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Gene Section
Short Communication

TCF3 (transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47))

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Identity

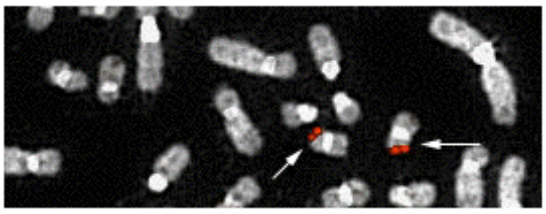
Other names: E2A, TCF3 (Trancription Factor 3), ITF1 Immunoglobulin Enhancer Binding, Factors E12/E47

HGNC (Hugo): TCF3

Location: 19p13.3

Local order: Proximal to ENL also in 19p13.3; LYL1 is in 19p13.2-p13.1 and ELL in 19p13.1.

DNA/RNA



Description

The E2A gene encodes two distinct basic helix-loop-helix transcription factors, E12 (ITF1) and E47 (TCF3) through alternative splicing.

Transcription

4,4 kb mRNA; coding sequence: 2,0 kb; alternate splicing --> E12 and E47, having different bHLH encoding exons (+ also E2-5).

Protein

Description

It forms homodimers and heterodimers with other basic helix-loop-helix transcription factors, such as ASCL1, MYOD1, TAL1, MYOG, NEUROG1, and TWIST1. It contains a transactivation domain (ADI) in N-term, a nuclear localization signal, activation domain II (ADII) (antiapoptotic), an ubiquitin ligase domain, a DNA binding motif, and a helix-loop-helix motif which mediates protein dimerisation in C-term.

Expression

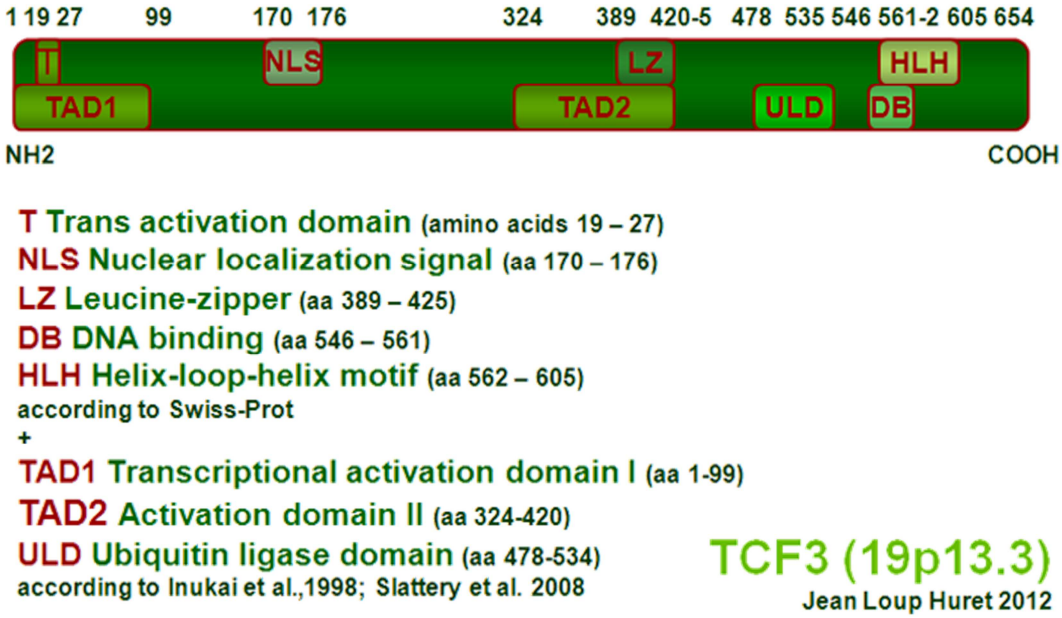
Widely expressed.

Localisation

Nuclear.

Function

Ubiquitously expressed during development and in areas of rapid cell proliferation and differentiation. Role in cell growth, cell commitment, and differentiation. Role in epithelial mesenchymal transition. During epithelial mesenchymal transition, TGF-beta upregulates E2A proteins. E2A proteins are down regulated by the ubiquitin pathway (review in Slattery et al., 2008). Essential for normal B-cell hematopoiesis.



TCF3 (19p13.3) protein and domains.

Homology

With other proteins with a helix-loop-helix dimerization domain signature, MYC type (MYC family, of which are MYC, LYL1, TAL1).

Implicated in

t(1;19)(q23;p13)/B-ALL --> hybrid gene: TCF3/PBX1

Disease

pre B-ALL mainly; CD19+, CD10+, CD9+ (review in Hunger, 1996).

Prognosis

Controversial data; associated with poor prognostic features.

