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Gene Section
Review

EPS8 (epidermal growth factor receptor pathway substrate 8)

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Identity

HGNC (Hugo): EPS8

Location: 12p12.3

DNA/RNA

Description

The EPS8 gene can be found on chromosome 12 at 12p12.3, starting at position 15664342 bp and ending at 15833601 bp from pter on the reverse strand. It contains 21 exons.

Transcription

The transcript consists of 4.1 kb and translates to a 822 residue protein.

Protein

Description

822 amino acids; contains pleckstrin homology (PH) domain at amino acids 69-129 and 381-414; contains Src homology (SH3) domain at amino acids 531-590; intertwined dimer.

Expression

Ubiquitous in adult; temporal expression in developing mouse embryo, in frontonasal neural crest cells, branchial arches, liver primordium, central nervous system and submandibular glands.

Localisation

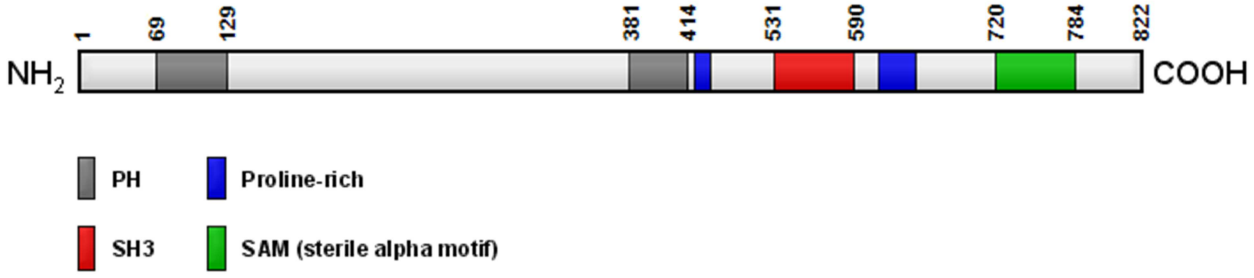
Plasma membrane; cytoplasm; perinuclear; possibly nuclear.

Function

Scaffolding protein; participates in signal transduction downstream of receptor tyrosine kinases (incl. EGFR, CSF1R, PDGFR); receptor endocytosis; cell motility; actin reorganization.

Homology

45 orthologues identified (Ensembl).
3 paralogues: EPS8L1; EPS8L2; EPS8L3.



Schematic representation of Homo sapiens EPS8.

Implicated in

Cancer

Note

Eps8 is reported to be expressed at elevated levels in a range of human malignancies, including breast cancer, pancreatic cancer, colon cancer and head and neck squamous cell carcinoma.

Oncogenesis

Overexpression of EPS8 has been reported to be sufficient to transform non-tumorigenic human cells to a tumorigenic phenotype. In a model system using murine fibroblasts, EPS8 overexpression led to enhanced mitogenic signaling and growth factor-dependent cellular transformation. Constitutive tyrosine phosphorylation of EPS8 has been documented in human tumor cell lines, although the significance of this for tumorigenesis remains to be established.

Breast cancer

Oncogenesis

EPS8 overexpression has been shown via integrated cDNA array comparative genomic hybridization and serial analyses of gene expression in a number of human breast cancer cell lines such as ductal carcinoma in situ cell lines, invasive ductal carcinomas and lymph node metastases, as novel candidate breast cancer oncogenes.

Pancreatic cancer

Oncogenesis

EPS8 was found to be overexpressed in multiple pancreatic tumors, with elevated levels primarily found in pancreatic ductal cells, cell lines derived from malignancies and ascites compared to lower levels in primary tumors and normal pancreatic tissues. EPS8 was reported to localize to the tips of F-actin filaments, filopodia, and the leading edge of the cells, and was therefore correlated with the migratory potential of tumor cells.

