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Gene Section
Mini Review

ZBTB33 (zinc finger and BTB domain containing 33)

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Identity

Other names: ZNF-kaiso; ZNF348

HGNC (Hugo): ZBTB33

Location: Xq24

DNA/RNA

Description

DNA consists of three exons, the third of which contains the coding region.

Transcription

Transcription of this gene produces transcript variants 1 (5324 bp) and 2 (5225 bp) that encode the same protein. Variant 2 lacks exon 2 in the 5' UTR.

Pseudogene

None.

Protein

Description

ZBTB33/Kaiso (hereafter Kaiso) is a member of the BTB/POZ (Broad complex, Tramtrak, Bric à brac/Pox virus and zinc finger)-zinc finger family of transcription factors.

Kaiso was originally identified in a yeast two-hybrid screen as a binding partner for the Armadillo repeat domain protein p120-catenin (CTNND1) and has subsequently been found to also interact with the p120-catenin-related protein delta-catenin. The N-terminal POZ/BTB domain mediates Kaiso interactions with N-CoR, the CTC-binding factor (CTCF), and Znf131, as well as Kaiso homodimerization.

Expression

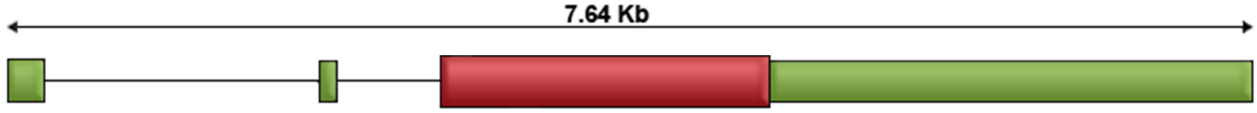
Kaiso is ubiquitously expressed.

Localisation

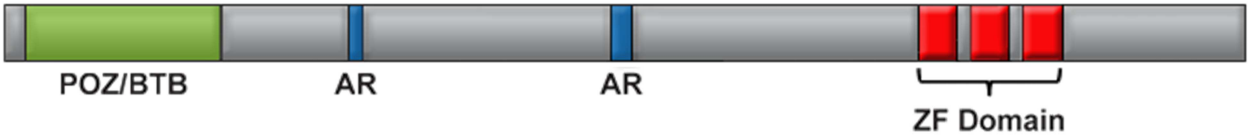
In various mammalian cell lines Kaiso localizes nearly exclusively to the nucleus, but in normal and tumor tissues Kaiso is predominantly detected in the cytoplasm. During mitosis a pool of Kaiso localizes to microtubles and centrosomes.

Function

Via its zinc finger domain, Kaiso binds DNA and functions as both a repressor and activator of transcription. Kaiso recognizes methylated CpG dinucleotides as well as a sequence-specific site (TCCTGCNA). While several genes are repressed by Kaiso (including matrilysin, siamois, c-Fos, cyclin-D1, c-Myc, Wnt11, MMP-7 and MTA2), rapsyn is the only reported gene to be activated by Kaiso.



ZBTB33/Kaiso genomic sequence (7.64 Kb) is composed of three exons (green). The coding region (red) is within exon 3.



ZBTB33/Kaiso contains an N-terminal POZ/BTB domain (green), two acidic regions (blue), and three C-terminal zinc finger domains (red).

Homology

Mus musculus - Zbtb33; Rattus norvegicus - Zbtb33; Xenopus laevis - zbtb33; Danio rerio - zbtb33; Pan troglodytes - ZBTB33; Bos Taurus - ZBTB33; Gallus gallus - ZBTB33.

Mutations

Note

None reported.

Implicated in

Lung cancer

Note

Immunohistochemical analysis of 294 cases of non-small cell lung cancer, including 50 cases of paired lymph node metastases, revealed a correlation of cytoplasmic Kaiso staining with poor prognosis, and shRNA-mediated knockdown of Kaiso enhances proliferative and invasive capabilities of several lung cancer cell lines.

Colon cancer

Note

Kaiso has been shown to repress expression of methylated tumor suppressor genes, and depletion of Kaiso sensitizes colon cancer cell lines to chemotherapy. Moreover, Kaiso is upregulated in intestinal tumors in mice, and a delayed onset of intestinal tumorigenesis is observed when Kaiso-null mice are crossed with the tumor-susceptible $Apc^{Min/+}$ mice.

Gastric cancer

Note

A study of the Helicobacter pylori-induced inflammatory response, which, if persistent, increases the risk for gastric adenocarcinoma, revealed that H. pylori induces nuclear translocation of the Kaiso-binding partner p120-catenin. Nuclear p120-catenin then relieves Kaiso-mediated repression of MMP-7, which is often overexpressed in premalignant and malignant gastric lesions.

Vertebrate development

Note

Injection of Xenopus laevis embryos with morpholinos targeting xKaiso leads to a developmental delay during gastrulation. Initially, Kaiso's roles in both general transcription repression and in regulation of canonical and non-canonical Wnt-signaling were thought to contribute to this phenotype, but subsequent studies determined that Kaiso's main role in early Xenopus development is restricted to the maintenence of transcriptional silencing. However, disruption of the Kaiso gene in mice did not reveal any abnormalities in development or gene expression.

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