

Gene Section

Short Communication

POU1F1 (POU class 1 homeobox 1)

Jean-Louis Franc, Denis Becquet, Anne-Marie François-Bellan

CRN2M, UMR7286 Aix-Marseille Universite, CNRS, Faculte de Medecine, Bd P. Dramard, Marseille, France (JLF, DB, AMFB)

Published in Atlas Database: February 2014

Online updated version : <http://AtlasGeneticsOncology.org/Genes/POU1F1ID46362ch3p11.html>
DOI: 10.4267/2042/54134

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2014 Atlas of Genetics and Cytogenetics in Oncology and Haematology

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 TSH β -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.

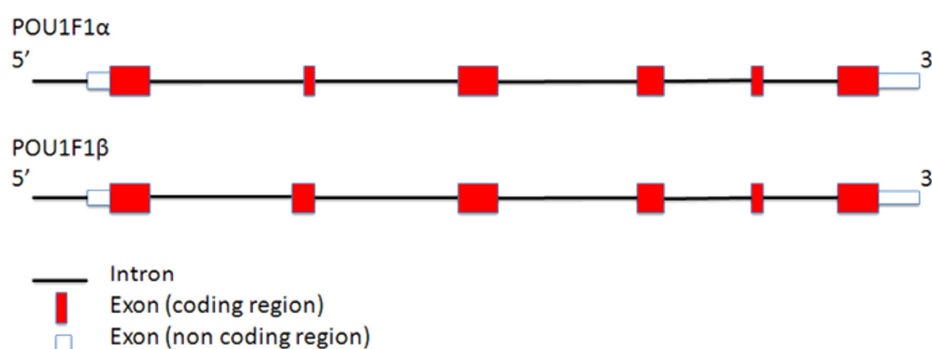
Protein

Description

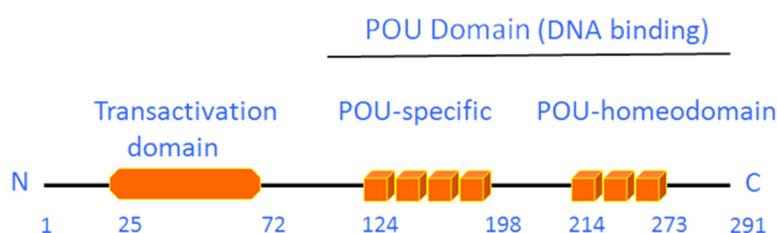
The main protein isoform expressed in pituitary cells is POU1F1 α .

This isoform, also named PIT-1.b or PIT-1 α , has 291 aa.

The predicted protein corresponding to POU1F1 β , also named PIT-1.a or PIT-1 β , 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 POU-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 acids 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 lactotrope 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

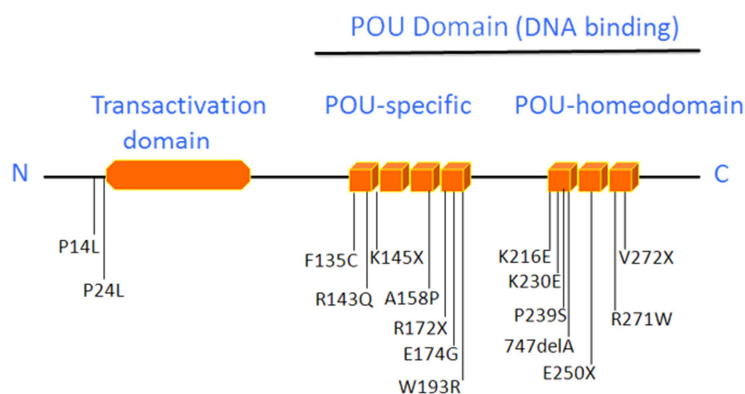
Prognosis

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).

