Familial gastrointestinal stromal tumors (GISTs)

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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 developed 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
Germline: 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


This article should be referenced as such: