MAPRE1 (Microtubule-associated protein, RP/EB family, member 1)

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Identity
Other names: EB1
HGNC (Hugo): MAPRE1
Location: 20q11.1-11.23
Location (base pair): 32,123,450 - 32,153,886 bp.

DNA/RNA
Description
22 Kb genomic locus, 5 introns.
Transcription
2540 bp open reading frame.

Protein
Description
268 amino acids; 35 kDa; EB1 was cloned in yeast two-hybrid screen as binding partner for the tumor suppressor APC (Adenomatous Polyposis Coli); EB1 is a microtubule plus end tracking protein (+tip). It contains a calponin homology domain and a leucine zipper.

Expression
EB1 is ubiquitously expressed. Protein levels remain similar throughout the cell cycle.

Localisation
EB1 targets to the plus ends of microtubules when they are polymerizing, producing a "comet tail" pattern. (Figure 1). The mechanism is treadmilling, in which new subunits are continually added at the tip. EB1 also shows additional weak binding to the microtubule lattice (along the length of the microtubule). EB1 targets to kinetochores moving anti-poleward. This is suspected to be due to binding to kinetochore microtubule plus ends rather than the kinetochore itself. Through its carboxyl terminus, EB1 localizes to centrosomes and spindle poles.

Note
The original name EB1 came from a yeast two hybrid screen "End Binding 1" is a nickname that was later applied when the protein was found to target to microtubule plus ends.

EB1-GFP fluorescence on polymerizing microtubule plus ends in a living PtK1 cell.
**Function**
The primary function identified to date is regulation of microtubule dynamic instability. Microtubules dynamically convert between growth (polymerization) and shrinkage (depolymerization). The transition from growth to shrinkage is called catastrophe, while the conversion from shrinkage to growth is called rescue. Microtubules also pause in their polymerization. EB1 reduces these pauses and reduces the frequency of catastrophes. EB1 increases the frequency of rescues. The net result is more stable, longer microtubules. This effect is predominantly seen during mitosis.

EB1 is important in maintaining the structure of the mitotic spindle. This is thought to be mediated by its effects on spindle microtubule dynamic instability. EB1 is important in spindle positioning within the cell. This is thought to be due to its effects on astral microtubule dynamic instability. In budding yeast, EB1 also plays a role in positioning the mitotic spindle through the bud neck. In this case, it is through microtubule dynamics as well direct binding to a protein at the bud tip, creating a physical link between the microtubule end and the cell cortex.

EB1 plays a role in linking kinetochores to kinetochore microtubules, which is important for chromosome stability. It is not known whether it regulates kinetochore microtubule dynamics or end-on attachment.

EB1 also has an independent role in anchoring microtubule minus ends to centrosomes.

**Protein-protein interactions:** Adenomatous Polyposis Coli (APC) tumor suppressor, polymerized tubulin (microtubules), p150glued/dynactin, CLIP-170, mDia, Pin2/TRF1, RhoGEF2 (drosophila), shortstop (drosophila).

**Homology**
MAPRE2, MAPRE3.

**Mutations**

**Note**
None known.

**Implicated in**

**Colon cancer**

**Disease**
Truncation of the Adenomatous Polyposis Coli (APC) protein is seen in Familial Adenomatous Polyposis (FAP) as well as most sporadic colon cancers. EB1 binds to the APC C-terminus, so its binding is lost in most truncations. Also lost are other APC binding partners including the transcription factor beta-catenin. The role of APC as a tumor suppressor is thought to be through the beta-catenin pathway. Some evidence in the mouse suggests that this is true.

However, there is increasing evidence that connections between APC and the cytoskeleton are important in cell migration, which could have an important role in colon cancer. One Italian FAP family has been reported in which APC is truncated distal to the beta-catenin binding site but including the EB1 binding site. There is no direct evidence of EB1 mutation in colon cancer, and a single report found no evidence of somatic mutations by reverse transcriptase single-strand conformational polymorphism (SSCP) analysis in 21 sporadic colorectal cancers and seven colorectal adenomas.

**Medulloblastoma**

**Disease**
A single report showed that EB1 is transcriptionally elevated in pediatric medulloblastoma. There is no direct evidence of EB1 mutation in medulloblastoma.

**Breakpoints**

**Note**
None known.

**References**


Berrueta L, Kraeft SK, Tirnauer JS, Schuyler SC, Chen LB, Hill DE, Pellman D, Bierer BE. The adenomatous polyposis coli-binding protein EB1 is associated with cytoplasmic and spindle microtubules. Proc Natl Acad Sci U S A. 1998 Sep 1;95(18):10596-601

Morrison EE, Wardlewth BN, Askham JM, Markham AF, Meredith DM. EB1, a protein which interacts with the APC tumour suppressor, is associated with the microtubule cytoskeleton throughout the cell cycle. Oncogene. 1998 Dec 31;17(26):3471-7


Askham JM, Moncur P, Markham AF, Morrison EE. Regulation and function of the interaction between the APC tumour suppressor protein and EB1. Oncogene. 2000 Apr 6;19(15):1950-8


Askham JM, Vaughan KT, Goodson HV, Morrison EE. Evidence that an interaction between EB1 and pd150(Glued) is required for the formation and maintenance of a radial microtubule array anchored at the centrosome. Mol Biol Cell. 2002 Oct;13(10):3627-45


Rogers SL, Rogers GC, Sharp DJ, Vale RD. Drosophila EB1 is important for proper assembly, dynamics, and positioning of the mitotic spindle. J Cell Biol. 2002 Sep 2;158(5):873-84

Tirnauer JS, Canman JC, Salmon ED, Mitchison TJ. EB1 targets to kinetochores with attached, polymerizing microtubules. Mol Biol Cell. 2002 Dec;13(12):4308-16


Ligon LA, Shelly SS, Tokito M, Holzbaur EL. The microtubule plus-end proteins EB1 and dynein have differential effects on microtubule polymerization. Mol Biol Cell. 2003 Apr;14(4):1405-17


Berrueta L, Tirnauer JS, Canman JC, Salmon ED, Mitchison TJ. EB1 targets to kinetochores with attached, polymerizing microtubules. Mol Biol Cell. 2002 Dec;13(12):4308-16

Wen Y, Eng CH, Schmoranzer J, Cabrera-Poch N, Morris EJ, Chen M, Wallar BJ, Alberts AS, Gundersen GG. EB1 and APC bind to mDia to stabilize microtubules downstream of Rho and promote cell migration. Nat Cell Biol. 2004 Sep;6(9):820-30

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