MED28 (mediator complex subunit 28)

Identity

Other names
1500003D12Rik
EG1
magicin

HGNC (Hugo) MED28
LocusID (NCBI) 80306
Location 4p15.32
Location_base_pair Starts at 17616273 and ends at 17626160 bp from pter (according to hg19-Feb_2009)

DNA/RNA

Note MED28 mRNA is identical to AF317679, AF358829, and AF321617 with the respective size of ~1, ~1.3, and ~3.2 kb (Wiederhold et al., 2004). They vary in the untranslated region, but share the same protein product.

protein

The full-length MED28 protein consists of 178 amino acids with a predicted molecular weight ~20 kDa (Wiederhold et al., 2004). MED28, an evolutionarily conserved protein, was identified as an endothelial-derived gene, EG-1 (Liu et al., 2002). MED28 was also identified as a Merlin-interacting protein by yeast two-hybrid screen (Wiederhold et al., 2004), where Merlin, the neurofibromatosis 2 (NF2) tumor suppressor protein, belongs to the Ezrin-Radixin-Moesin (ERM) family members. Affinity-binding assays demonstrated that MED28 interacted with the SH3 domains of Grb2 (Wiederhold et al., 2004). Accordingly, MED28 was also named as magicin, Merlin and Grb2 interacting cytoskeletal protein (Wiederhold et al., 2004). In addition, several Src family members, including Src, Fyn, and Lck, are also MED28-associated partners (Lee et al., 2006; Lu et al., 2006). Therefore, MED28/magicin/EG-1 may function as an adaptor/scaffold to relay cellular signaling (Lee et al., 2006). Furthermore, MED28 is also found in the nucleus where it is presumably involved in gene transcription as part of the Mediator complex (Sato et al., 2004). It is likely that MED28 shuttles between nucleus, cytoskeleton, and cytoplasm to convey its physiological role.

Expression MED28 is expressed in multiple human tissues (Wiederhold et al., 2004), with high expression in liver, placenta, and testis (Liu et al., 2002).

MED28-interacting proteins: Merlin, actin, Grb2 (Wiederhold et al., 2004), Fyn, Lck, Src (Lee et al., 2006; Lu et al., 2006), Mediator subunits (Sato et al., 2004).
Localisation: Cytoskeleton, cytoplasm, and nucleus (Sato et al., 2004; Wiederhold et al., 2004).

Function: MED28 may be involved in the regulation of numerous biological processes, including transcriptional regulation, cytoskeletal organization, signal transduction, cell proliferation, differentiation, angiogenesis, and migration (Beyer et al., 2007; Huang et al., 2012; Liu et al., 2002; Wiederhold et al., 2004; Yoon et al., 2010; Zhang et al., 2004).

Transcription regulation:
The Mediator complex is a set of protein coactivators that bridges DNA-binding transcription factors to transcriptional activation of the RNA polymerase II (pol II). MED28 was identified as a subunit of the mammalian Mediator complex by the multidimensional protein identification technology (MudPIT) (Sato et al., 2004). This identification indicates a role of MED28 in the regulation of gene transcription.

Cytoskeletal organization:
The implication of MED28 in cytoskeletal re-organization was based on the observation that MED28, similar to merlin, co-localizes with the actin cytoskeleton as determined by cofractionation, immunofluorescence and electron microscopy (Wiederhold et al., 2004).

Signal transduction:
Ectopic expression of MED28 led to increased phosphorylation of mitogen-activated protein kinases (MAPK) (Lu et al., 2005). In contrast, MED28-specific knockdown resulted in decreased expression of mitogen-activated protein kinase kinase 1 (MAP2K1/MEK1) in MCF7 cells (Huang et al., 2012). In addition, overexpression of MED28 resulted in the activation of c-Src (Lu et al., 2006) and MED28 can be phosphorylated at Y64 by Fyn, a Src family member (Lee et al., 2006). These data indicate that MED28 may function as a regulator of cellular signal transduction pathways.

Cell proliferation:
Ectopic overexpression of MED28 resulted in enhanced cell growth in immortal human embryonic kidney (HEK) 293 cells, and breast cancer cell lines, MCF7 and MDA-MB-231 (Lu et al., 2005). The HEK293 xenograft tumor growth was also stimulated in MED28-overexpressing cells (Lu et al., 2005).

Smooth muscle cell differentiation:
MED28 functions as a repressor of smooth muscle cell (SMC) differentiation (Beyer et al., 2007). MED28-specific knockdown resulted in up-regulation of several SMC-related genes and SMC phenotype, whereas ectopic expression of MED28 reversed the SMC morphology induced by MED28 knockdown (Beyer et al., 2007).

Angiogenesis:
MED28 expression was increased by two-fold in human umbilical vein endothelial cells (HUVECs) treated with either tumor conditioned media or specific angiogenic factors (Liu et al., 2002). This observation suggests a role of MED28 in angiogenesis.

