# DHX36

Probable ATP-dependent RNA helicase DHX36 also known as DEAH box protein 36 (DHX36) or MLE-like protein 1 (MLEL1) or G4 resolvase 1 (G4R1) or RNA helicase associated with AU-rich elements (RHAU) is an enzyme that in humans is encoded by the DHX36 gene. [4][5]

## Structure

Structurally, DHX36 is a 1008 amino acid-long modular protein that has been crystallized in a complex with a DNA G-quadruplex.<sup>[6]</sup> It consists of a ~440-amino acid helicase core comprising all signature motifs of the DEAH/RHA family of helicases with N- and C-terminal flanking regions of ~180 and ~380 amino acids, respectively. Part of the N-terminal flanking region forms an alphahelix called the DHX36-specific motif, which recognizes the 5'-most G-quadruplex quartet. The OBfold domain binds to the 3'-most G-tract sugar-phosphate backbone.<sup>[7]</sup> Like all the DEAH/RHA helicases, the helicase associated domain is located adjacent to the helicase core region and occupies 75% of the C-terminal region.<sup>[8]</sup>

## Function

DEAH/RHA proteins are RNA and DNA helicases typically characterized by low processivity translocation on substrates and the capability to bind/unwind non-canonical nucleic acid secondary structures. They are implicated in a number of cellular processes involving alteration of RNA secondary structure such as translation initiation, nuclear and mitochondrial splicing, and ribosome and spliceosome assembly. Based on their distribution patterns, some members of this DEAH/RHA protein family are believed to be involved in embryogenesis, spermatogenesis, and cellular growth and division. All

DHX36 exhibits a unique ATP-dependent guanine-quadruplex (G4) resolvase activity and specificity for its substrate *in vitro*. <sup>[10][11]</sup> DHX36 displays repetitive unwinding activity as a function of the thermal stability of the G-quadruplex substrate, characteristic of a number of other G-quadruplex resolvases such as the BLM/WRN helicases. <sup>[12][13]</sup> DHX36 binds G4-nucleic acid with subnanomolar affinity and unwinds G4 structures much more efficiently than double-stranded nucleic acid. Consistent with these biochemical observations, DHX36 was also identified as the major source of tetramolecular RNA-resolving activity in HeLa cell lysates.

Previous work showed that DHX36 associates with mRNAs and re-localises to stress granules (SGs) upon translational arrest induced by various environmental stresses.<sup>[14][15]</sup> A region of the first

105 amino acid was shown to be critical for RNA binding and re-localisation to SGs.

### DHX36

#### **Available structures**

PDB Ortholog search: PDBe (https://www.ebi.ac.uk/pdbe/searchResults.html?display=both&term=Q8VHK9% 20or%20Q9H2U1) RCSB (https://www.rcsb.org/search?q=rcsb\_polymer\_entity\_container\_identifiers.reference\_sequence\_identifiers.database\_name:UniProt%20AND%20rcsb\_polymer\_entity\_container\_identifiers.database\_accession:Q8VHK9,Q9H 2U1)

#### **List of PDB id codes**

2N16 (https://www.rcsb.or g/structure/2N16), 2N21 (ht tps://www.rcsb.org/structur e/2N21)

#### **Identifiers**

### **Aliases** DHX36 (https://www.

genenames.org/dat a/gene-symbol-repor t/#!/hgnc\_id/14410), DDX36, G4R1, MLEL1, RHAU, DEAH-box

helicase 36

### External IDs OMIM: 612767 (http

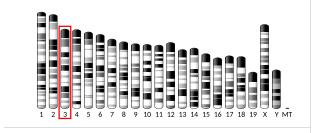
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12767); MGI:

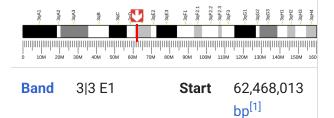
1919412 (http://www.informatics.jax.or

g/marker/MGI:19194 12); HomoloGene: 6356 (https://www.nc bi.nlm.nih.gov/entre z/query.fcgi?cmd=Re trieve&db=homologe ne&dopt=HomoloGen e&list\_uids=6356); GeneCards: DHX36 (h ttps://www.genecard s.org/cgi-bin/carddis p.pl?gene=DHX36); OMA:DHX36 orthologs (https://om abrowser.org/oma/v ps/n/a)

