

Gene Section

Mini Review

BRWD3 (bromodomain and WD repeat domain containing 3)

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Identity

Hugo: BRWD3

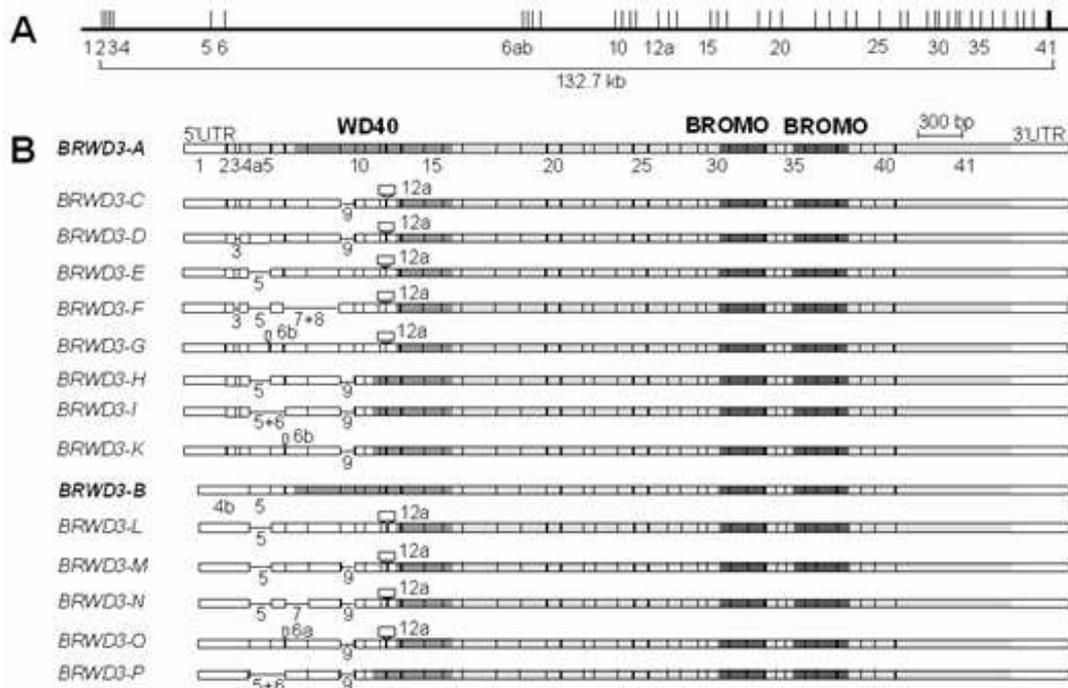
Other names: BRODL; FLJ38568

Location: Xq21.1

DNA/RNA

Description

44 exons spanning 132.7 kb genomic DNA.



Genomic organization (A) and transcript variants (B) of BRWD3. (A) Gene structure (drawn to scale): black boxes represent exons. (B) Transcripts (drawn to scale): boxes, exons; UTR, untranslated region; light shaded box, coding region; shaded and dark shaded boxes, nucleotide sequences coding for protein domains (WD40: WD40 tandem repeats; BROMO: bromodomain). For transcript variants BRWD3-C to BRWD3-P only the largest possible coding regions are indicated, though translation of different short proteins by using the start sites of BRWD3-A and BRWD3-B might also be possible.



Schematic representation of protein variants BRWD3-A and BRWD3-B as deduced from the transcripts. WD40: WD40 tandem repeats; BROMO: bromodomain. Translation initiation in exons 11 and 13 of transcripts BRWD3-C to BRWD3-P produces proteins, which retain four and three of the eight WD40 repeats, respectively.

Transcription

5.6-6.2 kb mRNA, coding sequence: 4.2-5.4 kb. Alternative splicing results in the expression of at least 15 transcript variants (BRWD3-A to BRWD3-P): The two most abundant transcript variants A and B are the result of alternative splicing of the first four exons (BRWD3-A contains exons 1 to 4, whereas BRWD3-B starts with an extended version of exon 4). BRWD3-C to BRWD3-P represent alternatively spliced variants of A and B, which contain additional exons 6a, 6b, and/or 12a and lack exons 3, 5, 6, 7, 8, and/or 9.

Pseudogene

None.

Protein

Description

The amino-terminal region consists of eight tandem WD40 repeats, which had been identified as the structural determinant of the beta-subunit of the G-proteins that mediating transmembrane signal transduction. The carboxy terminus is predicted to contain two bromodomains with the potential to mediate protein-protein interactions in DNA-binding proteins. BRWD3-C to BRWD3-P are amino-terminally truncated versions of BRWD3-A and BRWD3-B, which retain three or four of the eight WD40 repeats and both bromodomains.

Expression

Expressed in a variety of adult tissues (lymphocytes, brain, heart, kidney, placenta) and in fetal liver.

Function

By performing a systematic genomewide survey for genes required for JAK/STAT pathway activity (involved in cell proliferation and haematopoiesis), the *Drosophila* homologon of BRWD3 was isolated as a member of the JAK/STAT signalling cascade acting downstream of JAK. In vivo analysis demonstrated that disrupted *Drosophila* BRWD3 functions as a suppressor of leukemia-like blood cell tumors.

Homology

Drosophila melanogaster: BRWD3;
 Mouse: Brwd3;
 Pan troglodytes: BRWD3.

Implicated in

t(X;11)(q21;q23)

Note: In the tumour cells of one case of B-cell chronic lymphocytic leukemia (B-CLL), BRWD3 was affected by a translocation that rearranged the gene with ARHGAP20 (11q23). No fusion transcripts were generated. BRWD3 transcript expression is downregulated in B-CLL lymphocytes vs. CD19+ control B cells.

Disease

B-cell chronic lymphocytic leukemia.

Cytogenetics

t(X;11)(q21;q23).

Hybrid/Mutated Gene

ARHGAP20 - BRWD3.

Abnormal Protein

None detected.

References

Kalla C, Nentwich H, Schlotter M, Mertens D, Wildenberger K, Döhner H, Stilgenbauer S, Lichter P. Translocation *t*(X;11)(q13;q23) in B-cell chronic lymphocytic leukemia disrupts two novel genes. *Genes Chromosomes Cancer* 2005;42:128-143.

Müller P, Kutteneuler D, Gesellchen V, Zeidler MP, Boutros M. Identification of JAK/STAT signalling components by genome-wide RNA interference. *Nature* 2005;436:871-875.

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