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Gene Section
Short Communication

PASD1 (PAS domain containing 1)

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Identity

Other names: CT63, OXTES1
HGNC (Hugo): PASD1
Location: Xq28
Note: PASD1 gene encodes a protein thought to be a transcription factor (Entrez Gene). In normal tissues expression is restricted to immunologically protected sites (which lack MHC class I expression) such as the testes, however the demonstration of expression in haematological malignancies and a range of solid tumour cell lines indicates it is a cancer-testis antigen (Liggins et al., 2004a; Liggins et al., 2004b; Guinn et al., 2005; Cooper et al., 2006; Sahota et al., 2006).

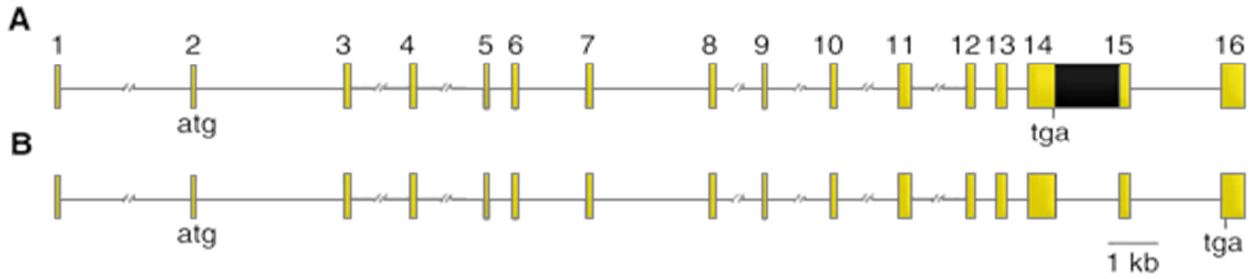
DNA/RNA

Description

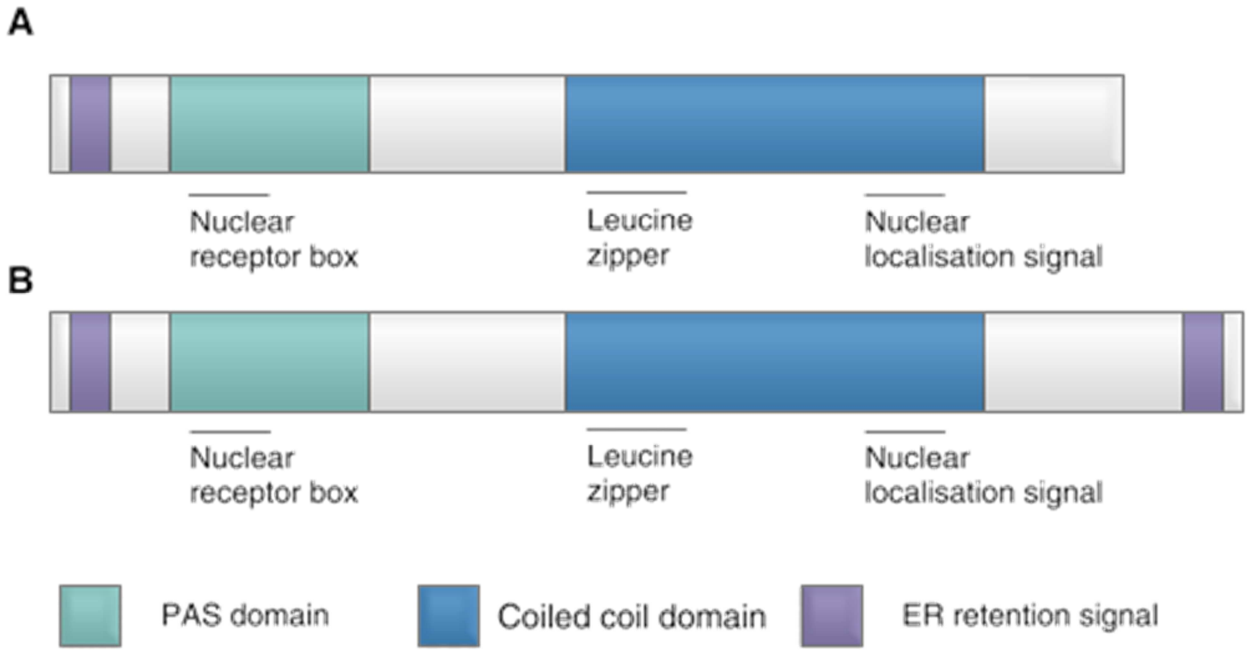
113205 bases.

Transcription

The PASD1 gene is alternatively spliced into two transcripts named PASD1_v1 and PASD1_v2. PASD1_v2 lacks intron 14 and a retained stop signal (Liggins et al., 2004a).
Differential splicing is predicted to create additional novel PASD1 isoforms as a protein smaller than PASD1_v1 and PASD1_v2 has been detected in OCi-Ly3 and FEPD cells (Cooper et al., 2006).
Transcripts found in 33% (4 of 12) acute myeloid leukaemia patients, 1 of 6 chronic myeloid leukaemia patients and 4 of 16 cell lines (Guinn et al., 2005).
Transcripts have been found in 5 of 11 multiple myeloma cell lines including THIEL and RPMI8226, and 14 of 16 primary multiple myeloma samples (Sahota et al., 2006), 22 of 25 B- and T-cell malignancy cell lines (Liggins et al., 2010).



