HLF (hepatic leukemia factor)
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Identity
HGNC (Hugo): HLF
Location: 17q22

DNA/RNA

DNA diagram

Transcription
3.9 kb.

Protein

Protein diagram

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 bZIP (basic region leucine zipper) transcription factors; PAR and bZIP 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 subunit (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 bZIP 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


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


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