

Gene Section

Mini Review

AMOT (angiomotin)

Roshan Mandrawalia, Ranjan Tamuli

Department of Biotechnology, Indian Institute of Technology Guwahati, Guwahati-781 039, Assam, India (RM, RT)

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Identity

Other names: KIAA1071

HGNC (Hugo): AMOT

Location: Xq23

DNA/RNA

Description

DNA size 66.31 kb, mRNA size 6888 bp, 12 exons.

Protein

Description

Angiomotin protein is 1084 amino acid residues in length. It contains two coiled coil domains 429-689

(261), 721-751 (31), a PDZ-binding motif 1081-1084 (4), a SMC_prok_B region 429-549 (121), and an angiomotin_C terminal 599-794 (196). Phosphorylations occur on S305, S312, S712, S714, T717, Y719, and T1061. Phosphorylated upon DNA damage, probably by ATM or ATR.

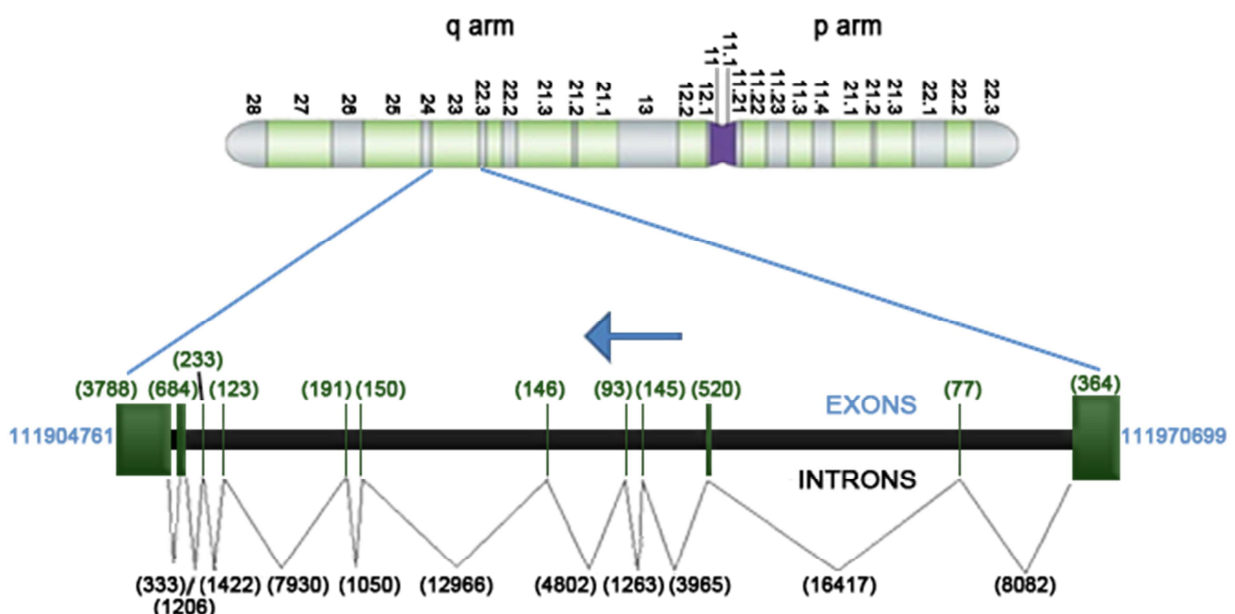
Isoforms:

