Atlas of Genetics and Cytogenetics
in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Cancer Prone Disease Section

Mini Review

Familial gastrointestinal stromal tumors (GISTs)

Lidia Larizza, Alessandro Beghini

Department of Biology and Genetics for Medical Sciences, Medical Faculty, University of Milan, Via Viotti 3/5, 20133 Milan, Italy (LL, AB)

Published in Atlas Database: September 1998

Online updated version : http://AtlasGeneticsOncology.org/Kprones/GastroISTID10029.html
DOI: 10.4267/2042/37492

Identity

Note

A recently described familial cancer syndrome characterized by development of multiple GISTs in different family members.

Inheritance

Autosomal dominant.

Clinics

Phenotype and clinics

Symptoms are attributable to development of benign and malignant GISTs.

Hyperpigmentation and mast-cell disease may be associated.

- Etiology: GISTs originate from the CD34+/KIT+ interstitial cells of Cajal (ICCs) which development depends on the SCF/KIT interaction; germline/somatic KIT mutations in familial/solitary GISTs.

- Pathology: mesenchymal tumours developped in the gastrointestinal wall mainly characterized by positivity for both KIT and CD34; precursor tumour cells are likely ICCs that are located in and near the circular muscle layer of the stomach, small intestine and large intestine.

Genes involved and proteins

KIT

Location

4q12

DNA/RNA

Description: 21 exons

Protein

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

Mutations

Germinal: Small deletion of one of two consecutive valine residues (codon 559 or 560, GTTGTT).

Somatic: In frame deletions (550del27, 551del15, 559del6) and missense mutations (Lys 550Ile and Val559Asp); all mutations, clustered in exon 11, lead to constitutive phosphorylation and kinase activation.

References

Hirota S, Isozaki K, Moriyama Y, Hashimoto K, Nishida T, Ishiguro S, Kawano K, Hanada M, Kurata A, Takeda M, Muhammad Tunio G, Matsuzawa Y, Kanakura Y, Shinomura Y, Kitamura Y. Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors. Science. 1998 Jan 23;279(5350):577-80

Nishida T, Hirota S, Taniguchi M, Hashimoto K, Isozaki K, Nakamura H, Kanakura Y, Tanaka T, Takabayashi A, Matsuda H, Kitamura Y. Familial gastrointestinal stromal tumours with germline mutation of the KIT gene. Nat Genet. 1998 Aug;19(4):323-4

This article should be referenced as such:

Larizza L, Beghini A. Familial gastrointestinal stromal tumors (GISTs). Atlas Genet Cytogenet Oncol Haematol. 1999; 3(1):43.