Structure of the PASD1 gene from which (A) PASD1_v1 and (B) PASD1_v2 and transcribed. Lines indicate introns, boxes exons, the filled box the retained intron in PASD1_v1, "atg" the predicted start site and "tga" the predicted stop site (Liggins et al., 2004a).



Schematic illustration of the functional domains within the PASD1 protein. PASD1a protein translated from PASD1_v1 (A) and PASD1b translated from PASD1_v2 (B) are shown (Liggins et al., 2004a).

Protein

Description

Contains a Per Arnt Sim (PAS) domains in the N-terminal regions between aa 32-94 and aa 41-137 (Liggins et al., 2004a).

Expression

Expression highest in G361 (melanoma) and SW480 (colorectal adenocarcinoma) cell lines of a panel of nine tested.

Expression in 25 of 68 solid tumours on matched tumour/normal arrays (Liggins et al., 2004a).

Expression restricted in normal tissues, placenta and testes, not detected in panel of normal tissue cDNAs.

Expression also found in K562, Jurkats (T-cell leukaemia), Hn5 (head and neck cancer) and highest in H1299 (lung cancer) cell lines by real-time PCR (Guinn et al., 2005).

Of the normal tissues expression was restricted to testes and not found in a range of normal tissues including brain, liver, kidney, placenta, breast, uterus or ovary (Guinn et al., 2005; Cooper et al., 2006).

Expression of PASD1 was demonstrated in OCI-Ly3 (non-germinal centre diffuse large B-cell lymphoma-derived cells), FEDP (ALK-negative anaplastic large-cell lymphoma), Granta519 (mantle cell lymphoma) KM-H2 (Hodgkin's lymphoma), K562 (chronic myeloid leukaemia) and Thiel (multiple myeloma) cell lines and 21/51 diffuse large B-cell lymphoma patients, 4/9 mantle cell lymphoma, 4/15 follicular lymphomas and a range of other tumour cells from patients with haematological malignancies (Cooper et al., 2006).

Expression has been detected in the multiple myeloma cell lines THIEL and RPMI8226, in the testis and in two of four primary multiple myeloma tumour samples (Sahota et al., 2006).

Not found in 78 basal cell carcinoma by real-time PCR (Ghafouri-Fard et al., 2010).

Localisation

In normal tissues expression was only found in the nuclei of a subpopulation of spermatogonia near the basal membrane in the testicular tubules (Cooper et al., 2006).

PASD1 protein has shown variable expression. In OCI-Ly3 cells, PASD1 expression was found on the membrane and in the cytoplasm.

Nuclear staining of KM-H2, K562 and Thiel cells, nuclear and cytoplasmic staining of Granta519 (Cooper et al., 2006).

Function

The protein is thought to be a transcription factor (Entrez Gene). No role in human cell cycle (Denniss and Guinn, unpublished data).

Detected by virtue of patient humoral responses (Liggins et al., 2004b; Guinn et al., 2005), it has shown to stimulate $CD3^+$ (Guinn et al., 2005), $CD4^+$ (Ait-Tahar et al., 2011) and $CD8^+$ T cell responses (Ait-Tahar et al., 2009; Joseph-Pietras et al., 2010; Hardwick et al., submitted) in mixed lymphocyte reactions (MLR) and cytotoxic T lymphocyte (CTL) assays.

Homology

PASD1 has been identified in cow, chicken and mouse where it is known as GM1141 (Entrez Gene). Similarity to the CLOCK gene in mice which is essential for circadian behaviour.

Implicated in

Diffuse large B-cell lymphoma (DLBCL)

Note

DLBCL is the most common type of non-Hodgkins lymphoma and is caused by malignant mature B lymphocytes. Around half the number of patients diagnosed die from the disease (Alizadeh et al., 2000). Using gene expression patterns two types of DLBCL have been identified, 'germinal centre B-like DLBCL' and 'activated B-like DLBCL' (Alizadeh et al., 2000). PASD1 antigen is recognized by DLBCL patient sera (Liggins et al., 2004b)

Prognosis

Germinal centre markers CD10, BCL6 and non-germinal centre marker MUM1 have been used to identify prognosis and survival of DLBCL patients. CD10 or BCL6 expression predicted better overall survival but MUM1 expression suggested worse overall survival (Hans et al., 2004). Germinal centre type associated with good prognosis. Patients with non-germinal centre type showed serum reactivity with PASD1, and PASD1_v2 expression was restricted to non-germinal cell lines (Liggins et al., 2004a).

Acute myeloid leukaemia (AML) and chronic myeloid leukaemia (CML)

Note

PASD1 was recognized by 35% of AML, 6% of CML and 10% of DLBCL sera but not the normal donor sera. Expression was found in 33% (4 of 12) AML and 17% (1 of 6) chronic myeloid leukaemia patient samples (Guinn et al., 2005) by RT-PCR and confirmed by RQ-PCR.

Multiple myeloma

Note

Cancer of the plasma cells in bone marrow. PASD1 expression has been seen in multiple myeloma cell lines by RT-PCR and in primary multiple myeloma samples by Q-PCR at presentation and previously treated cases (Sahota et al., 2006).

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