

Gene Section

Review

FLT3 (FMS-like tyrosine kinase 3)

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Identity

Other names: CD135; FLK2 (Fetal liver kinase 2); STK1 (Stem cell kinase 1)

Location: 13q12

DNA/RNA

Description

The FLT3 gene contains 24 exons and spans at least 96 kb of DNA; the exact size of the gene is unknown because there is a large intron (>50 kb) between exon 2 and exon 3.

Transcription

3.7 kb; 2979 bp open reading frame.

Protein

Description

993 amino acids; FLT3 is a class III receptor tyrosine kinase (RTK) structurally related to the receptors for platelet derived growth factor (PDGF), colony stimulating factor 1 (CSF1), and KIT ligand (KL); these RTK contain five immunoglobulin-like domains in the extracellular region and an intracellular tyrosine kinase domain split in two by a specific hydrophilic insertion (kinase insert); immunoprecipitation of the human FLT3 protein results in the appearance of a minor band of Mr 130 000 and a major band of Mr 155 000/160 000; the high-molecular-weight band corresponds to the mature, N-glycosylated form, and the low-molecular-weight band to the immature, high mannose-containing form; N-linked glycosylations account for 50 000 daltons.

Expression

FLT3 expression was described on bone marrow CD34-positive cells, corresponding to multipotential, myeloid and B-lymphoid progenitor cells, and on monocytic cells; FLT3 expression is restricted to cells of the fetal liver expressing high levels of CD34; in addition, the FLT3 protein is expressed on blast cells from most ANLL and B-ALL.

Localisation

Functional mature form is at the plasma membrane.

Function

FLT3 receptor function can be defined by the activity of its ligand (FL); FL is an early acting factor and supports the survival, proliferation and differentiation of primitive hemopoietic progenitor cells.

Mutations

Somatic

An internal tandem duplication in the juxtamembrane domain-coding sequence of the gene was found in 20% of acute non lymphocytic leukemias (ANLL) and in a small number of myelodysplasia; the duplicated sequence belongs to exon 11 but sometimes involves intron 11 and exon 12; these FLT3 gene mutations are significantly associated with leukocytosis in M1 and M2 but not in M4/5 ANLL, and are associated with an unfavorable prognosis regardless of the FAB subtype.

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