

Gene Section

Mini Review

DDX43 (DEAD (Asp-Glu-Ala-Asp) box polypeptide 43)

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Published in Atlas Database: January 2007

Online updated version: <http://AtlasGeneticsOncology.org/Genes/DDX43ID40288ch6q13.html>
DOI: 10.4267/2042/38413

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Identity

Hugo: DDX43

Other names: HAGE (for Helicase AntiGen); DKFZp434H2114

Location: 6q13

Local order: between markers GATA11B08 and D6S284.



Probe(s) - Courtesy Mariano Rocchi.

Note: This gene was isolated as a cDNA by applying a subtraction approach named representational difference analysis (RDA). Rhabdomyosarcoma LB23-SAR was used as the source of tester cDNA that was subtracted with driver cDNA, a mixture of human uterus, breast, heart, and colon cDNA.

DNA/RNA

Transcription

The transcript is about 2.2 kb. Gene HAGE is weakly transcribed in normal tissues: the level of expression was estimated to represent only 0.2% of the level found in the LB23-SAR reference cell line. The only exception is testis, which shows a level of expression comparable to that of LB23-SAR. Gene HAGE was found to be expressed in 90 out of 383 tumor samples of different histological types, well above the level in normal tissues; about 5% of the positive samples showed a level of expression above 10% of the level of LB23-SAR, and 7% showed a level of expression

between 1-10%. Expression of HAGE was induced in fibroblasts after treatment with the demethylating agent, 5-aza-2'-deoxycytidine.

Protein

Description

The largest open reading frame comprises 1,944 nucleotides and encodes a protein of 648 amino acids (72,871 Da). The pKi of the protein is 9.29.

Function

Comparison with databases revealed that HAGE shows 55% similarity with the human p68 protein, an ATP-dependent RNA helicase that is a member of the DEAD-box proteins. Four motifs that are present in members of the DEAD box family are conserved in the HAGE protein. However, ATPase and helicase activities of HAGE were not demonstrated.

Mutations

Note: No mutation was observed in the HAGE cDNA isolated from LB23-SAR.

Implicated in

Tumors

Note: HAGE expression can be induced by demethylating agent 5-azadeoxycytidine, suggesting that demethylation plays a role in the activation of these genes in tumors. Activation of HAGE in tumor cells most likely results therefore from the genome-wide demethylation process that is known to occur in these cells.

Oncogenesis

HAGE is not the first case of a DEAD-box protein that is overexpressed in tumors. Moreover, it worth noting that one out of 42 discovered mutated human tumor antigens is produced by a point mutation in a gene named MUM-3. This gene encodes a protein with homology with members of the RNA helicase family. These observations suggest that mutated or overexpressed helicases may contribute to tumoral transformation or progression.

References

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This article should be referenced as such:

De Plaen E. DDX43 (DEAD (Asp-Glu-Ala-Asp) box polypeptide 43). *Atlas Genet Cytogenet Oncol Haematol.*2007;11(2):119-120.