Cell migration:
The role of MED28 in cell migration was demonstrated in both estrogen receptor (ER)-positive and negative human breast cancer cell lines (Huang et al., 2012; Lee et al., 2011). Ectopic expression of MED28 increased cell migration and invasion in MCF7 and MDA-MB-231 breast cancer cells (Huang et al., 2012; Lee et al., 2011). Investigation of the underlying mechanisms revealed that MED28 activates epidermal growth factor (EGF)-stimulated migration through induction of matrix metalloproteinase 9 (MMP9) in EGFR-overexpressing MDA-MB-231 cells (Lee et al., 2011). In addition, MED28 can also regulate cell migration through the mitogen-activated protein kinase kinase 1 (MAP2K1; MEK1)-dependent MMP2 activation, which is independent of EGF stimulation (Huang et al., 2012). These lines of evidence support the role of MED28 in cell migration, implying that MED28 might be responsible for cancer metastasis.
Homology
MED28 has significant homology to a mouse cDNA (94%), fish, and a fly cDNA (31%) (Liu et al., 2002; Wiederhold et al., 2004). The mouse MED28 gene is located on chromosome 5 (45520229..45529284).

Implicated in
Various cancers
MED28 expression is elevated in cancers including breast, colorectal, and prostate cancers, suggesting a role of MED28 in malignant phenotype of epithelial-derived cancers (Liu et al., 2002; Zhang et al., 2004). Further tissue microarray (TMA) analysis on a set of breast cancer population also showed elevated MED28 expression in the ductal carcinoma in situ (DCIS) and invasive ductal carcinoma lesions (Yoon et al., 2010). Such elevated MED28 expression independently predicts poor survival (Yoon et al., 2010). These data indicate that MED28 may be a potential therapeutic target in cancer intervention. Indeed, MED28 suppression via either siRNA lentivirus or polyclonal antibody resulted in decreased growth of both MCF7 and MDA-MB-231 cell lines and their corresponding xenograft tumors in mice (Lu et al., 2007). Furthermore, the in vitro application of phytochemical resveratrol potently inhibited EGF-stimulated cell migration via suppression of MED28 in MDA-MB-231 breast cancer cells (Lee et al., 2011).

Prognosis
The evidence supporting MED28 as a prognostic factor is emerging. MED28 peptide was detectable in serum and urine of a small set of breast cancer patients (Lu et al., 2007). In addition, statistical analysis on the correlation between MED28 and survival time or time-to-relapse indicates that MED28 is a significant predictor of malignant breast cancer (Yoon et al., 2010).

External links
Nomenclature
- HGNC (Hugo): MED28 24628
- Entrez Gene (NCBI): MED28 80306 mediator complex subunit 28
- Atlas: MED28ID50131ch4p15
- AceView (NCBI): MED28
- Genatlas (Paris): MED28
- euGene (Indiana): 80306
- SOURCE (Stanford): NM_025205

Genomic and cartography
- Ensembl: MED28 - 4p16 [CytoView]
- Mapping of homologs: MED28
- OMIM: 610311

Gene and transcription
- Genbank (Entrez): AF317678 AF317679 AF317680 AF318059 AF358829
- RefSeq transcript (SRS): NM_025205
- RefSeq transcript (Entrez): NM_025205
- RefSeq genomic (SRS): AC_000136 NC_000004 NT_006316 NW_001838900
RefSeq genomic (Entrez) | AC_000136 NC_000004 NT_006316 NW_00183900

Consensus coding sequences : CCDS (NCBI) | MED28

Cluster EST : Unigene | Hs.731966 [ SRS ] Hs.731966 [ NCBI ]

Alternative Splicing Gallery | ENSG00000118579

Gene Expression | MED28 [ NCBI-GEO ] MED28 [ EBI-ARRAY_EXPRESS ]

Protein : pattern, domain, 3D structure

UniProt/SwissProt | Q9H204 (SRS) Q9H204 (Uniprot)

With graphics : InterPro | Q9H204

Splice isoforms : SwissVar | Q9H204 (SwissVar)

Domains : Interpro (SRS) | Mediator_Med28

Domains : Interpro (EBI) | Mediator_Med28

Related proteins : CluSTr | Q9H204

Domain families : Pfam (SRS) | Med28 (PF11594)

Domain families : Pfam (Sanger) | Med28 (PF11594)

Domain families : Pfam (NCBI) | pfam11594

Blocks (Seattle) | Q9H204

Human Protein Atlas | ENSG00000118579

HPRD | 14381

IPI | IPI00097532 IPI00966840

Protein Interaction databases

DIP (DOE-UCLA) | Q9H204

IntAct (EBI) | Q9H204

FunCoup | ENSG00000118579

REACTOME | MED28

BioGRID | MED28

InParanoid | Q9H204

Interologous Interaction database | Q9H204

IntegromeDB | MED28

Polymorphism : SNP, mutations, diseases

SNP Single Nucleotide Polymorphism (NCBI) | MED28

SNP (GeneSNP Utah) | MED28

Genetic variants : HAPMAP | MED28

Somatic Mutations in Cancer : COSMIC | MED28

CONAN: Copy Number Analysis | MED28

Mutations and Diseases : HGMD | MED28

OMIM | 610311

GENETests | 610311

Disease Genetic Association | MED28

Huge Navigator | MED28 [HugePedia] MED28 [HugeCancerGEM]