## **Gene location (Mouse)**



**Chr.** Chromosome 3 (mouse)<sup>[1]</sup>



End 62,507,004 bp<sup>[1]</sup>

## **RNA expression pattern**

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(http:// biogps. org/)

### **Gene ontology**

# Molecular function

- nucleotide binding (htt p://amigo.geneontology.o rg/amigo/term/GO:00001 66)
- DNA binding (http://amig o.geneontology.org/amig o/term/G0:0003677)
- ATP-dependent activity, acting on DNA (http://ami go.geneontology.org/ami go/term/G0:0008094)
- helicase activity (http://a migo.geneontology.org/a migo/term/G0:0004386)
- G-quadruplex RNA binding (http://amigo.gen eontology.org/amigo/ter m/G0:0002151)
- histone deacetylase binding (http://amigo.gen eontology.org/amigo/ter m/G0:0042826)
- G-quadruplex DNA binding (http://amigo.gen eontology.org/amigo/ter m/G0:0051880)
- protein binding (http://am igo.geneontology.org/ami go/term/G0:0005515)
- nucleic acid binding (htt p://amigo.geneontology.o rg/amigo/term/GO:00036 76)
- double-stranded RNA binding (http://amigo.gen

- eontology.org/amigo/ter m/G0:0003725)
- hydrolase activity (http:// amigo.geneontology.org/ amigo/term/G0:001678
   7)
- ATP binding (http://amig o.geneontology.org/amig o/term/G0:0005524)
- telomerase RNA binding (http://amigo.geneontolo gy.org/amigo/term/GO:0 070034)
- RNA binding (http://amig o.geneontology.org/amig o/term/G0:0003723)
- single-stranded DNA binding (http://amigo.gen eontology.org/amigo/ter m/G0:0003697)
- magnesium ion binding (http://amigo.geneontolo gy.org/amigo/term/GO:0 000287)
- RNA polymerase II cisregulatory region sequence-specific DNA binding (http://amigo.gen eontology.org/amigo/ter m/G0:0000978)
- mRNA 3'-UTR binding (htt p://amigo.geneontology.o rg/amigo/term/GO:00037 30)
- DNA helicase activity (htt p://amigo.geneontology.o

- rg/amigo/term/G0:00036 78)
- 3'-5' RNA helicase activity (http://amigo.geneontolo gy.org/amigo/term/GO:0 034458)
- mRNA 3'-UTR AU-rich region binding (http://ami go.geneontology.org/ami go/term/G0:0035925)
- metal ion binding (http:// amigo.geneontology.org/ amigo/term/GO:004687
   2)
- mRNA 5'-UTR binding (htt p://amigo.geneontology.o rg/amigo/term/GO:00480 27)
- pre-miRNA binding (htt p://amigo.geneontology.o rg/amigo/term/G0:00708 83)

# Cellular component

- chromosome (http://ami go.geneontology.org/ami go/term/G0:0005694)
- telomere (http://amigo.ge neontology.org/amigo/ter m/G0:0000781)
- extracellular exosome (ht tp://amigo.geneontology. org/amigo/term/G0:0070 062)
- cytosol (http://amigo.gen eontology.org/amigo/ter m/G0:0005829)

- nucleus (http://amigo.ge neontology.org/amigo/ter m/G0:0005634)
- cytoplasm (http://amigo. geneontology.org/amigo/ term/G0:0005737)
- mitochondrion (http://am igo.geneontology.org/ami go/term/G0:0005739)
- cytoplasmic stress granule (http://amigo.gen eontology.org/amigo/ter m/G0:0010494)
- nuclear speck (http://ami go.geneontology.org/ami go/term/G0:0016607)
- axon (http://amigo.geneo ntology.org/amigo/term/ G0:0030424)
- dendrite (http://amigo.ge neontology.org/amigo/ter m/G0:0030425)
- cell projection (http://ami go.geneontology.org/ami go/term/G0:0042995)
- perikaryon (http://amigo. geneontology.org/amigo/ term/G0:0043204)

# Biological process

- RNA processing (http://a migo.geneontology.org/a migo/term/G0:0006396)
- regulation of transcription, DNAtemplated (http://amigo. geneontology.org/amigo/ term/GO:0006355)

