

# Gene Section

## Short Communication

# PHLDA1 (pleckstrin homology-like domain, family A, member 1)

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## Abstract

Short communication on PHLDA1, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

## Identity

**Other names:** DT1P1B11, PHRIP, TDAG51

**HGNC (Hugo):** PHLDA1

**Location:** 12q21.2

**Local order:** Minus strand.

## DNA/RNA

### Description

PHLDA1 gene contains 2 exons, 1 intervening sequence and spans 6,3 kb of genomic DNA.

### Transcription

1,2 kb mRNA.

### Pseudogene

Not identified.

## Protein

### Description

The PHLDA1 gene encodes for a 401 amino acid protein that is a member of the evolutionarily conserved pleckstrin homology-like domain family.

PHLDA1 protein has a modular structure containing a central pleckstrin homology-like domain (PHL) and proline-glutamine (PQ) and proline-histidine (PH) repeats in the C-terminal region (see figure above).

### Expression

PHLDA1 is widely expressed in mammalian tissues displaying cytoplasmic, vesicle membrane, plasma membrane and nuclear subcellular localization. PHLDA1 expression is up-regulated by estrogen, IGF-1 (insulin-like growth factor 1), FGF (fibroblast growth factor), TPA (phorbol ester), and ER (endoplasmic reticulum)-stress agents such as homocysteine, tunicamycin, and farnesol.

### Localisation

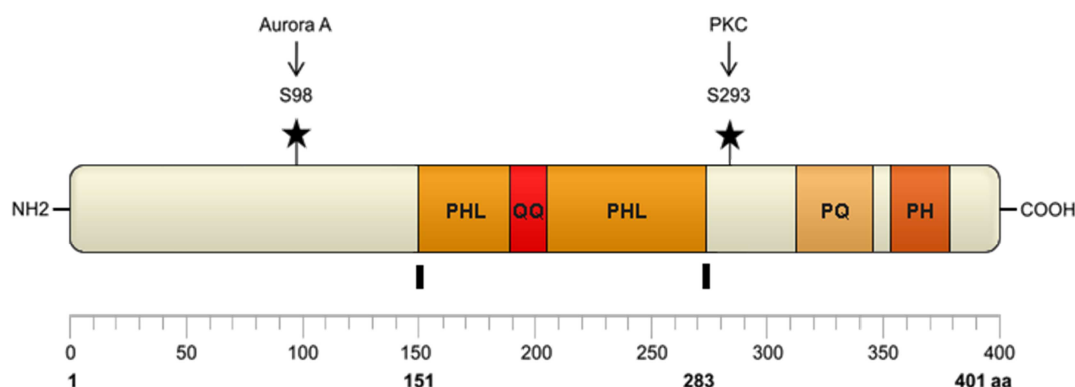
Cytoplasm, vesicle membrane, plasma membrane, nucleus.

### Function

Protein binding. Several evidences have implicate PHLDA1 as a potential transcriptional activator that acts as a pro-apoptotic and antiproliferative factor, however the mechanisms by which PHLDA1 mediates cell survival is still under investigation.

### Homology

PHLDA2 (pleckstrin homology-like domain, family A, member 2) and PHLDA3 (pleckstrin homology-like domain, family A, member 3) are paralogs for PHLDA1.



**Schematic representation of the modular structure of PHLDA1 protein.** PHL: pleckstrin homology-like domain spanning amino acids residues from 150 to 283; QQ: proline/glutamine rich sequence (aa residues from 189 to 204); PQ: proline-glutamine tracts (aa residues from 311 to 346); PH: proline-histidine-rich tracts (aa residues from 352 to 389); \*: indicates phosphorylation sites.

## Mutations

### Note

Short genetic variation - dbSNP: rs139162669, rs73385441, rs74620794, rs147230079, rs76437300, rs186978611, rs140610935, rs144470255, rs79545253, rs147644129.

## Implicated in

### Melanoma

#### Note

PHLDA1 expression was associated with reduced cell growth and colony formation and with increased apoptotic rates and drug sensitivity in melanoma cell lines. Loss of PHLDA1 has been correlated with melanoma progression (Neef et al., 2002).

### Breast cancer

#### Note

Down-regulation of PHLDA1 mRNA and protein expression is frequently observed in primary invasive breast tumours.

Down-regulation of PHLDA1 protein has been shown to be a strong predictor of poor prognosis for breast cancer patients, indicating that reduced PHLDA1 expression contribute for breast cancer progression and might serve as useful prognostic biomarker of disease outcome (Nagai et al., 2007).

### Oral cancer

#### Note

Reduced expression of PHLDA1 was observed in 60,7% of oral squamous cell carcinomas (OSCC), especially in well-differentiated tumors.

Positive PHLDA1 immunostaining was associated with advanced clinical stages of the disease, suggesting that PHLDA1 has a functional role in oral tumorigenesis.

Overall and disease-free survival rates were

significantly better in patients with tumors that were negative for PHLDA1, and a multivariate analysis suggested that PHLDA1 is an independent prognostic factor in OSCC patients (Coutinho-Camillo et al., 2013).

### Colon cancer

#### Note

Altered PHLDA1 expression has been shown to be associated with the process of intestinal tumorigenesis (Sakthianandeswaren et al., 2011).

### Basal cell carcinoma

#### Note

PHLDA1 has also been shown to be a follicular and epithelial stem cell marker (Ohyama et al., 2006; Sakthianandeswaren et al., 2011) with potential to differentiates between trichoepithelioma and basal cell carcinoma (Sellheyer and Nelson, 2011).

### Atherosclerosis

#### Note

In vivo and in vitro studies demonstrated that increased PHLDA1 expression induced by homocysteine promotes detachment-mediated programmed cell death and contributes to the development of atherosclerosis (Hossain et al., 2003).

Genetic variant in an intergenic region of the PHLDA1 gene (rs2367446) has been shown to be associated with the development of cardiovascular diseases (Hossain et al., 2013).

### Epilepsy

#### Note

PHLDA1 expression has been shown to be higher in the anterior temporal neocortex from patients with intractable epilepsy when compared with the levels observed in the neocortex from the control group, suggesting a possible association of PHLDA1 in the physiopathology of the disease (Xi et al., 2007).

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