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Cancer Prone Disease Section

Mini Review

Familial / sporadic 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 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: Simple in frame deletions, point mutations, deletion and point mutations are mainly clustered in exon 11 (from codon 550 to 584), but a few have been also identified in exon 9 and exon 13; all mutations are predicted to lead to constitutive phosphorylation and kinase activation.

The percentage of GISTs positive for c-kit mutations in exon 11 has been estimated to be 57%.

Use of c-kit mutation as unfavourable prognostic marker is under debate.

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

Sakurai S, Fukasawa T, Chong JM, Tanaka A, Fukayama M. C-kit gene abnormalities in gastrointestinal stromal tumors (tumors of interstitial cells of Cajal. Jpn J Cancer Res. 1999 Dec;90(12):1321-8

Taniguchi M, Nishida T, Hirota S, Isozaki K, Ito T, Nomura T, Matsuda H, Kitamura Y. Effect of c-kit mutation on prognosis of gastrointestinal stromal tumors. Cancer Res. 1999 Sep 1;59(17):4297-300

Lux ML, Rubin BP, Biase TL, Chen CJ, Maclure T, Demetri G, Xiao S, Singer S, Fletcher CD, Fletcher JA. KIT extracellular and kinase domain mutations in gastrointestinal stromal tumors. Am J Pathol. 2000 Mar;156(3):791-5

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