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Gene Section
Short Communication

POU1F1 (POU class 1 homeobox 1)

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Abstract

Short communication on POU1F1, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Identity

Other names: CPHD1, GHF-1, PIT1, POU1F1a, Pit-1

HGNC (Hugo): POU1F1

Location: 3p11.2

DNA/RNA

Note

The anterior pituitary-specific transcription factor POU1F1 was initially identified and cloned as a transactivator of prolactin (PRL), growth hormone (GH), and TSHβ-subunit genes (Bodner et al., 1988; Ingraham et al., 1988). Transcription produces 2 alternatively spliced mRNAs α (NM_000306.2) and β (NM_001122757.1).

Description

The human POU1F1 gene is composed of 6 exons (Theill et al., 1992).

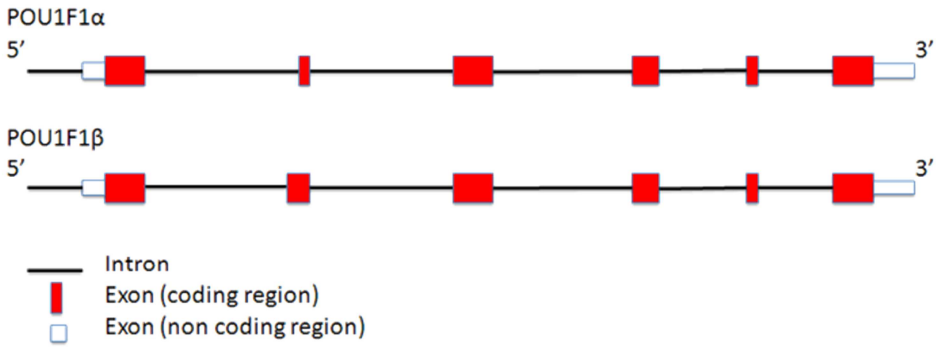
Transcription

Two transcripts have been reported for this gene.

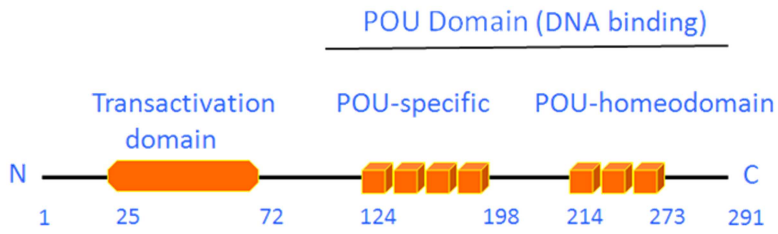
Protein

Description

The main protein isoform expressed in pituitary cells is POU1F1α.
This isoform, also named PIT-1.b or PIT-1α, has 291 aa.
The predicted protein corresponding to POU1F1β, also named PIT-1.a or PIT-1β, has 317 aa and acts as a repressor in pituitary cells (Theill et al., 1992; Jonsen et al., 2009). POU1F1 is structurally related to the POU family of transcriptional regulators, containing a characteristic POU domain divided into two regions, the POU-specific and homeo subdomains.



Structure of POU1F1 gene and its transcripts encoded on minus strand of chromosome 3.



The POUs-specific domain consists of 75 amino acids, comprises 4 α-helices, and contributes to the DNA binding specificity and protein / protein interactions (Ingraham et al., 1990; Jacobson et al., 1997). The homeodomain is composed of 60 amino and contains 3 α-helices. The N-terminal part of POU1F1 is involved in the transcriptional activity. POU1F1 binds as a dimer to most DNA response elements (for review see Phillips and Luisi, 2000).

Expression

The expression of POU1F1 is largely restricted in the pituitary gland in somato- thyreo- and lacto-trope cells, but this factor is also expressed in some extrapituitary tissues and cell lines, including the mammary gland (Gil-Puig et al., 2002).

Localisation

The localization of POU1F1 is nuclear.

Function

POU1F1 is a member of the POU family of transcription factors. This factor is required for terminal differentiation of the somatotrope, lactotrope and thyrotrope cell types (Ingraham et al., 1988; Cohen et al., 1996). This factor is also implicated in the cell growth and prevents the apoptotic cell death (Pellegrini et al., 2006).

Mutations

Note

In humans, mutation in the POU1F1 gene has been shown to be responsible for combined pituitary hormone deficiency (for review see Quentien et al., 2006) (see below).

Implicated in

Pituitary adenoma

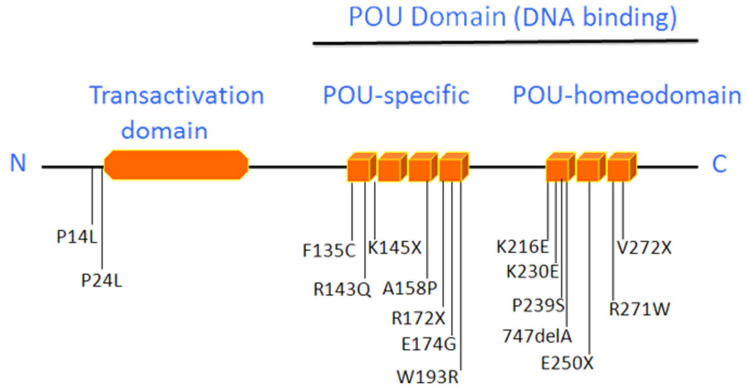
Prognosis

POU1F1 is overexpressed in GH, PRL and TSH pituitary adenomas (Asa et al., 1993; Delhase et al., 1993; Pellegrini et al., 1994) and the increased expression in adenomas is compatible with the role of POU1F1 in cell proliferation. Interestingly, human non-functioning pituitary adenomas also express POU1F1, especially it was expressed in all alpha SU positive nonfunctioning adenomas (Osamura et al., 1999).

Combined pituitary hormone deficiency (CPHD)

Prognosis

In humans, mutation in the POU1F1 gene has been shown to be responsible for combined pituitary hormone deficiency. This syndrome is a disease characterized by the lack of PRL, GH, and TSHbeta produced by the somato- lacto- and thyreo-tropes cells. At least sixteen distinct recessive or dominant POU1F1 mutations have been described to date (Cushman et al., 2002; Dattani, 2005). The molecular mechanisms underlying their effects can be dominant inhibition of transcription or inability to bind to DNA. The R271W mutation is the most commonly occurring POU1F1 gene defect (Radovick et al., 1992). Other mutations, such as F135C, show a decreased transactivation activity although the DNA binding property is conserved (Vallette-Kasic et al., 2001).



Location of the Pit-1 gene mutation.

Breast carcinoma

Prognosis

POU1F1 was expressed in normal human breast tissue but its mRNA expression levels is significantly higher in breast adenocarcinoma. This deregulation promotes tumor growth and metastasis (Gil-Puig et al., 2005; Ben-Batalla et al., 2010).

Acute myeloid leukemia

Prognosis

In acute myeloid leukemia POU1F1 has been identified as a new fusion partner of NUP98 gene (Lisboa et al., 2013).

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