Cytogenetics

Two different forms:
- the balanced t(1;19);
- the unbalanced form, with 2 normal chromosomes 1, a der(19), and a normal chromosome19: --> partial trisomy for 1q23-1qter and monosomy for 19p13.3-pter;
additional anomalies: in half of the cases; they are various.

Hybrid/Mutated gene

5' TCF3 - 3' PBX1; breakpoints are clustered on both genes.

Abnormal protein

N-term transcriptional activation domains from TCF3 fused to the Hox cooperative motif and homeodomain of C-term PBX1.

Oncogenesis

Potent transcriptional activator; pleiotropic transforming activity.

t(12;19)(p13;p13)/B-ALL --> hybrid gene: TCF3/ZNF384

Disease

Pro-B acute lymphoblastic leukemia with expression of myeloid antigens (La Starza et al., 2005; Zhong et al., 2008).

Prognosis

Relatively good prognosis.

Cytogenetics

The t(12;19)(p13;p13) is cryptic.

Hybrid/Mutated gene

5' TCF3 - 3' ZNF384

t(13;19)(q14;p13)

Disease

Only one case to date, an adult patient with pre B-ALL; she achieved complete remission (Barber et al., 2007).

Hybrid/Mutated gene

The translocation involves TCF3 and an unknown partner in 13q14.

t(17;19)(q22;p13)/B-ALL --> hybrid gene: TCF3/HLF

Disease

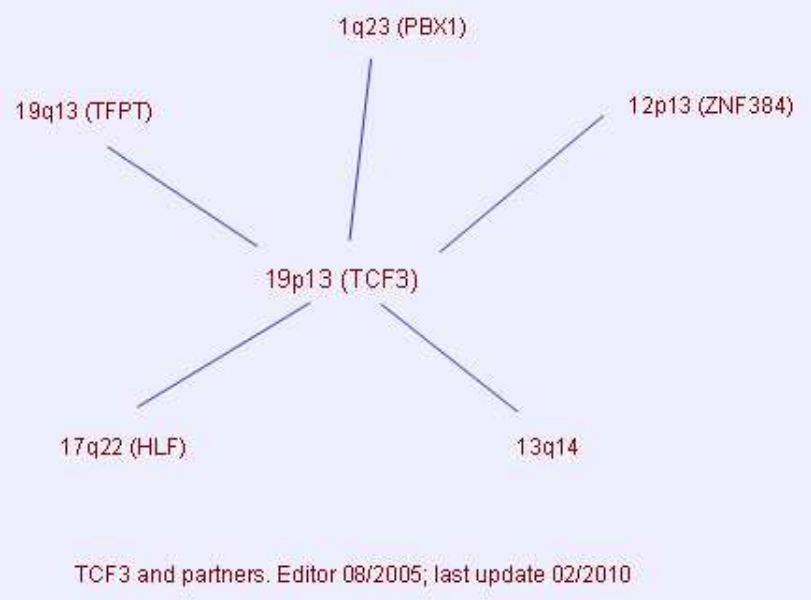
Childhood B-ALL (Raimondi et al., 1991; Hunger et al., 1992; Inaba et al., 1992; Devaraj et al., 1994; Mathew et al., 2001; Takahashi et al., 2001; Ribeiro et al., 2002; Yeung et al., 2006; Barber et al., 2007).

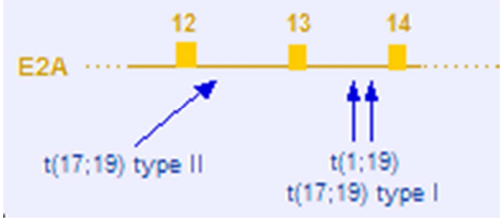
Prognosis

Poor prognosis is likely.

Hybrid/Mutated gene

5' TCF3 - 3' HLF





Abnormal protein
N-term transcriptional activation domains from TCF3 fused to the basic leucine zipper from HLF C-term.

Oncogenesis
TCF3/HLF homodimers bind to promoter/enhancer elements of downstream target genes.

t(19;19)(p13;q13)/B-ALL --> hybrid gene: TCF3/TFPT

Disease
Childhood pre-B cell acute lymphoblastic leukemia (Brambillasca et al., 1999).

Cytogenetics
This chromosome rearrangement is cryptic.

Hybrid/Mutated gene
5' TCF3 - 3' TFPT

Abnormal protein
Retains the transactivation domain of TCF3, but with a truncation in TFPT, due to the frequent occurrence of a stop codon.

Breakpoints

Note
Breakpoints: 1- in t(1;19): are located (and dispersed) in the intron 13, and remove the bHLH domain; 2- in t(17;19) type I: are so far located at a given nucleotide in intron 13; in t(17;19) type II: are located in intron 12.

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