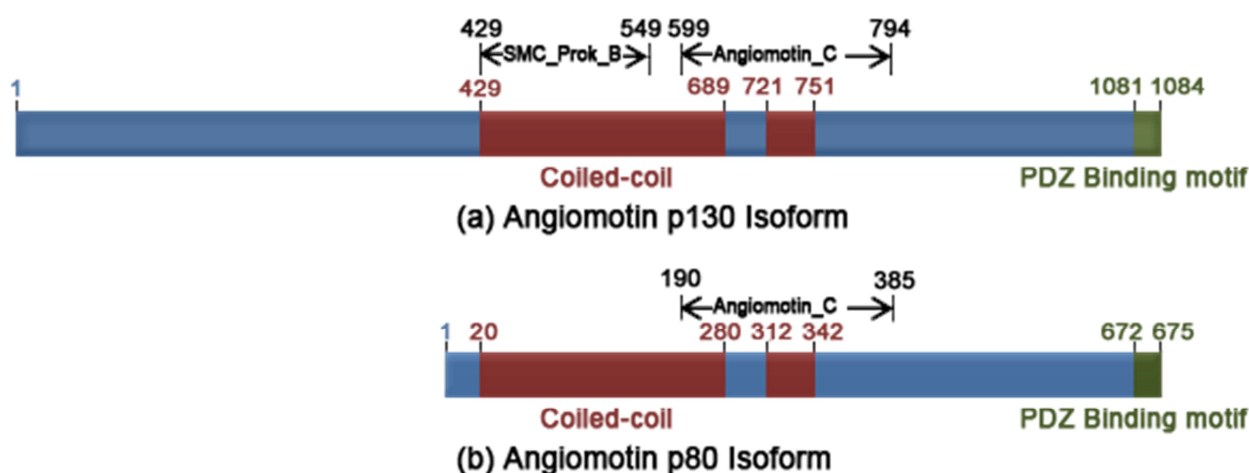
- Isoform 1: p130 angiomotin

1084 amino acids, 118085 Da. This isoform has been chosen as the 'canonical' sequence.

- Isoform 2: p80 angiomotin

675 amino acids, 72540 Da. The isoform differs from the canonical sequence with N-terminal alternative splicing region 1-409 (409) missing, which mediates the binding of angiomotin to F-actin stress fibres. The SMC_prok_B region is also missing in this isoform.





Expression

Expressed in placenta and skeletal muscle. Predominantly expressed in endothelial cells of capillaries, larger vessels of the placenta.

Localisation

Cell junction, tight junction. Localized on the cell surface. May act as a transmembrane protein.

Function

Mediates inhibitory effect of angiostatin on tube formation and the migration of endothelial cells toward growth factors during the formation of new blood vessels in the larger vessels of the placenta. Isoform-1 is found to control cell shape by association with F-actin fibres through N-terminal part of protein. The isoform 2 (p80) promotes angiogenesis, in part, by conferring a hypermigratory phenotype to endothelial cells.

Homology

The percent identity below represents identity of AMOT over an aligned region in Unigene.

Mus musculus: 88.1 (percent identity)

Oryctolagus cuniculus: 79

Sus scrofa: 72

Danio rerio: 68.9

Fugu rubripes: 65

Xenopus laevis: 61.8

Caenorhabditis elegans: 46

Saccharomyces cerevisiae: 47

Drosophila melanogaster: 36

Mutations

Note

Several polymorphisms have been found but none of them has shown any association with a disease. Furthermore, endothelial cells expressing mutated angiomotins have been reported failure in their function, including failure to migrate and inhibition of angiogenesis. Mutation with deletion of three amino

acids from PDZ-binding motif results in inhibition of chemotaxis, embryos with this mutation may lead to death on embryonic day 9.5.

Implicated in

Breast cancer

Note

Angiomotin is linked to angiogenesis and aggressive nature of breast tumours. Angiomotin shows high level of expression in mammary tissues during tumour stages as compared to normal expression level (33.1 ± 11 in normal versus 86.5 ± 13.7 in tumour tissues, $p=0.0003$). Significant high expression was found in aggressive tumours (grade 2, grade 3 and with nodal involvement) compared with less aggressive grade 1 tumour ($p<0.001$ and $p=0.05$ respectively). Angiogenesis is the essential process in the development and spread of breast cancer, by providing blood supply to tumours and escape route for tumour cells to other part of the body.

Hemangioendothelioma invasion

Disease

Angiomotin expression promotes hemangioendothelioma invasion. Expression of human angiomotin in mouse aortic endothelial (MAE) cells results in stabilization of tubes in the Matrigel assay. Cells from the established tubes invaded into the solidified matrigel, however, cells expressing a functional mutant lacking the PDZ protein interaction motif did not migrate and form tubes. Angiomotin may promote angiogenesis by both stimulating invasion as well as stabilizing established tubes.

Endothelial cell migration and tube formation

Note

Upon expression of angiomotin in HeLa cells, angiomotin bound and internalized fluorescein-labeled angiostatin, a circulating inhibitor of angiogenesis. In endothelial cells, angiomotin protein is localized to the

leading edge of migrating cells and results in increased cell migration. Angiomin-transfected MAE cells bind and respond to angiostatin by inhibition of cell migration and tube formation, which suggest that angiomin regulates endothelial cell migration and tube formation.

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