

Gene Section

Mini Review

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

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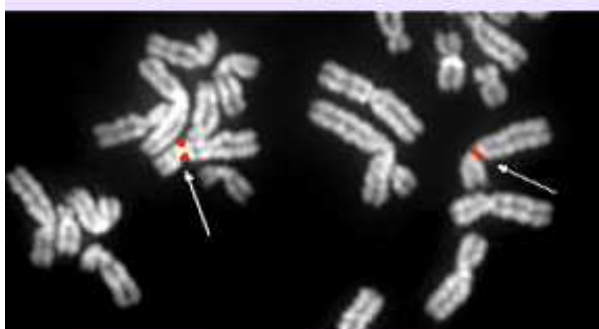
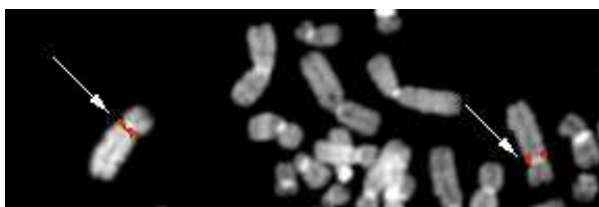
Identity

Other names: SCFR (Stem Cell Factor Receptor); CD117

HGNC (Hugo): KIT

Location: 4q12

Local order: centromere-PDGFRa-KIT-KDR-telomere.



bA74L18 (top) and bA586A2 (bottom)

KIT (4q12) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

Description

Spans 89 kb; 21 exons; size of intron 1: 37,4 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 aminoacids.

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 by a kinase insert (KI) in an ATP-binding region and in the phosphotransferase domain.

Expression

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

Localisation

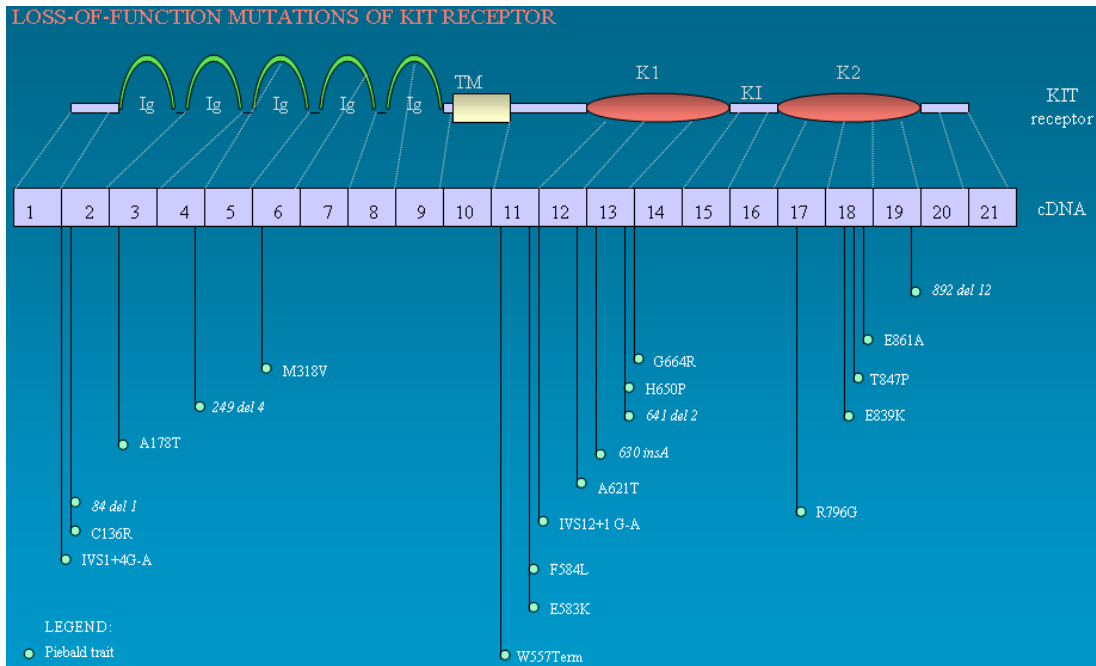
Plasma membrane.

