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Gene Section
Short Communication

MIEN1 (migration and invasion enhancer 1)

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Identity

Other names: C17orf37, C35, ORB3, RDX12, XTP4

HGNC (Hugo): MIEN1

Location: 17q12

DNA/RNA

Description

MIEN1 DNA contains 4 coding exons over 1,63 kb on the minus strand between ERBB2 and GRB7 on human chromosome 17q12. It is also neighbouring mRNA4728.

Transcription

Transcript (NC_000017.100) length: 1006 bps. Transcription was reported in a variety of cell lines and organs, mainly using gene expression arrays (EMBL-EBI).

Pseudogene

None identified.

Protein

Description

MIEN1 is a small (12 kDa) membrane bound protein found in a variety of human tumours (Evans et al., 2006).
Its main function is to induce cell invasion and it may be involved in metastasis (Dasgupta et al., 2011; Dasgupta and Vishwanatha, 2007; Katz et al., 2010).

Expression

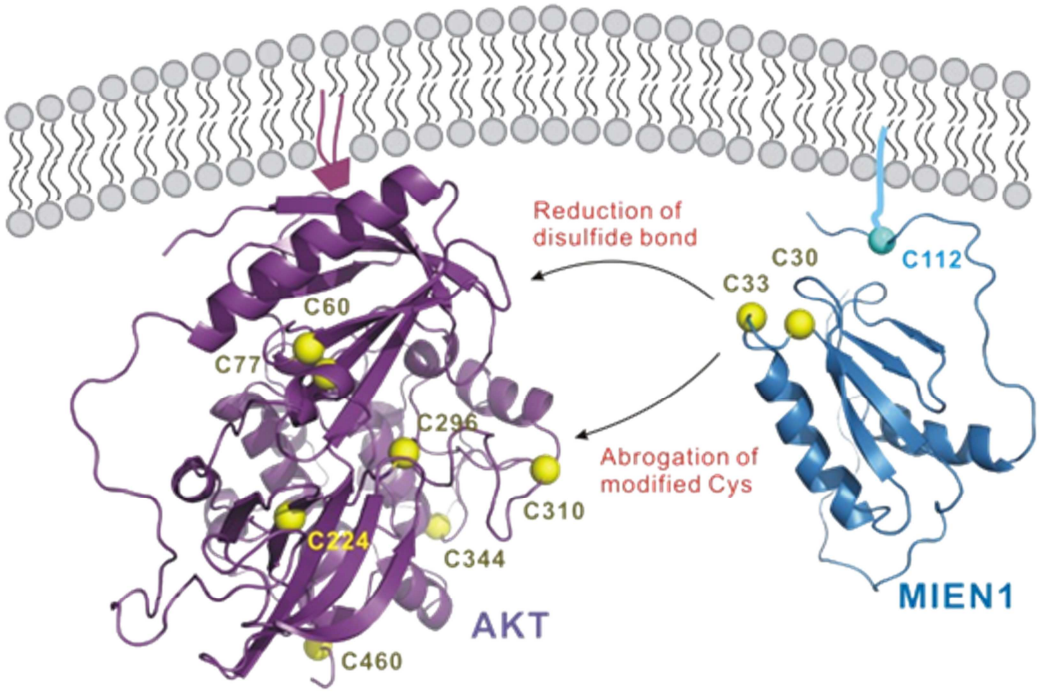
MIEN1 is almost exclusively expressed in human tumours, with the notable exception of Leydig cells in testes (Evans et al., 2006).

Localisation

MIEN1 protein is membrane bound and its stability depends on its localization (our unpublished observations). MIEN1 contains a CVIL amino acid sequence in the C-terminal, which fits the prenylation motif CaaX (Evans et al., 2006). Based on several physical properties, such as size, flexibility, membrane buried preference, and presence of leucine as the X residue, MIEN1 is predicted to be geranylgeranylated in vivo by GGTI enzyme, resulting in the addition of 20-carbon isoprenoid moiety.

Function

The MIEN1 sequence EATYLELASAVKEQYPGIEI conforms to a prototypical immuno-receptor tyrosine-based activation motif (ITAM). ITAMs, such as this of C35 rely on Syk protein kinase for their signaling capacities (Katz et al., 2010). The most commonly reported consequence of MIEN1 over-expression is the induction of cell motility and invasion (Dasgupta et al., 2011; Katz et al., 2010). High levels of MIEN1 expression lead to epithelial to mesenchymal transition in breast cell lines (Katz et al., 2011a). However, intermediate levels lead to a cancer phenomenon rarely observed in experimental models, collective invasion (Katz et al., 2011b).



With permission by Hsu et al. (Hsu et al., 2012).

Homology

MIEN1 is very highly conserved among six higher eukaryotic species (identities >77%) but does not seem to have orthologues in microbial organisms (Evans et al., 2006).
MIEN1 contains an ITAM motif which is prevalent in immune receptors as well as oncogenic viruses.

