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Gene Section
Mini Review

EGLN1 (egl nine homolog 1 (C. elegans))

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Identity

Hugo: EGLN1
Other names: C1orf12; DKFZp761F179; ECYT3; HIFPH2; HPH-2; PHD2; SM-20; SM20; ZMYND6
Location: 1q42.2

DNA/RNA

Description

EGLN1 gene is located on chromosome 1, location 229568054-229627413. Gene spans 61293 bases and has 5 exons.

Transcription

PHD2 expression is strongly induced in hypoxia by the HIF-1alpha transcription factor. Primary transcript length is 5936 bases. On mRNA level two splice variants have been proposed, lacking exons 3 or 4, but these have not been confirmed on protein level.

Protein

Description

PHD2 protein is 426 amino acids long and approximately 46 kDa. It has a zf-MYND domain (aa 21-58) and a 2-OG-FeII-oxygenase domain (aa 205-391).

Expression

Ubiquitous.

Localisation

Predominantly cytoplasmic.

Function

PHD2 is a member of the 2-oxoglutarate-dependent, non-haem iron binding dioxygenases.
PHD2 post-translationally regulates the levels of hypoxia-inducible factor-alpha (HIF-alpha) subunits in normoxic conditions by hydroxylating them in an oxygen-dependant manner on specific proline residues. This enables recognition of HIF by the VHL ubiquitin ligase complex and subsequent degradation of HIF by the proteasome. In hypoxic conditions the hydroxylation is significantly decreased, and the HIF-alpha subunits are stabilized. PHD2 is considered the main HIF-1alpha regulator in normoxic and mildly hypoxic conditions.

Homology

EGLN1 has two paralogs: EGLN2 and EGLN3 homologs have been found in all multicellular organisms investigated.

Mutations

Note: Homozygous deletion confers embryonic lethality in mouse.

Germinal

Heterozygous mutations have been associated with familial erythrocytosis. Currently three point mutations: G1112A → Arg371His, C950G → Pro317Arg, C1129T → Gln377X, one deletion: 606delG → frameshift, and one insertion: 840_841insA → frameshift have been reported.

Implicated in

Familial erythrocytosis (ECYT3)

Note: ECYT3 is characterized by increased serum hemoglobin and hematocrit, but with normal serum erythropoietin levels.

Disease

Characterized EGLN1 mutations result in the loss of catalytic function and thereby aberrant erythropoietin expression.

Head and neck squamous cell carcinoma

Note: Increased expression levels and nuclear translocation have been associated with the aggressiveness of the carcinoma.

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