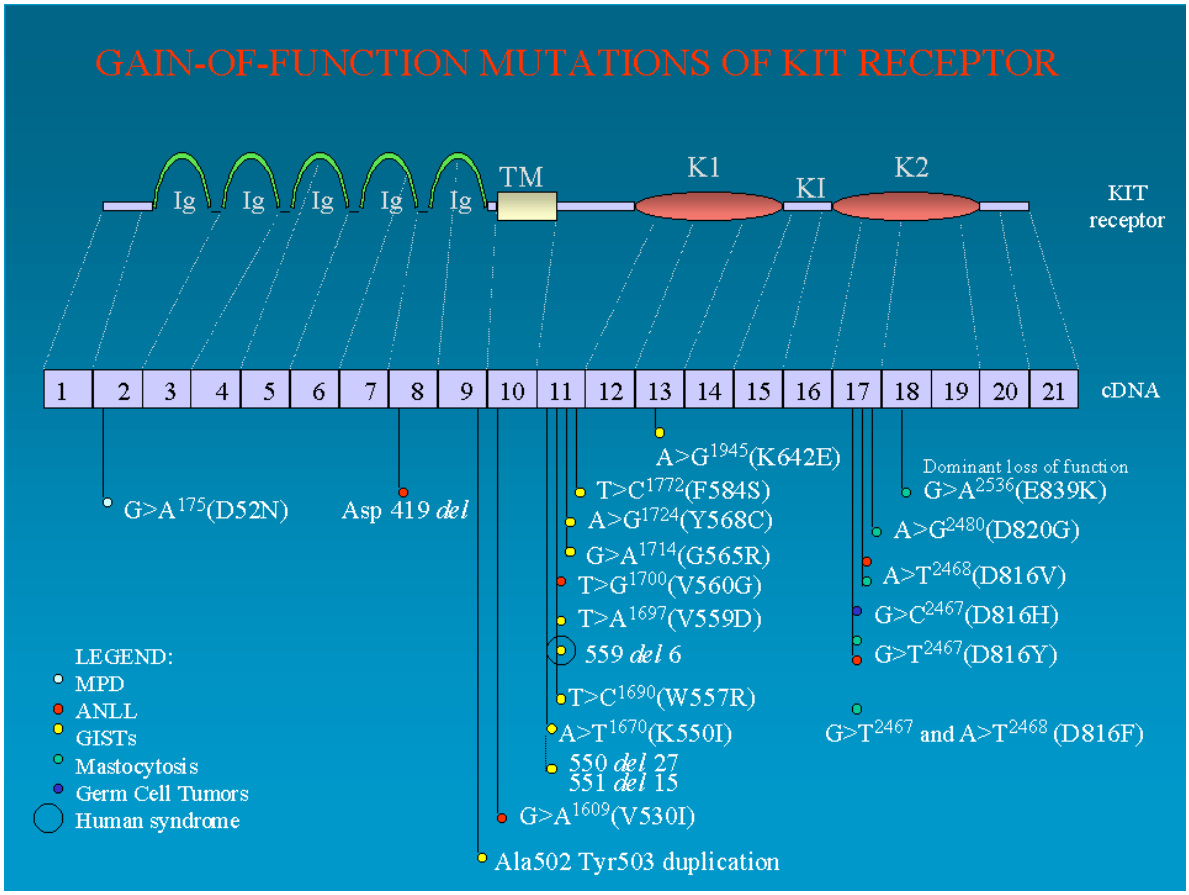
Plasma membrane.

Function

SCF/MGF receptor with tyrosine kinase activity; binding of ligand (SCF) induces receptor dimerization, autophosphorylation and signal transduction via molecules containing SH2-domains.

Homology

With CSF-1R, PDGFRb, PDGFRa, and FLT3.



Mutations

Germinal

In piebaldism, and in familial gastrointestinal stromal tumours (see below).

Somatic

In aggressive mastocytosis, mast cell leukemia, AML with mast cell involvement, myeloproliferative disorders, colon carcinoma and gastrointestinal stromal tumours.

Implicated in

Piebaldism

Disease

Autosomal dominant disorder of pigmentation; loss of function abnormalities of the c-KIT gene have been demonstrated in 59% of the typical patients.

Familial gastrointestinal stromal tumours and sporadic gastrointestinal stromal tumours (GISTs)

Disease

GISTs are the most common mesenchymal tumors in the human digestive tract; they originate from KIT-expressing cells (ICCs), and were found to have activating c-KIT mutations in the juxtamembrane domain.

Systemic mast cell disease (SMCD)

Disease

Mast cell hyperplasia in the bone marrow, liver, spleen, lymph nodes, gastrointestinal tract and skin; gain of function mutations have been detected in a few patients.

Prognosis

Depending on the four clinical entities recognized: indolent form, form associated with hematologic disorder, aggressive SMCD and mast cell leukemia;

leukemic transformation with mast cell involvement is characterized by rapid progression of disease with a survival time less than 1 year.

Oncogenesis

Clinical features of malignant hematopoietic cell growth are influenced by the time, the location of c-KIT mutative events, and the number of associated lesions.

To be noted

Note

Loss of expression of c-KIT appears to be associated with progression of some tumors (melanoma) and autocrine/paracrine stimulation of the c-KIT/SCF system may participate in human solid tumors such as lung, breast, testicular and gynecological malignancies.

References

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