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Gene Section
Mini Review

INTS6 (integrator complex subunit 6)

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Identity

Hugo: INTS6
Other names: DICE1; deleted in cancer 1; DBI-1; DDX26; INT6
Location: 13q14.3

DNA/RNA

Description

The DICE1 gene consists of 18 exons and contains a GpC-rich promoter.

Transcription

A major transcript of 4.4 kb and a minor transcript of 6.9 kb was detected in fetal and adult tissues. In adult heart, brain and skeletal muscle an additional smaller transcript of 4 kb has been detected by Northern blot analysis. The DICE1 cDNA consists of 3665 bp with a coding sequence of 2661 bp; an alternatively spliced variant generated by skipping of exon 3 has been detected specifically in brain.

Pseudogene

Presumably LOC285634 at 5p13.1.

Protein

Description

For the DICE1 protein 887 amino acids were predicted. A protein of approximately 100 kDaltons was detected by coupled in vitro transcription and translation. The Int6 protein was purified as an approximately 110 kDaltons polypeptide component of a nuclear Integrator complex.

Localisation

Mainly nuclear localisation.

Function

Predicted motifs of DICE1 protein were a von willebrand factor a (VWFA) domain of nuclear proteins, nuclear sorting signals and a DEAD box of ATP-dependent helicases. Ectopic expression of DICE1 cDNA in tumour cells suppresses colony formation and in cell culture. The Int6 protein was purified as a subunit of a RNA polymerase II multiprotein complex with roles in transcriptional regulation and RNA processing.

Homology

Weak homology to members of the helicase superfamily II.

Mutations

Note: Mutations in the coding sequence of DICE1/DDX26 have been infrequently detected in tumour cells.

Somatic

Frequent loss of heterozygosity (LOH) has been observed in lung, esophageal and prostate carcinomas. Promoter hypermethylation concomitant with reduced mRNA expression has been observed in lung and prostate carcinomas. In esophageal squamous cell carcinomas missense mutations V431I, R658Q have been detected. In prostate cancer cell line LNCaP missense mutation D546G has been described.

Implicated in

Functional inactivation of the DICE1 gene has been implicated in:

Tumorigenesis of sporadic lung carcinomas, esophagus carcinomas, prostate carcinomas and possibly other sporadic carcinomas

Abnormal Protein

A 6.3 kb fusion cDNA of a Notch-like with Dice1 cDNA (DBI-1) was detected in mouse cell line TC4. Overexpression of DBI-1 cDNA in IGF-IR transformed mouse cells compromised the mitogenic response to IGF-1 and interfered with anchorage-independent growth.

Oncogenesis

Downregulation of DICE1 mRNA was detected in 7 of 8 non-small cell lung carcinoma cell lines by Northern blot analysis. Microdissected non-small cell lung carcinomas showed reduced or absent expression of DICE1 mRNA by RT-PCR. Promoter hypermethylation was found in tumour cells with downregulated DICE1 expression. Aberrantly sized transcripts were detected in two non-small cell lung carcinoma cell lines. A reduced DICE1 expression was also observed in prostate cancer cell lines DU145 and LNCaP by real-time RT-PCR. DICE1 promoter hypermethylation was detected in 6 of 10 microdissected prostate cancer samples. Ectopic expression of DICE1 cDNA inhibited colony formation of human non-small cell lung carcinoma cell lines and prostate carcinoma cell lines and suppressed anchorage-independent growth of IGF-IR transformed mouse cells.

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