Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

# Gene Section
## Mini Review

# DHX9 (DEAH (Asp-Glu-Ala-His) box polypeptide 9)

**Frédéric Guénard, Francine Durocher**

Cancer Genomics Laboratory, Oncology and Molecular Endocrinology Research Centre, CRCHUL, CHUQ and Laval University, Québec, G1V 4G2, Canada (FG, FD)

Published in Atlas Database: July 2009

Online updated version : http://AtlasGeneticsOncology.org/Genes/DHX9ID702ch1q25.html
DOI: 10.4267/2042/44773



## Identity

**Other names:** DDX9; LKP; NDHII; RHA; NDH2; leukophysin

**HGNC (Hugo):** DHX9

**Location :** 1q25.3

## DNA/RNA

### Description

The gene spans 48.5 kb and is composed of 27 exons.

### Transcription

Transcription start is 163 bp upstream of first ATG of the DHX9 ORF. The translation start site is located in exon 2 and there is a sole isoform ubiquitously expressed.

### Pseudogene

DHX9 pseudogene (DHX9P) is located at 13q22.

## Protein

### Description

Monomeric 140 kDa protein. Human DHX9 is 1270 amino acids. It contains an helicase catalytic domain flanked by two double-stranded RNA binding domains (dsRBD) at the N-terminus and an RGG-box at the C terminus. A bidirectional nuclear transport domain is located at the C terminus.

### Expression

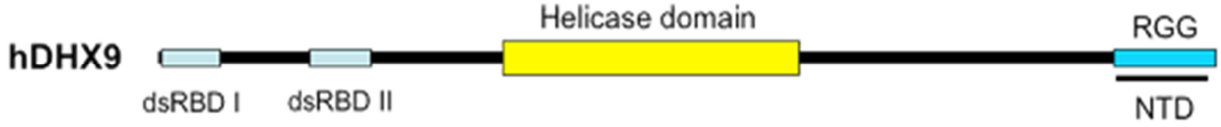
All tissues tested, ubiquitous expression.

### Localisation

DHX9 shuttles between the nucleus and the cytoplasm.

### Function

DHX9 is a nucleic-acid helicase that unwinds double-stranded DNA and RNA in a nucleotide dependent manner. It acts as a transcriptional coactivator which stimulates transcription by interacting with the transcriptional coactivator CBP/p300, the breast cancer protein BRCA1, the RNA polymerase II and has an important role in the assembly of STAT6 transcriptosome.
DHX9 plays a role in regulating chromatin structure by interacting physically and functionally with topoisomerase IIa.
It mediates the attachment of nuclear ribonucleoprotein complexes to actin filaments, which may be related to RNA processing and transport.




**Structure of DHX9**. dsRBD, double-stranded RNA binding domain; RGG, arginine and glycine-rich region; NTD, nuclear transport domain.

DHX9 interacts with the survival motor neuron which plays a role in the assembly and regeneration of small nuclear ribonucleoproteins and spliceosomes.
DHX9 acts as a nuclear shuttle protein promoting the export of mRNA transcripts through binding to TAP and HAP95.
In the cytoplasm, DHX9 is preferentially associated with actively translating polyribosomes and is necessary for efficient translation of RNAs that contain a highly structured 5'UTR.
DHX9 might be necessary for maintaining genomic stability as it plays a role in promoting the DNA processing function of WRN. Overexpression of a truncated DHX9 peptide prevents normal BRCA1 function, such as BRCA1 association with nuclear foci following DNA damage. DHX9 associates with gH2AX after DNA damage, suggesting a role for DHX9 in DNA repair.
DHX9 is also necessary for early embryonic development in mice.

### Homology

Sequence analysis revealed that DHX9 contains seven helicase core motifs that are conserved among the DEX[D/H] helicase superfamily. DHX9 is highly conserved among man, cow, mouse, worm, and fruit fly.

## Mutations

**Note**
DHX9 truncating mutations were reported to affect the interaction with BRCA1 and RNA polymerase II, and to result in decreased transcriptional activity of BRCA1.
In mammals, DHX9-knockout mice are embryonic lethal for homozygous DHX9 mutants. DHX9 is thus necessary for early embryonic development in mice. It was also suggested that DHX9 is required for the survival and differentiation of embryonic ectoderm.
DHX9 maps to chromosome 1q25 near a major susceptibility locus for prostate cancer.

