Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

KITLG (KIT ligand)

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Published in Atlas Database: June 2000

Online updated version : http://AtlasGeneticsOncology.org/Genes/MGFID142.html
DOI: 10.4267/2042/37633

This article is an update of : Beghini A, Larizza L. MGF (Mast cell growth factor). Atlas Genet Cytogenet Oncol Haematol 1999;3(1):6-7.

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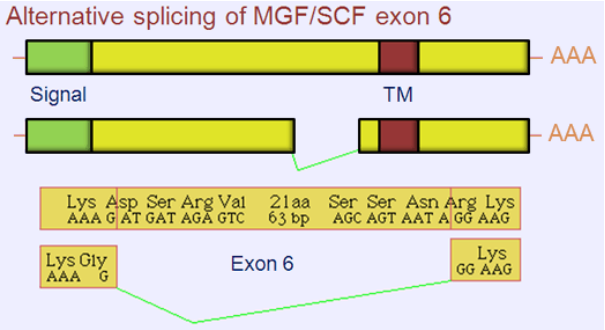
Identity

Other names: MGF (Mast Cell Growth Factor); SCF (Stem Cell factor)

HGNC (Hugo): KITLG

Location: 12q22

DNA/RNA



Description

Genomic sequence not known; 9 exons.

Transcription

1,4 Kb mRNA; alternative splicing gives rise to different transcripts, mainly represented by those for a membrane and a soluble form.

Protein

Description

The membrane bound form is a surface molecule of 248 aa, that includes 23 aa of the highly hydrophobic transmembrane domain; the second form corresponds to a soluble protein constituted by the first 165 aa of the extracellular domain released by a posttranslational processing, consisting in a proteolytic cleavage of the mature SCF in the extracellular juxtamembrane region; the full length transcripts encode for a transmembrane precursor of the soluble protein; an alternative splicing that involves the region corresponding to exon 6 of the SCF cDNA, which contains the proteolytic cleavage site, encodes for a surface molecule.

Expression

SCF transcripts have been found in the cells surrounding kit-positive cells, such as granulosa and Sertoli cells, bone marrow stromal cells and in fibroblasts, keratinocytes and mature granulocytes; SCF expression of peripheral lymphocytes and monocytes is still controversial.

Localisation

Plasma membrane or interstitial space.

Function

SCF/MGF binding of receptor KIT, with tyrosine kinase activity, induces receptor dimerization, autophosphorylation and signal transduction via molecules containing SH2-domains; the soluble and the transmembrane protein have a different biological activity; the soluble form mainly stimulates cellular proliferation; the membrane-bound isoform induces an activation of the receptor more prolonged than the soluble one.

Homology

With PDGFRb, PDGFRa, and CSF-1.

Mutations

Germinal

Human mutations are yet unknown in human MGF/SCF gene; mouse mutations at the murine steel (Sl) locus that encodes MGF are known and give rise to deficiencies in pigment cells, germ cells, and blood cells; in particular the steel-Dickie (Sld) mouse has a 4.0-kb intragenic deletion that truncates the Sl coding sequence; Sld mice are only capable of encoding a soluble truncated growth factor that lacks both transmembrane and cytoplasmic domains.

Implicated in

Mastocytosis

Disease

In skin from patients with mastocytosis, MGF was found prevalently free in the dermis and in extracellular spaces between keratinocytes suggesting the presence of a soluble form of the protein; altered distribution of mast cell growth factor in the skin of patients with cutaneous mastocytosis is consistent with abnormal production of the soluble form of the factor, resulting by an increased cleavage of SCF with excessive release of a soluble form from the normally membrane bound form; no sequence abnormalities were detected in MGF mRNA.

Gynecological tumors

Disease

Findings obtained on three cervical carcinomas (ovarian serous adenocarcinoma, small cell carcinoma and ovarian immature teratoma) and two gynecological cancer cell lines (ME180 and HGCM) demonstrate coexpression of c-Kit receptor and SCF; these observations are consistent with the possibility that an autocrine activation of SCF/KIT system might be involved in gynecological malignancies.

Small-cell lung cancer

Disease

SCF is expressed in small-cell lung cancer (SCLC); abundant expression of SCF and c-Kit mRNA was seen in 32% of SCLC cell lines and 66% of SCLC tumors; an autocrine mechanism in the pathogenesis of SCLC is strongly suggested.

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This article should be referenced as such:

Larizza L, Beghini A. KITLG (KIT ligand). Atlas Genet Cytogenet Oncol Haematol. 2000; 4(3):99-100.