Mutations

Note
A single SNP, rs3809717, was described with no bearing on breast cancer risk (attributed originally to the ERBB2 gene, (Einarsdóttir et al., 2006)).

Implicated in

Carcinomas

Note
Several carcinomas (breast, ovarian, and gastro-intestinal cancers) show high expression of the ERBB2 amplicon containing the MIEN1 gene.

Breast cancer

Disease
Over-expression of ERBB2 amplicon is seen in ~20% of breast cancers and it confers worse biological behavior and clinical aggressiveness in breast cancer.
Breast cancers can have up to 25 to 50 copies of the ERBB2 amplicon.
MIEN1 is one of the core ERBB2 genes which are always over-expressed with ERBB2/HER2 (Kauraniemi et al., 2003).

Prognosis
The prognosis of MIEN1 over-expressing breast cancer is indistinguishable from those of ERBB2 over-expressing breast cancers, due to the common amplification (Katz et al., 2010).

Prostate cancer

Disease
MIEN1 is highly overexpressed in prostate cancer, where it modulates the Akt activity as a membrane bound adapter protein (Dasgupta et al., 2009). MIEN1 is post-translationaly modified by addition of prenyl groups that translocates the protein to the inner face of the plasma membrane.
Ectopic expression of MIEN1 activates Akt and cascades downstream signaling through NF-κB pathway upregulating expression of several migratory and invasive genes (Dasgupta et al., 2011).
MIEN1 may act as a scaffolding protein blocking PTEN binding to Akt; however, the exact mechanism is not known.

Prognosis
Unkown.

References

Kauraniemi P, Kuukasjärvi T, Sauter G, Kallioniemi A. Amplification of a 280-kilobase core region at the ERBB2 locus leads to activation of two hypothetical proteins in breast cancer. Am J Pathol. 2003 Nov;163(5):1979-84

Einarsdóttir K, Rosenberg LU, Humphreys K, Bonnard C, Palmgren J, Li Y, Li Y, Chia KS, Liu ET, Hall P, Liu J, Wedrén S. Comprehensive analysis of the ATM, CHEK2 and ERBB2 genes in relation to breast tumour characteristics and survival:

a population-based case-control and follow-up study. Breast Cancer Res. 2006;8(6):R67

Evans EE, Henn AD, Jonason A, Paris MJ, Schiffhauer LM, Borrello MA, Smith ES, Sahasrabudhe DM, Zauderer M. C35 (C17orf37) is a novel tumor biomarker abundantly expressed in breast cancer. Mol Cancer Ther. 2006 Nov;5(11):2919-30

Dasgupta S, Vishwanatha JK.. Role of C17orf37/MGC14832 in prostate cancer cell proliferation and migration. FASEB J. 2007; 21(5):A289-b.

Dasgupta S, Wasson LM, Rauniyar N, Prokai L, Borejdo J, Vishwanatha JK.. Novel gene C17orf37 in 17q12 amplicon promotes migration and invasion of prostate cancer cells. Oncogene. 2009 Aug 13;28(32):2860-72. doi: 10.1038/onc.2009.145. Epub 2009 Jun 8.

Katz E, Dubois-Marshall S, Sims AH, Faratian D, Li J, Smith ES, Quinn JA, Edward M, Meehan RR, Evans EE, Langdon SP, Harrison DJ.. A gene on the HER2 amplicon, C35, is an oncogene in breast cancer whose actions are prevented by inhibition of Syk. Br J Cancer. 2010 Jul 27;103(3):401-10. doi: 10.1038/sj.bjc.6605763. Epub 2010 Jul 13.

Dasgupta S, Cushman I, Kpetemey M, Casey PJ, Vishwanatha JK.. Prenylated c17orf37 induces filopodia formation to promote cell migration and metastasis. J Biol Chem. 2011 Jul 22;286(29):25935-46. doi: 10.1074/jbc.M111.254599. Epub 2011 May 31.

Katz E, Dubois-Marshall S, Sims AH, Gautier P, Caldwell H, Meehan RR, Harrison DJ.. An in vitro model that recapitulates the epithelial to mesenchymal transition (EMT) in human breast cancer. PLoS One. 2011a Feb 15;6(2):e17083. doi: 10.1371/journal.pone.0017083.

Katz E, Verleyen W, Blackmore CG, Edward M, Smith VA, Harrison DJ.. An analytical approach differentiates between individual and collective cancer invasion. Anal Cell Pathol (Amst). 2011b;34(1-2):35-48. doi: 10.3233/ACP-2011-0003.

Hsu CH, Shen TL, Chang CF, Chang YY, Huang LY.. Solution structure of the oncogenic MIEN1 protein reveals a thioredoxin-like fold with a redox-active motif. PLoS One. 2012;7(12):e52292. doi: 10.1371/journal.pone.0052292. Epub 2012 Dec 20.

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