## Implicated in

### Lung cancer

**Note**
DHX9 is over-expressed in tumor samples compared to normal lung tissues. There was a tendency for higher expression levels in small cell lung cancer compared to non-small cell carcinomas.

**Prognosis**
There was no correlation with tumor stage and survival.

### Breast cancer

**Note**
Involvement of DHX9 in breast cancer susceptibility was analyzed in a cohort of breast cancer individuals from non-BRCA1/BRCA2 French Canadian families. This study did not identify any deleterious truncating mutation or aberrant splicing in the DHX9 gene. It was concluded that studies on much bigger cohorts are needed to fully evaluate the association of variants identified with breast cancer risk.

### Systemic lupus erythematosus (SLE)

**Note**
Anti-DHX9 is a new serologic marker for SLE. The production of anti-DHX9 may depend on a process restricted to early SLE, or it may be highly sensitive to treatment.

**Disease**
Systemic lupus erythematosus (SLE) is a largely genetically based disease in which environmental factors are also involved. SLE is an autoimmune disease characterized by autoantibody production and involvement of multiple organ systems. Variable manifestations and outcome reflect the clinical heterogeneity of the disease. It is characterized by acute and chronic inflammation of various tissues of the body including joints, kidneys, mucous membranes, and blood vessel walls.

**Prognosis**
Among patients with SLE, anti-DHX9 was common in young patients and at an early stage of the disease.

## References

Lee CG, Eki T, Okumura K, Nogami M, Soares Vda C, Murakami Y, Hanaoka F, Hurwitz J. The human RNA helicase A (DDX9) gene maps to the prostate cancer susceptibility locus at chromosome band 1q25 and its pseudogene (DDX9P) to 13q22, respectively. Somat Cell Mol Genet. 1999 Jan;25(1):33-9

Zhang S, Herrmann C, Grosse F. Nucleolar localization of murine nuclear DNA helicase II (RNA helicase A). J Cell Sci. 1999 Aug;112 ( Pt 16):2693-703

Tang H, Wong-Staal F. Specific interaction between RNA helicase A and Tap, two cellular proteins that bind to the constitutive transport element of type D retrovirus. J Biol Chem. 2000 Oct 20;275(42):32694-700

Westberg C, Yang JP, Tang H, Reddy TR, Wong-Staal F. A novel shuttle protein binds to RNA helicase A and activates the retroviral constitutive transport element. J Biol Chem. 2000 Jul 14;275(28):21396-401

Aratani S, Fujii R, Oishi T, Fujita H, Amano T, Ohshima T, Hagiwara M, Fukamizu A, Nakajima T. Dual roles of RNA helicase A in CREB-dependent transcription. Mol Cell Biol. 2001 Jul;21(14):4460-9

Fujii R, Okamoto M, Aratani S, Oishi T, Ohshima T, Taira K, Baba M, Fukamizu A, Nakajima T. A Role of RNA Helicase A in cis-Acting Transactivation Response Element-mediated Transcriptional Regulation of Human Immunodeficiency Virus Type 1. J Biol Chem. 2001 Feb 23;276(8):5445-51

Yang JP, Tang H, Reddy TR, Wong-Staal F. Mapping the functional domains of HAP95, a protein that binds RNA helicase A and activates the constitutive transport element of type D retroviruses. J Biol Chem. 2001 Aug 17;276(33):30694-700

Zhang S, Buder K, Burkhardt C, Schlott B, Görlach M, Grosse F. Nuclear DNA helicase II/RNA helicase A binds to filamentous actin. J Biol Chem. 2002 Jan 4;277(1):843-53

Aratani S, Fujii R, Fujita H, Fukamizu A, Nakajima T. Aromatic residues are required for RNA helicase A mediated transactivation. Int J Mol Med. 2003 Aug;12(2):175-80

Schlegel BP, Starita LM, Parvin JD. Overexpression of a protein fragment of RNA helicase A causes inhibition of endogenous BRCA1 function and defects in ploidy and cytokinesis in mammary epithelial cells. Oncogene. 2003 Feb 20;22(7):983-91

Zhou K, Choe KT, Zaidi Z, Wang Q, Mathews MB, Lee CG. RNA helicase A interacts with dsDNA and topoisomerase IIalpha. Nucleic Acids Res. 2003 May 1;31(9):2253-60

Argasinska J, Zhou K, Donnelly RJ, Hay RT, Lee CG. A functional interaction between RHA and Ubc9, an E2-like enzyme specific for Sumo-1. J Mol Biol. 2004 Jul 30;341(1):15-25