Colon cancer

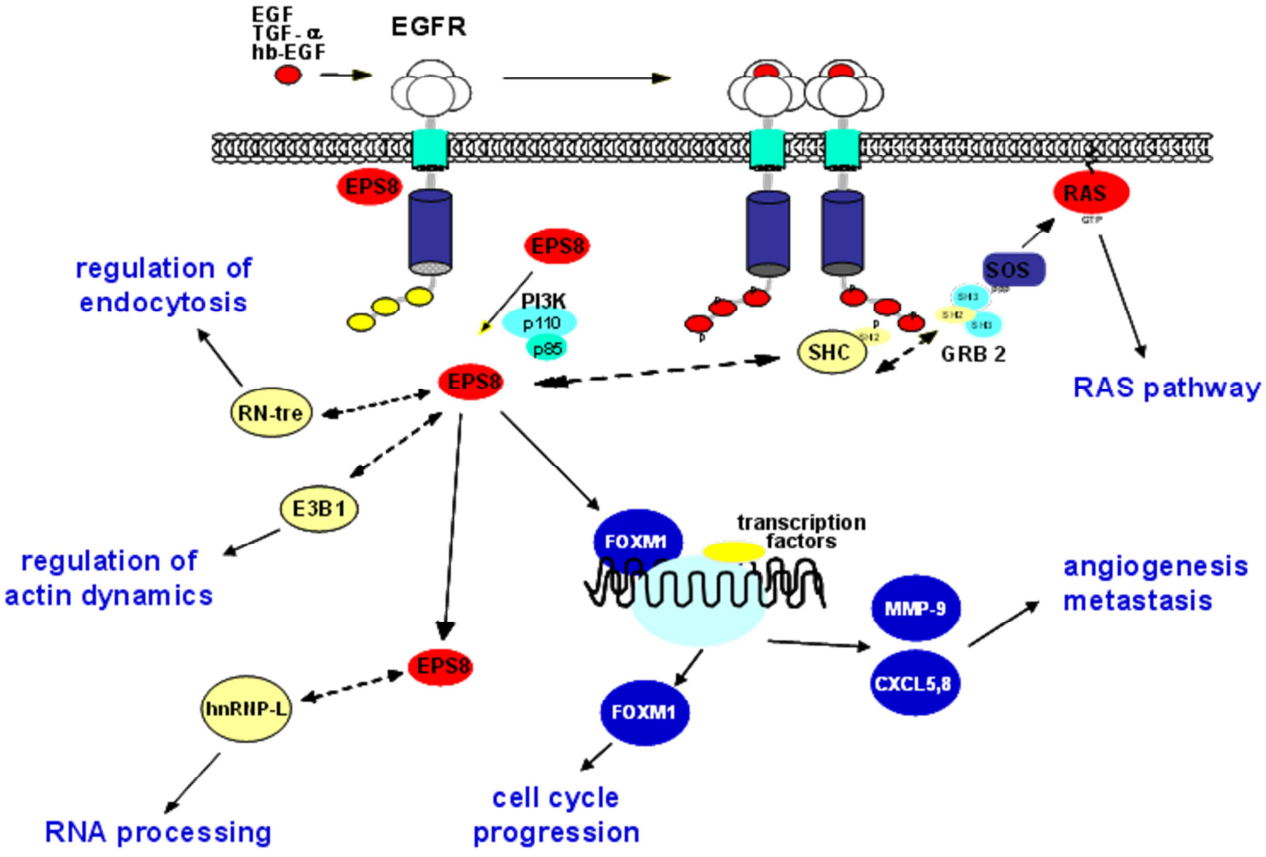
Oncogenesis

EPS8 was found to be overexpressed in the majority of colorectal tumors compared to their normal counterparts. It was also found to modulate FAK expression and together, EPS8 and FAK were found to play an important role in cell locomotion.

Head and neck squamous cell carcinoma

Oncogenesis

Greater expression of EPS8 was found in malignant head and neck squamous cell carcinoma cell lines (HN12) compared to the primary tumor derived cells (HN4) from the same patient. Ectopic overexpression of EPS8 in HN4 cells led to increased cell proliferation and migration in vitro and tumorgenicity in vivo.



Signaling processes involving EPS8. Dashed lines, direct protein interactions; blue circles, effector proteins.

Knockdown of EPS8 in HN12 cells led to reduced migration in vitro and reduced tumorgenicity in vivo. EPS8 was found to mediate alphavbeta6 and alpha5beta1 integrin dependent activation of Rac1 and resulting cell migration. Suppression of either EPS8 or Rac1 resulted in reduced cell motility of the same tumor cells, however constitutive expression of Rac1 rescued reduced cell migration in EPS8 knockdown cells. Therefore EPS8 and Rac1 likely modulate integrin-dependent tumor cell motility. FOXM1, a cell cycle related transcription factor, was found to be upregulated in tumor cells with elevated EPS8. Further studies showed cell proliferation and migration due to EPS8 occurs in part by FOXM1 deregulation and induction of CXC-chemokine expression, which is mediated by PI3K and AKT-dependent mechanisms.

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