Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section

Mini Review

ROBO1 (roundabout, axon guidance receptor, homolog 1 (Drosophila))

Oliver Doebler, Joern Groene

Vivantes Clinic Auguste Viktoria, Department of Surgery, Berlin, Germany (OD), Charite - Campus Benjamin Franklin, Department of Surgery, Berlin,Germany (JG)

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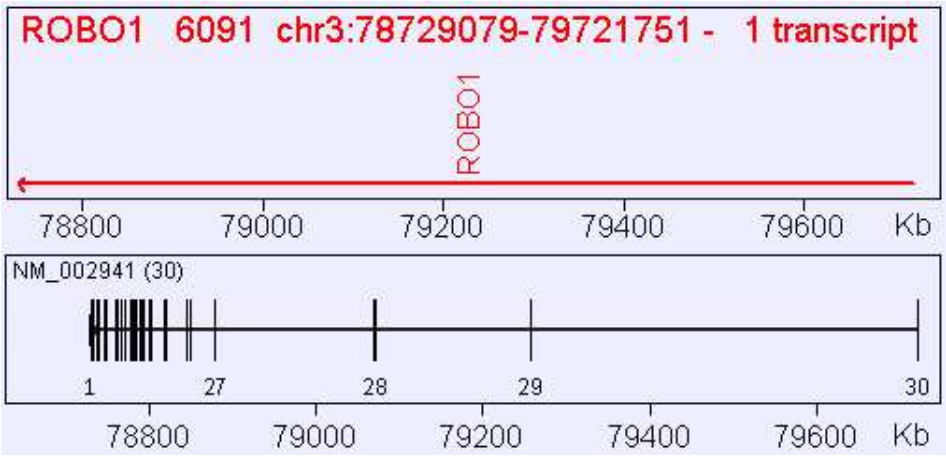
Identity

Other names: DUTT1; FLJ21882; MGC131599; MGC133277; SAX3

HGNC (Hugo): ROBO1

Location: 3p12.3



DNA/RNA

Description

30 exons, 30 coding exons, 992672 bp of genomic DNA.

Transcription

Two mRNA transcript variants. Transcript variant 1 contains of 6629 b coded by 30 exons. Transcript variant 2 utilizes an alternate exon that contains a different 5'UTR and translation start site than that of variant 1. The N-terminus differs from isoform a encoded by variant 1. Transcript variant 2 contains of 6456 b coded by 28 exons.

Pseudogene

None known.

Protein

Description

ROBO1 is a single-pass type 1 membrane protein and interacts with SLIT1 and SLIT2. ROBO1 belongs to the immunglobulin super family of ROBO proteins. It contains of 3 fibronectin type-III domains and 5 immunoglobuline-like C2-type domains. There are 3

protein isoforms existing of ROBO1 produced by alternative splicing.

Expression

ROBO1 expression is seen in a number different tissues and organs.

Localisation

ROBO1 proteins are located in the cellular membrane as a transmembrane protein.

Function

Receptor for SLIT1 and SLIT2 which are thought to act as molecular guidance cue in cellular migration, including axonal navigation at the ventral midline of the neural tube and projection of axons to different regions during neuronal development. In axon growth cones, the silencing of the attractive effect of NTN1 by SLIT2 may require the formation of a ROBO1-DCC complex. Robo1 plays also a role in cell-adhesion. ROBO1 may be required for lung development. It is indicated that ROBO/SLIT is involved in angiogenic mechanisms whereas endothelial cells expressing ROBO1 receptors are attracted by SLIT2 which is secreted by human tumor cells.

Homology

There are 3 paralogs of human ROBO1: ROBO2, ROBO3 and ROBO4. Orthologs have been identified in mouse, rat, cow, dog, chimpanzee.

Implicated in

Lung cancer

Oncogenesis

A deletion of chromosome 3 allele and dysfunction or lack of ROBO1 receptors might be an early somatic genetic change in lung tumor development (Xian et al., 2001; Dallol et al., 2002b; Tsujiuchi et al., 2004; Xian et al., 2004).

Breast cancer

Oncogenesis

Breast cancer tumors and tumor cell lines show a suppressed expression of ROBO1 gene (Dallol et al., 2002a; Dallol et al., 2002b).

Prostate cancer

Oncogenesis

Human prostate tumors and tumor cell lines show an overexpression of ROBO1 gene (Bonner et al., 2003).

Angiogenesis of malignant tumors

Oncogenesis

ROBO1 gene is highly expressed in tumor vessel endothelium. Blocking of ROBO1 receptors causes loss of microvessel density in tumors e.g. malignant melanoma, colorectal cancer (Wang et al., 2003; Suchting et al., 2005; Groene et al., 2006; Legg et al., 2008).

Colorectal cancer

Oncogenesis

ROBO1 gene is overexpressed in human colorectal cancer tumor probes and colorectal cancer cell lines (Groene et al., 2006).

Cervical cancer

Oncogenesis

Cervical Cancer exhibits highly complex genomic alterations. These include hemizygous deletions at 4p15.3, 10q24, 5q35, 3p12.3, and 11q24, the chromosomal sites of SLIT-ROBO pathway genes (Narayan et al., 2006).

Hepatocellular carcinoma

Oncogenesis

ROBO1, a member of the immunoglobulin superfamily, is highly expressed in hepatocellular carcinoma, whereas it showes only a limited distribution in normal liver tissue. Strikingly, the ectodomain of ROBO1 was detected not only in the culture medium of liver cancer cell lines (PLC/PRF/5, HepG2, etc.) but also in sera from hepatocellular carcinoma patients (Ito et al., 2006).

T-acute lymphoblastic leukaemia

Oncogenesis

ROBO1 gene alterations were detected in subpopulations with childhood T-acute lymphoblastic leukaemia (Haltrich et al., 2007).

Nasopharyngeal carcinoma

Oncogenesis

In an inducible Epstein-Barr virus (EBV) nasopharyngeal cell line was a increased expression of ROBO1 detected that may be cause a role in this tumor carcinogenesis (Lee et al., 2008).

Dyslexia

Disease

Dyslexia may be caused by partial haplo-insufficiency for ROBO1 in rare families. A slight disturbance in neuronal axon crossing across the midline between brain hemispheres, dendrite guidance, or another function of ROBO1 may manifest as a specific reading disability in humans (Hannula-Jouppi et al., 2005; Fisher and Francks, 2006; McGrath et al., 2006; Shastry, 2007; Paracchini et al., 2007).

Autism

Disease

Gene expression analysis shows a reduced expression for ROBO1 in the autistic patient group and may play a role in pathogenesis of autism (Anitha et al., 2008).

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