Genomic Variants | MED28

snp3D : Map Gene to Disease | 80306

http://atlasgeneticsoncology.org/Genes/MED28ID50131ch4p15.html

2012/11/28
<table>
<thead>
<tr>
<th>General knowledge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homologs:</td>
</tr>
<tr>
<td>HomoloGene</td>
</tr>
<tr>
<td>Homology/Alignments:</td>
</tr>
<tr>
<td>Family Browser (UCSC)</td>
</tr>
<tr>
<td>Phylogenetic Trees/Animal Genes:</td>
</tr>
<tr>
<td>TreeFam</td>
</tr>
<tr>
<td>Chemical/Protein Interactions:</td>
</tr>
<tr>
<td>CTD</td>
</tr>
<tr>
<td>Chemical/Pharm GKB Gene</td>
</tr>
<tr>
<td>Clinical trial</td>
</tr>
<tr>
<td>Cancer Resource (Charite)</td>
</tr>
<tr>
<td>Ontology : AmiGO</td>
</tr>
<tr>
<td>actin binding</td>
</tr>
<tr>
<td>protein binding</td>
</tr>
<tr>
<td>nucleus</td>
</tr>
<tr>
<td>nucleolus</td>
</tr>
<tr>
<td>transcription, DNA-dependent</td>
</tr>
<tr>
<td>regulation of transcription, DNA-dependent</td>
</tr>
<tr>
<td>negative regulation of smooth muscle cell differentiation</td>
</tr>
<tr>
<td>Ontology : EGO-EBI</td>
</tr>
<tr>
<td>actin binding</td>
</tr>
<tr>
<td>protein binding</td>
</tr>
<tr>
<td>nucleus</td>
</tr>
<tr>
<td>nucleolus</td>
</tr>
<tr>
<td>transcription, DNA-dependent</td>
</tr>
<tr>
<td>regulation of transcription, DNA-dependent</td>
</tr>
<tr>
<td>negative regulation of smooth muscle cell differentiation</td>
</tr>
<tr>
<td>Other databases</td>
</tr>
<tr>
<td>Probes: Imagenes</td>
</tr>
<tr>
<td>MED28 Related clones (RZPD - Berlin)</td>
</tr>
<tr>
<td>Literature</td>
</tr>
<tr>
<td>PubMed</td>
</tr>
<tr>
<td>20 Pubmed reference(s) in Entrez</td>
</tr>
<tr>
<td>PubGene</td>
</tr>
<tr>
<td>MED28</td>
</tr>
<tr>
<td>iHOP</td>
</tr>
<tr>
<td>MED28</td>
</tr>
</tbody>
</table>

**Bibliography**

**Identification of a novel endothelial-derived gene EG-1.**
Liu C, Zhang L, Shao ZM, Beatty P, Sartippour M, Lane TF, Barsky SH, Livingston E, Nguyen M.
PMID 11779215

**A set of consensuses mammalian mediator subunits identified by multidimensional protein identification technology.**
PMID 15175163

**Magiein, a novel cytoskeletal protein associates with the NF2 tumor suppressor merlin and Grb2.**
Oncogene. 2004 Nov 18;23(54):8815-25.
PMID 15467741

**Expression pattern of the novel gene EG-1 in cancer.**
PMID 15161706

**The novel gene EG-1 stimulates cellular proliferation.**
PMID 16024617

**Magiein associates with the Src-family kinases and is phosphorylated upon CD3 stimulation.**
Lee MF, Beauchamp RL, Beyer KS, Gusella JF, Ramesh V.
PMID 16899217

**EG-1 interacts with c-Src and activates its signaling pathway.**
Lu M, Zhang L, Sartippour MR, Norris AJ, Brooks MN.
PMID 16064398

**Mediator subunit MED28 (Magiein) is a repressor of smooth muscle cell differentiation.**
Beyer KS, Beauchamp RL, Lee MF, Gusella JF, Naar AM, Ramesh V.
PMID 17845860
Targeted inhibition of EG-1 blocks breast tumor growth.
Lu M, Saritipour MR, Zhang L, Norris AJ, Brooks MN.
PMID 17568184

Elevated MED28 expression predicts poor outcome in women with breast cancer.
Yoon NK, Maresh EI, Elshimali Y, Li A, Horvath S, Seligson DB, Chia D, Goodglick L.
PMID 20584319

Resveratrol modulates MED28 (Magicin/EG-1) expression and inhibits epidermal growth factor (EGF)-induced migration in MDA-MB-231 human breast cancer cells.
Lee MF, Pan MH, Chiu YS, Cheng AC, Huang H.
PMID 21942447

MED28 regulates MEK1-dependent cellular migration in human breast cancer cells.
Huang CY, Chou YH, Hsieh NT, Chen HH, Lee MF.
PMID 22495818


This paper should be referenced as such:

This paper is referenced by INIST as such:


For comments and suggestions or contributions, please contact us

jlhuret@AtlasGeneticsOncology.org.