Tetsuka T, Uranishi H, Sanda T, Asamitsu K, Yang JP, Wong-Staal F, Okamoto T. RNA helicase A interacts with nuclear factor kappaB p65 and functions as a transcriptional coactivator. Eur J Biochem. 2004 Sep;271(18):3741-51

Wei X, Pacyna-Gengelbach M, Schlüns K, An Q, Gao Y, Cheng S, Petersen I. Analysis of the RNA helicase A gene in human lung cancer. Oncol Rep. 2004 Jan;11(1):253-8

Zhang S, Grosse F. Multiple functions of nuclear DNA helicase II (RNA helicase A) in nucleic acid metabolism. Acta Biochim Biophys Sin (Shanghai). 2004 Mar;36(3):177-83

Zhang S, Köhler C, Hemmerich P, Grosse F. Nuclear DNA helicase II (RNA helicase A) binds to an F-actin containing shell that surrounds the nucleolus. Exp Cell Res. 2004 Feb 15;293(2):248-58

Zhang S, Schlott B, Görlach M, Grosse F. DNA-dependent protein kinase (DNA-PK) phosphorylates nuclear DNA helicase II/RNA helicase A and hnRNP proteins in an RNA-dependent manner. Nucleic Acids Res. 2004;32(1):1-10

Zhong X, Safa AR. RNA helicase A in the MEF1 transcription factor complex up-regulates the MDR1 gene in multidrug-resistant cancer cells. J Biol Chem. 2004 Apr 23;279(17):17134-41

Friedemann J, Grosse F, Zhang S. Nuclear DNA helicase II (RNA helicase A) interacts with Werner syndrome helicase and stimulates its exonuclease activity. J Biol Chem. 2005 Sep 2;280(35):31303-13

Aratani S, Oishi T, Fujita H, Nakazawa M, Fujii R, Imamoto N, Yoneda Y, Fukamizu A, Nakajima T. The nuclear import of RNA helicase A is mediated by importin-alpha3. Biochem Biophys Res Commun. 2006 Feb 3;340(1):125-33

Hartman TR, Qian S, Bolinger C, Fernandez S, Schoenberg DR, Boris-Lawrie K. RNA helicase A is necessary for translation of selected messenger RNAs. Nat Struct Mol Biol. 2006 Jun;13(6):509-16

Roy BB, Hu J, Guo X, Russell RS, Guo F, Kleiman L, Liang C. Association of RNA helicase a with human immunodeficiency virus type 1 particles. J Biol Chem. 2006 May 5;281(18):12625-35

Toretsky JA, Erkizan V, Levenson A, Abaan OD, Parvin JD, Cripe TP, Rice AM, Lee SB, Uren A. Oncoprotein EWS-FLI1 activity is enhanced by RNA helicase A. Cancer Res. 2006 Jun 1;66(11):5574-81

Välineva T, Yang J, Silvennoinen O. Characterization of RNA helicase A as component of STAT6-dependent enhanceosome. Nucleic Acids Res. 2006;34(14):3938-46

Ishiguro A, Ideta M, Mikoshiba K, Chen DJ, Aruga J. ZIC2-dependent transcriptional regulation is mediated by DNA-dependent protein kinase, poly(ADP-ribose) polymerase, and RNA helicase A. J Biol Chem. 2007 Mar 30;282(13):9983-95

Robb GB, Rana TM. RNA helicase A interacts with RISC in human cells and functions in RISC loading. Mol Cell. 2007 May 25;26(4):523-37

Prahl M, Vilborg A, Palmberg C, Jörnvall H, Asker C, Wiman KG. The p53 target protein Wig-1 binds hnRNP A2/B1 and RNA Helicase A via RNA. FEBS Lett. 2008 Jun 25;582(15):2173-7

Guénard F, Labrie Y, Ouellette G, Beauparlant CJ, Durocher F. Genetic sequence variations of BRCA1-interacting genes AURKA, BAP1, BARD1 and DHX9 in French Canadian families with high risk of breast cancer. J Hum Genet. 2009 Mar;54(3):152-61

*This article should be referenced as such:*

Guénard F, Durocher F. DHX9 (DEAH (Asp-Glu-Ala-His) box polypeptide 9). Atlas Genet Cytogenet Oncol Haematol. 2010; 14(6):547-549.