- ossification (http://amig o.geneontology.org/amig o/term/G0:0001503)
- response to exogenous dsRNA (http://amigo.gen eontology.org/amigo/ter m/G0:0043330)
- response to virus (http:// amigo.geneontology.org/ amigo/term/G0:000961
   5)
- transcription, DNAtemplated (http://amigo. geneontology.org/amigo/ term/GO:0006351)
- positive regulation of telomere maintenance (ht tp://amigo.geneontology. org/amigo/term/G0:0032 206)
- RNA secondary structure unwinding (http://amigo. geneontology.org/amigo/ term/G0:0010501)
- positive regulation of type I interferon production (http://amigo. geneontology.org/amigo/ term/GO:0032481)
- positive regulation of transcription by RNA polymerase II (http://ami go.geneontology.org/ami go/term/G0:0045944)
- telomerase RNA stabilization (http://amig

- o.geneontology.org/amig o/term/G0:0090669)
- immune system process (http://amigo.geneontolo gy.org/amigo/term/GO:0 002376)
- positive regulation of myeloid dendritic cell cytokine production (htt p://amigo.geneontology.o rg/amigo/term/GO:00027 35)
- regulation of transcription by RNA polymerase III (http://ami go.geneontology.org/ami go/term/G0:0006359)
- regulation of translation (http://amigo.geneontolo gy.org/amigo/term/GO:0 006417)
- multicellular organism development (http://amig o.geneontology.org/amig o/term/G0:0007275)
- spermatogenesis (http:// amigo.geneontology.org/ amigo/term/G0:000728
   3)
- positive regulation of gene expression (http://a migo.geneontology.org/a migo/term/GO:0010628)
- negative regulation of translation (http://amigo. geneontology.org/amigo/ term/G0:0017148)

- cell differentiation (http:// amigo.geneontology.org/ amigo/term/GO:003015
   4)
- positive regulation of mRNA 3'-end processing (http://amigo.geneontolo gy.org/amigo/term/GO:0 031442)
- DNA duplex unwinding (h ttp://amigo.geneontolog y.org/amigo/term/G0:00 32508)
- cellular response to heat (http://amigo.geneontolo gy.org/amigo/term/GO:0 034605)
- cellular response to UV (h ttp://amigo.geneontolog y.org/amigo/term/GO:00 34644)
- positive regulation of IkappaB kinase/NFkappaB signaling (http:// amigo.geneontology.org/ amigo/term/GO:004312
   3)
- regulation of mRNA stability (http://amigo.ge neontology.org/amigo/ter m/G0:0043488)
- G-quadruplex DNA unwinding (http://amigo. geneontology.org/amigo/ term/GO:0044806)
- innate immune response (http://amigo.geneontolo

- gy.org/amigo/term/GO:0 045087)
- regulation of embryonic development (http://amig o.geneontology.org/amig o/term/G0:0045995)
- defense response to virus (http://amigo.geneontolo gy.org/amigo/term/G0:0 051607)
- positive regulation of cardioblast differentiation (http://ami go.geneontology.org/ami go/term/G0:0051891)
- positive regulation of transcription initiation from RNA polymerase II promoter (http://amigo.g eneontology.org/amigo/t erm/G0:0060261)
- positive regulation of dendritic spine morphogenesis (http://a migo.geneontology.org/a migo/term/GO:0061003)
- 3'-UTR-mediated mRNA destabilization (http://am igo.geneontology.org/ami go/term/G0:0061158)
- positive regulation of nuclear-transcribed mRNA catabolic process, deadenylation-dependent decay (http://amigo.gene ontology.org/amigo/ter m/GO:1900153)

- positive regulation of hematopoietic progenitor cell differentiation (http:// amigo.geneontology.org/ amigo/term/GO:190153
   4)
- cellular response to arsenite ion (http://amig o.geneontology.org/amig o/term/G0:1903843)
- positive regulation of telomere maintenance via telomere lengthening (http://amigo.geneontolo gy.org/amigo/term/GO:1 904358)
- positive regulation of intracellular mRNA localization (http://amig o.geneontology.org/amig o/term/G0:1904582)
- positive regulation of cytoplasmic translation (http://amigo.geneontolo gy.org/amigo/term/GO:2 000767)

Sources:Amigo (http://amigo.geneontolog y.org/) / QuickGO (https://www.ebi.ac.u k/QuickGO/)

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# External links

- Group Yoshikuni Nagamine homepage (https://web.archive.org/web/20100621120450/http://www.fmi.ch/research/groupleader/?group=27)
- Group Steven Akman homepage (https://crchd.cancer.gov/research/pi\_akman.html)

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