EGLN1 (egl nine homolog 1 (C. elegans))
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Published in Atlas Database: January 2008
Online updated version: http://AtlasGeneticsOncology.org/Genes/EGLN1ID44140ch1q42.html
DOI: 10.4267/2042/38569
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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-alphas) subunits in normoxic conditions by hydroxylating them in an oxygen-dependent 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.

Germinald
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.

### References


Berra E, Benizri E, Ginouvès A, Volmat V, Roux D, Pouyssegur J. HIF prolyl-hydroxylase 2 is the key oxygen sensor setting low steady-state levels of HIF-1alpha in normoxia. EMBO J 2003;22:4082-4090.