References

- Bodner M, Castrillo JL, Theill LE, Deerinck T, Ellisman M, Karin M. The pituitary-specific transcription factor GHF-1 is a homeobox-containing protein. *Cell*. 1988 Nov 4;55(3):505-18
- Ingraham HA, Chen RP, Mangalam HJ, Elsholtz HP, Flynn SE, Lin CR, Simmons DM, Swanson L, Rosenfeld MG. A tissue-specific transcription factor containing a homeodomain specifies a pituitary phenotype. *Cell*. 1988 Nov 4;55(3):519-29
- Ingraham HA, Flynn SE, Voss JW, Albert VR, Kapiloff MS, Wilson L, Rosenfeld MG. The POU-specific domain of Pit-1 is essential for sequence-specific, high affinity DNA binding and DNA-dependent Pit-1-Pit-1 interactions. *Cell*. 1990 Jun 15;61(6):1021-33
- Radovick S, Nations M, Du Y, Berg LA, Weintraub BD, Wondisford FE. A mutation in the POU-homeodomain of Pit-1 responsible for combined pituitary hormone deficiency. *Science*. 1992 Aug 21;257(5073):1115-8
- Theill LE, Hattori K, Lazzaro D, Castrillo JL, Karin M. Differential splicing of the GHF1 primary transcript gives rise to two functionally distinct homeodomain proteins. *EMBO J*. 1992 Jun;11(6):2261-9
- Asa SL, Puy LA, Lew AM, Sundmark VC, Elsholtz HP. Cell type-specific expression of the pituitary transcription activator pit-1 in the human pituitary and pituitary adenomas. *J Clin Endocrinol Metab*. 1993 Nov;77(5):1275-80
- Delhase M, Vergani P, Malur A, Velkeniers B, Teugels E, Trouillas J, Hooghe-Peters EL. Pit-1/GHF-1 expression in pituitary adenomas: further analogy between human adenomas and rat SMtTW tumours. *J Mol Endocrinol*. 1993 Oct;11(2):129-39
- Pellegrini I, Barlier A, Gunz G, Figarella-Branger D, Enjalbert A, Grisoli F, Jaquet P. Pit-1 gene expression in the human pituitary and pituitary adenomas. *J Clin Endocrinol Metab*. 1994 Jul;79(1):189-96
- Cohen LE, Wondisford FE, Radovick S. Role of Pit-1 in the gene expression of growth hormone, prolactin, and thyrotropin. *Endocrinol Metab Clin North Am*. 1996 Sep;25(3):523-40
- Jacobson EM, Li P, Leon-del-Rio A, Rosenfeld MG, Aggarwal AK. Structure of Pit-1 POU domain bound to DNA as a dimer: unexpected arrangement and flexibility. *Genes Dev*. 1997 Jan 15;11(2):198-212
- Osamura RY, Tahara S, Komatsubara K, Itoh Y, Kajiwara H, Kurotani R, Sanno N, Teramoto A. Pit-1 positive alpha-subunit positive nonfunctioning human pituitary adenomas: a dedifferentiated GH cell lineage? *Pituitary*. 1999 May;1(3-4):269-71
- Phillips K, Luisi B. The virtuoso of versatility: POU proteins that flex to fit. *J Mol Biol*. 2000 Oct 6;302(5):1023-39
- Vallette-Kasic S, Pellegrini-Bouiller I, Sampieri F, Gunz G, Diaz A, Radovick S, Enjalbert A, Brue T. Combined pituitary hormone deficiency due to the F135C human Pit-1 (pituitary-specific factor 1) gene mutation: functional and structural correlates. *Mol Endocrinol*. 2001 Mar;15(3):411-20
- Cushman LJ, Showalter AD, Rhodes SJ. Genetic defects in the development and function of the anterior pituitary gland. *Ann Med*. 2002;34(3):179-91
- Gil-Puig C, Blanco M, Garcia-Caballero T, Segura C, Pérez-Fernández R. Pit-1/GHF-1 and GH expression in the MCF-7 human breast adenocarcinoma cell line. *J Endocrinol*. 2002 Apr;173(1):161-7
- Dattani MT. Growth hormone deficiency and combined pituitary hormone deficiency: does the genotype matter? *Clin Endocrinol (Oxf)*. 2005 Aug;63(2):121-30
- Gil-Puig C, Seoane S, Blanco M, Macia M, Garcia-Caballero T, Segura C, Perez-Fernandez R. Pit-1 is expressed in normal and tumorous human breast and regulates GH secretion and cell proliferation. *Eur J Endocrinol*. 2005 Aug;153(2):335-44
- Pellegrini I, Roche C, Quentien MH, Ferrand M, Gunz G, Thirion S, Bagnis C, Enjalbert A, Franc JL. Involvement of the pituitary-specific transcription factor pit-1 in somatolactotrope cell growth and death: an approach using dominant-negative pit-1 mutants. *Mol Endocrinol*. 2006 Dec;20(12):3212-27
- Quentien MH, Barlier A, Franc JL, Pellegrini I, Brue T, Enjalbert A. Pituitary transcription factors: from congenital deficiencies to gene therapy. *J Neuroendocrinol*. 2006 Sep;18(9):633-42
- Jonsen MD, Duval DL, Gutierrez-Hartmann A. The 26-amino acid beta-motif of the Pit-1beta transcription factor is a dominant and independent repressor domain. *Mol Endocrinol*. 2009 Sep;23(9):1371-84
- Ben-Batalla I, Seoane S, Garcia-Caballero T, Gallego R, Macia M, Gonzalez LO, Vizoso F, Perez-Fernandez R. Deregulation of the Pit-1 transcription factor in human breast cancer cells promotes tumor growth and metastasis. *J Clin Invest*. 2010 Dec;120(12):4289-302
- Lisboa S, Cerveira N, Bizarro S, Correia C, Vieira J, Torres L, Mariz JM, Teixeira MR. POU1F1 is a novel fusion partner of NUP98 in acute myeloid leukemia with t(3;11)(p11;p15). *Mol Cancer*. 2013 Jan 18;12:5

This article should be referenced as such:

Franc JL, Becquet D, François-Bellan AM. POU1F1 (POU class 1 homeobox 1). *Atlas Genet Cytogenet Oncol Haematol*. 2014; 18(10):728-730.