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

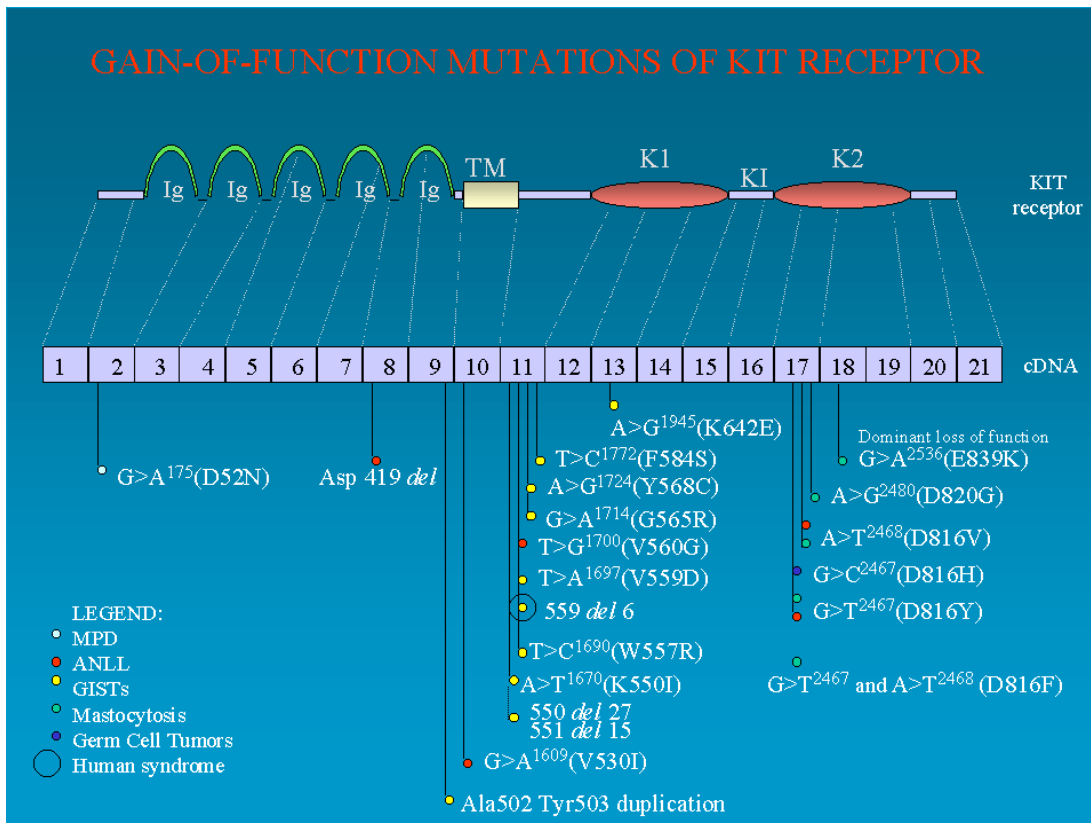
Note: See diagrams: Loss-of-function mutations, and Gain-of-function mutations.

Germinal

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

Somatic

In aggressive mastocytosis, mast cell leukemia, ANLL with/without mast cell involvement, myeloproliferative disorders, colon carcinoma and gastrointestinal stromal tumours and germ cell tumors (GCCs).



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 often have activating c-kit mutations clustered 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 are detected in most 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.

Core binding factor leukemias (ANLL-M2 with t(8;21) (link), (ANLL-M4Eo with inv(16))

Disease

Characterized by disruption and loss of CBFa2/AML1 - CBFb/PEBP2b function.

Myelomonoblastic leukemia cells are marked by combined positivity for the stem cell antigens CD34, CD117 and high frequency of c-kit mutations (see Figure on CBF leukemia and KIT mutations).

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.

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