Gene Section
Review

EPHB6 (EPH receptor B6)

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Identity

Other names: HEP, MGC129910, MGC129911
HGNC (Hugo): EPHB6
Location: 7q34

DNA/RNA

Note
EphB6 is located on chromosome 7q33-q35.

Description

Size: 16056 bases.
Orientation: plus strand.

Transcription

EphB6 mRNA size is 4044 bp.

Pseudogene

Not reported.

The chromosomal location of EPHB6 is indicated at interval q33-q35. Adapted from GeneCards.

Schematic representation of various domains in EphB6 protein.
**Protein**

**Note**
The crystal structure of EphB6 has not yet been determined. However, based on amino acid sequence and domain arrangement it is classified as a type I transmembrane protein.

It has a highly conserved N-terminal domain in the extracellular region that is involved in ligand recognition and binding (Labrador et al., 1997). The N-terminal domain is followed by a cysteine rich region and two fibronectin type-III repeats. These repeats are involved in mediating protein-protein interactions and receptor dimerization (Lackmann et al., 1998).

The intracellular region contains a juxtamembrane domain, a conserved kinase domain, a sterile α-motif (SAM) domain and a PSD95/Dlg/ZO1 (PDZ) domain (Kalo and Pasquale, 1999).

**Description**

Eph (erythropoietin producing hepatocellular carcinoma) receptors belong to a family of receptor tyrosine kinases, which are activated by binding to ephrin ligands.

These receptors are involved in a diverse array of signal transduction processes in humans.

Such diversity of signaling and the resulting functional output is partly attributed to differential expression and interactions among these receptors. Based on sequence homology and affinity for ephrin ligands, Eph receptors are classified into A and B groups. EphB6 is a kinase-deficient receptor (Gurniak and Berg, 1996) that has been shown to interact with two kinase-active receptors, namely, EphB2 and EphA2 (Fox and Kandpal, 2011). Ephrin B2 has been reported as a ligand for this receptor (Munthe et al., 2000).

The loss of EphB6 expression in breast carcinoma cell lines has been correlated to their invasiveness (Fox and Kandpal, 2004; Fox and Kandpal, 2006), and its role as a tumor suppressor has also been reported (Fox and Kandpal, 2009; Yu et al., 2010).

**Expression**

Eph receptors are expressed in a wide variety of tissues and cells (Andres et al., 1994; Fox et al., 1995; Ciossek et al., 1995; Lickliter et al., 1996; Muñoz et al., 2002).

In addition to other tissues and cells, EphB6 receptor expression has been shown in breast, prostate, thymus, mature T-cells and leukemia cells (Shimoyama et al., 2000; Luo et al., 2001; Luo et al., 2002; Fox and Kandpal, 2004; Fox and Kandpal, 2006). EphB6 deficient mice develop normally and do not display any abnormality in their general appearance (Shimoyama et al., 2002).

**Localisation**

Cellular. EphB6 is a transmembrane protein.

**Function**

A variety of Eph receptors and their ligands are involved in regulating cell pattern formation during organogenesis (Xu and Wilkinson, 1997; Flanagan and Vanderhaeghen, 1998; Holmberg et al., 2000; Leighton et al., 2001; Kullander et al., 2001; Gerlai, 2001).

EphB6 has been shown to facilitate T-cell activation (Luo et al., 2002). Metastasis/invasion suppressor role of EphB6 in non-small cell lung carcinoma and breast carcinoma (Müller-Tidow et al., 2005; Fox and Kandpal, 2009) suggests its involvement in cell adhesion and migration.

**Homology**

Amino acid homology between EphB6 and other EphB family members varies between 47% and 60%. Mouse and human homologs of EphB6 share greater than 90% amino acid identity (Gurniak and Berg, 1996; Matsuoka et al., 1997). The kinase domain in EphB6 is mutated.

**Implicated in**

**Non-small cell lung cancer**

**Note**

Altered levels and loss of EphB6 expression have been found in non-small cell lung carcinoma (Tang et al., 1999a; Müller-Tidow et al., 2005; Yu et al., 2010).

**Breast cancer**

**Note**

EphB6 silencing has been observed in breast carcinoma cell lines and some tumors (Fox and Kandpal, 2004; Fox and Kandpal, 2006; Fox and Kandpal, 2009; Truit et al., 2010). Molecular profiling of breast carcinoma cells with or without EphB6 expression has revealed significant changes in proteins as well as miRNAs (Kandpal, 2010; Bhushan and Kandpal, 2011). However, elevated levels of EphB6 have also been reported in breast tumor specimens (Brantley-Sieders et al., 2011).

**Melanoma**

**Note**

The progression of melanoma to metastasis has been correlated to progressive decrease of EphB6 expression (Hafner et al., 2003).

**Neuroblastoma**

**Note**

The levels of EphB6 have been characterized as prognostic indicators in neuroblastoma (Tang et al., 1999b; Tang et al., 2000).

**Leukemia and T-cell development**

**Note**

EphB6 expression has been implicated in T-cell development, and altered levels of this protein have been observed in leukemia and lymphoma cells (Shimoyama et al., 2000).
Colorectal and colon cancer

Note
In familial colorectal cancer EphB6 gene shows two missense mutations in germline. These two mutations include change of alanine to proline at position 321 (A321P) and glycine to valine (G914V) at position 914 (Gylfe et al., 2010). Deletions of EphB6 gene locus have also been reported in colon cancer (Ashktorab et al., 2010).

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