

Gene Section

Mini Review

HLF (hepatic leukemia factor)

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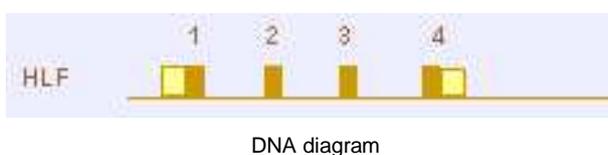
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Identity

HGNC (Hugo): HLF

Location: 17q22

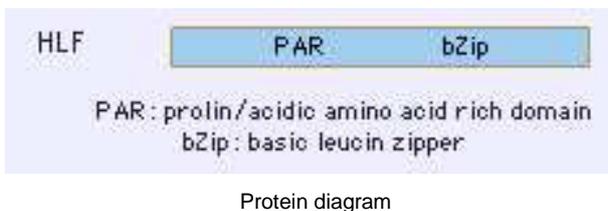
DNA/RNA



Transcription

3.9 kb.

Protein



Description

295 amino acids, MW 43 kDa.

Expression

HLF is normally expressed in hepatocytes and liver-derived cell lines, and, to a lesser extent, in lung, kidney and neurons of the central nervous system; it is not expressed in hematopoietic tissues or cell lines.

Localisation

Nuclear.

Function

The normal function of HLF is largely unknown; HLF is a member of the PAR (proline and acidic amino acid-rich region) subfamily of b/ZIP (basic region leucine zipper) transcription factors; PAR and b/ZIP proteins bind to the DNA as dimers; HLF acts as a transcriptional transactivator; there are evidences that HLF protein transactivates factor VIII and factor IX genes, by binding as a homodimer (HLF/HLF) or a heterodimer with one albumin D-element binding protein sub unit (HLF/DBP), to multiple sites in the promoter of these genes; in the mouse central nervous system ontogeny, HLF expression increases markedly with synaptogenesis, suggesting that HLF plays a role in the function of adult differentiated neurons.

Homology

Other members of the b/ZIP PAR subfamily; in mammals: albumin D-element binding protein (DBP) and thyrotroph embryonic factor/ vitellogenin gene binding protein (TEF/VBP); like HLF, they are transcription activators; the three proteins have an ability to form heterodimers with one another through the leucine-zipper domain; in other species: vitellogenin binding protein (VBP) in the chicken and Ces-2 gene in the nematode *Caenorhabditis elegans*.

Implicated in

t(17;19)(q22;p13) in acute lymphoblastic leukemia --> E2A - HLF fusion gene

Disease

Childhood pro-B cell acute lymphoblastic leukemia.

Prognosis

Poor prognosis is likely.

Abnormal protein

Fusion encodes a protein which contains the AD1 and AD2 transactivation domains of E2A, linked to the bZIP DNA binding/ protein dimerization region of HLF.

Oncogenesis

E2A-HLF alters the apoptotic pathway of pro-B lymphocytic cells, leading to the survival of defective cells that would normally be eliminated; it is to be noted that, in normal tissues, there is no evidence in favour of a role of native HLF in apoptosis regulation.

References

Inaba T, Roberts WM, Shapiro LH, Jolly KW, Raimondi SC, Smith SD, Look AT. Fusion of the leucine zipper gene HLF to the E2A gene in human acute B-lineage leukemia. *Science*. 1992 Jul 24;257(5069):531-4

Hunger SP. Chromosomal translocations involving the E2A gene in acute lymphoblastic leukemia: clinical features and molecular pathogenesis. *Blood*. 1996 Feb 15;87(4):1211-24

Hunger SP, Li S, Fall MZ, Naumovski L, Cleary ML. The proto-oncogene HLF and the related basic leucine zipper protein

TEF display highly similar DNA-binding and transcriptional regulatory properties. *Blood*. 1996 Jun 1;87(11):4607-17

Inukai T, Inaba T, Yoshihara T, Look AT. Cell transformation mediated by homodimeric E2A-HLF transcription factors. *Mol Cell Biol*. 1997 Mar;17(3):1417-24

Newcombe K, Glassco T, Mueller C. Regulation of the DBP promoter by PAR proteins and in leukemic cells bearing an E2A/HLF translocation. *Biochem Biophys Res Commun*. 1998 Apr 17;245(2):633-9

Begbie M, Mueller C, Lillicrap D. Enhanced binding of HLF/DBP heterodimers represents one mechanism of PAR protein transactivation of the factor VIII and factor IX genes. *DNA Cell Biol*. 1999 Feb;18(2):165-73

Hitzler JK, Soares HD, Drolet DW, Inaba T, O'Connell S, MG Rosenfeld, Morgan JI, Look AT. Expression patterns of the hepatic leukemia factor gene in the nervous system of developing and adult mice. *Brain Res*. 1999 Feb 27;820(1-2):1-11

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