Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section
Mini Review

FGFR1 (Fibroblast Growth Factor Receptor 1)

Marie-Josèphe Pébusque

INSERM U119, IFR 57, 27 Blvd Lei Roure, 13009 Marseille, France (MJP)

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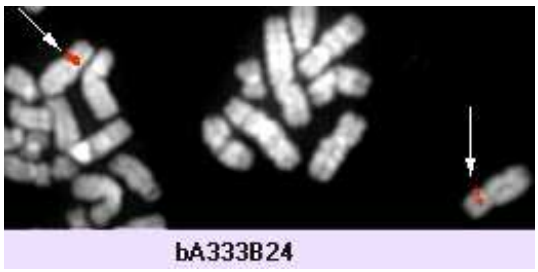
Identity

Other names: BFGFR (basic fibroblast growth factor receptor); FLT2 (FMS-like tyrosine kinase 2); FLG (FMS-like gene); CEK; FGFBR; N-SAM

Location: 8p11



FGFR1 (8p12) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

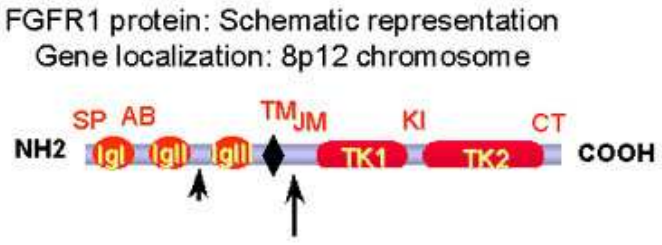
Transcription

2.7 mRNA.

Protein

Description

822 amino acids; 100-135 kDa glycoprotein from a 90-115 kDa



The extracellular domain contains a signal peptide (SP), two (IgII, IgIII) or three (IgI, IgII, and IgIII) Ig-like domains, followed by the transmembrane domaine (TM), and an intracellular domain comprising a juxtamembrane domain (JM), two tyrosine kinase subdomains (TK1, TK2) interrupted by a short kinase insert (KI), and a C-terminal-tail (CT).
The acidic box (AC) indicated in the extracellular domain is a specific feature of FGF receptors.
Vertical arrow indicates the localization of the breakpoint in the 8p12 myeloproliferative disorder;
Arrowhead indicates the position of FGFR1 germline mutation in the Pfeiffer syndrome

protein core; tyrosine kinase receptor; contains four major domains: an extracellular domain with 2 or 3 Ig-like loops, a transmembrane domain and an intracellular domain, a juxtamembrane domain, and an intracellular domain composed of the tyrosine kinase domain (two kinase domains interrupted by a short kinase insert), and a C-terminal tail.

Localisation

Plasma membrane.

Function

FGF receptor with tyrosine kinase activity; binding of ligand (FGF) in association with heparan sulfate proteoglycans induces receptor dimerization, autophosphorylation and signal transduction.

Homology

With other FGFR (FGFR2, FGFR3, and FGFR4).

Implicated in

Stem-cell myeloproliferative disorder associated with chromosomal translocations involving 8p12; to date, seven FGFR1 partners have been described (see below)

Disease

Stem-cell myeloproliferative disorder characterized by T- or B-cell lymphoblastic leukemia/lymphoma, myeloid hyperplasia, and peripheral blood eosinophilia, and it generally progresses to acute myeloid leukemia; specific to the 8p12 chromosomal region.

Prognosis

Very poor (median survival: 12 months).

Cytogenetics

The 7 translocations are:
-t(6;8)(q27; p12) involving FOP (FGFR1 Oncogene Partner);
-t(8;9)(p12;q33) involving CEP110 (Centrosome protein 110);
-t(8;11)(p12;p15);
-t(8;12)(p12;q15);
-t(8;13)(p12;q12) involving FIM (Fused In Myeloproliferative disorder also called ZNF198 or RAMP);
-t(8;17)(p12;q25);
-t(8;19)(p12;q13.3);
additional anomalies: in the t(8;9)(p12;q33): +der(9), +21; in the t(8;13)(p12;q12): +8, +der(13), +21.

Hybrid/Mutated gene

-5' FOP - 3' FGFR1 in the t(6;8),
-5' CEP110 - FGFR1 in the t(8;9),
-5' FIM/ZNF198 - 3' FGFR1 in the t(8;13).

Abnormal protein

Three fusion transcripts are identified: FOP-FGFR1, CEP110-FGFR1, and FIM-FGFR1; they encode large proteins containing the N-term of either FOP or CEP110, or FIM, and the catalytic domain of FGFR1 at their C-term:
-N-term leucine-rich region from FOP fused to the catalytic domain of FGFR1;
-N-term leucine zipper motifs from CEP110 fused to the catalytic domain of FGFR1;
-N-term zinc fingers from FIM fused to the Tyrosine kinase domain of FGFR1in C-term.

Oncogenesis

Constitutive activation of FGFR1.

Pfeiffer syndrome (inborn disease)

Disease

One form of Pfeiffer syndrome, an autosomal dominant craniosynostosis syndrome with broad thumbs and usually no mental deficiency, is due to a mutation in amino acid 252 (Pro252Arg substitution) of FGFR1.

Breast cancer

Disease

Gene amplification and overexpression in sporadic breast tumors.

References

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