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Gene Section
Mini Review

BRD4 (bromodomain containing 4)

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Identity

Hugo: BRD4
Other names: HUNK1; MCAP
Location: 19p13
Location_base_pair: position 15252262-15209302 on the chromosome 19 genomic sequence.

DNA/RNA

Description

The gene consists of 20 exons that span approximately 43 kb of genomic DNA in the centromere-to-telomere orientation. The translation initiation codon and stop codon are located to exon 2 and exon 20, respectively.

Transcription

Two isoforms of BRD4 have been reported. The 'BRD4 long isoform' corresponds to the ordinary full length transcript while the 'BRD4 short isoform' corresponds to an alternative splicing variant lacking exons 12-20. The 'BRD4 long variant' encodes a 6.0 kb transcript and the 'BRD4 short variant' encodes a 4.4 kb transcript.

Protein

Description

BRD4 belongs to the BET subgroup of the bromodomain superfamily and contains 2 bromodomains and a conserved ET-domain.
The open reading frame encodes a 1362 amino acid protein with a molecular weight of 200 kDa.

Expression

Northen blot analysis has shown an ubiquitous normal expression of both BRD4 isoforms.

Localisation

Nuclear.

Function

A striking feature of BRD4 is its association with euchromatic regions of mitotic chromosomes. By this association, the protein exerts its function as regulator of cell cycle progression from G2 to M but also in the G1 to S transition. It has also been suggested that the association of BRD4 to chromatin is important for the transmission of a transcriptional memory during cell division.

Implicated in

Carcinoma with t(15;19)(q14;p13) translocation.

Prognosis

Carcinoma with t(15;19) translocation is invariably fatal with a rapid clinical course when located to the midline thoracic, head and neck structures. One tumor, displaying the cytogenetic and molecular cytogenetic features of carcinoma with t(15;19) translocation, but located to the iliac bone, has been reported as successfully cured.

Cytogenetics

t(15;19)(q14;p13) [reported breakpoints: t(15;19)(q11-15;p13)].

Hybrid/Mutated Gene

The t(15;19)(q14;p13) results in a BRD4-NUT chimeric gene where exon 10 of BRD4 is fused to exon 2 of NUT.

Abnormal Protein

The BRD4-NUT fusion protein is composed of the N-terminal of BRD4 (amino acids 1-720 out of 1372) and almost the entire protein sequence of NUT (amino acids 6-1127). The N-terminal of BRD4 includes bromodomains 1 and 2 and other, less well characterized functional domains.

Oncogenesis

It has been suggested that the oncogenic effect of the NUT-BRD4 fusion is caused not only by the abnormal regulation of NUT by BRD4 promoter elements but also by the consequent ectopic expression of NUT in non-germinal tissues.

Breakpoints

Note: The vast majority of reported 19p breakpoints were assigned to band 19p13, the exception being the cytogenetic interpretation of a 19q13 breakpoint reported once. The reported breakpoints on chromosome 15 have varied (15q11-q15).

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