Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section

Mini Review

ZNF217 (zinc finger protein 217)

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Identity

Hugo: ZNF217
Other names: 13009; FLJ14031; ZABC1
Location: 20q13.2

DNA/RNA

Description

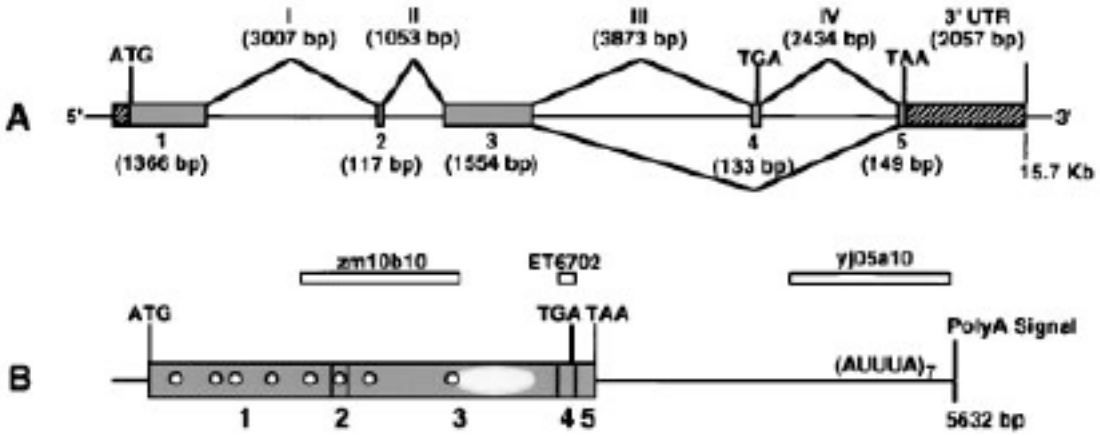
5 exons.

Transcription

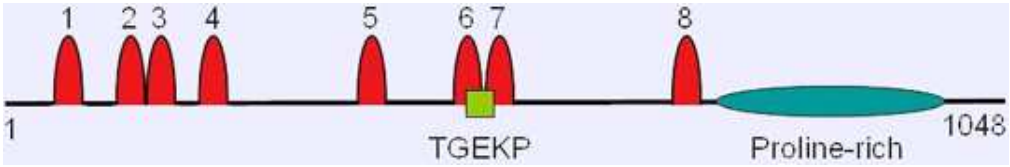
Exon 4 encodes a TGA termination codon and is alternatively processed.

Pseudogene

None.



Genomic organization of ZNF217. (A) The genomic organization of the five exons with encoded initiation and termination codons that make up ZNF217. Hatched boxes represent known 59- and 39-untranslated regions (UTR) in the cDNA. The sizes of exons and introns appear below and above the map, respectively. (B) The map of the 5632-bp ZNF217 cDNA. Vertical bars represent exon boundaries. The relative positions of the predicted eight C2H2 Kruppel-like zinc finger motifs are indicated by white circles. The position of the proline-rich putative transcription activator domain is shown as a hatched oval. AUUUA motifs are indicated in the 39-untranslated region. The relative locations of three ESTs are shown in boxes.



Eight C2H2 zinc fingers and a proline-rich domain. Conserved linker sequence, TGEKP, reported to bind DNA with high affinity

Protein

Description

Full-length ZNF217 cDNAs encode two open reading frames of 1,062 and 1,108 amino acids, due to alternative splicing of exon 4. Each predicted protein has eight C2H2 zinc fingers and a proline-rich domain. Sequence analysis of ZNF217 indicates a strong resemblance to members of the Kruppel-like family of zinc finger proteins. The eight zinc finger domains in ZNF217 are interspersed throughout the ZNF217 sequence and their pattern does not appear to fall into one of the three classes of C2H2 zinc finger proteins; triple-C2H2, multiple-adjacent, and separated-paired fingers. The sixth and seventh zinc fingers in ZNF217 are separated by the conserved linker sequence, TGEKP, reported to bind DNA with high affinity. Database analysis indicates that this paired zinc finger region aligns with those in several members of the Delta-EF1/ZFH-1 family of two-handed zinc-finger homeodomain proteins, including Smad-Interacting Protein 1 (SIP-1).

Expression

ZNF217 is expressed at low levels in normal tissues.

Localisation

Nuclear

Function

ZNF217 protein localizes to the nucleus and co-immunoprecipitates with complexes containing the transcriptional corepressors CoREST and CtBP, histone deacetylases HDAC1 and HDAC2, and histone methyltransferases G9a and Eu-HMTase1. This strongly suggests that ZNF217 may function as part of a transcriptional repressor complex.

Implicated in

The findings that ZNF217 can immortalize human mammary epithelial cells, and that its amplification is associated with poor prognosis, suggest that it may play roles in both early and late stage breast cancer. ZNF217 can attenuate apoptotic signals resulting from telomere dysfunction as well as from doxorubicin-induced DNA damage, while silencing ZNF217 with siRNA restores sensitivity to doxorubicin. Moreover, elevated ZNF217 leads to increased phosphorylation of Akt, whereas inhibition of the phosphatidylinositol 3 kinase pathway and Akt phosphorylation decreases ZNF217 protein levels and increases sensitivity to doxorubicin. These results suggest that ZNF217 may promote neoplastic transformation by increasing cell survival during telomeric crisis, and may promote later stages of malignancy by increasing cell survival during chemotherapy.

References

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