

# Gene Section

## Mini Review

# ATF2 (activating transcription factor 2)

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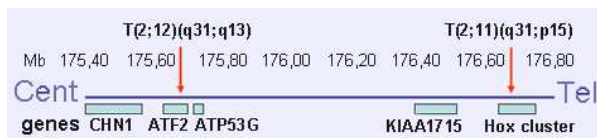
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## Identity

**Hugo:** ATF2

**Other names:** CREB1; CRE-BP1; CREB2; CREBP1; HB16; MGC111558; TREB7; Cyclic AMP-dependent transcription factor ATF-2; cAMP response element-binding protein CRE- BP1

**Location:** 2q31.1



## DNA/RNA

### Description

Gene size: 115.93Kb.



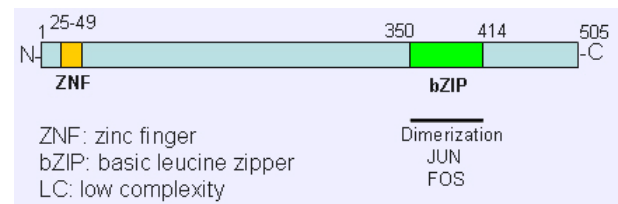
ATF2 gene structure based on data available in the Ensembl release 44. Upstream non-coding exons (green). Coding exons (pink), 3' untranslated sequence (red). The size of the exons in nucleotides is indicated below each exon. Exon number is indicated within the exon.

### Transcription

Initiation codon located in exon 4. Normal message is 2109 nucleotides. Some alternatively spliced RNA messages have been detected; but they are likely to represent splicing intermediates since no protein has been detected/expressed from these alternative messages in humans.

## Protein

**Note:** Protein of 505 aminoacids and a size of 52.27 kDa. Functions as a dimer, either homodimer or heterodimer with proteins of the jun family (e.g.: c-Jun, c-Fos).



### Localisation

Nuclear protein.

### Function

Transcription factor which binds to the cAMP-responsive element (CRE) (consensus: 5'-GTGACGT[AC][AG]-3'). ATF2 binds DNA as a dimer. The specificity of the DNA target sequence that is recognized by dimers containing ATF2 is different depending on whether it is a homodimer or it forms a heterodimer with another JUN protein.

## Mutations

**Note:** Lung cancer.

### Somatic

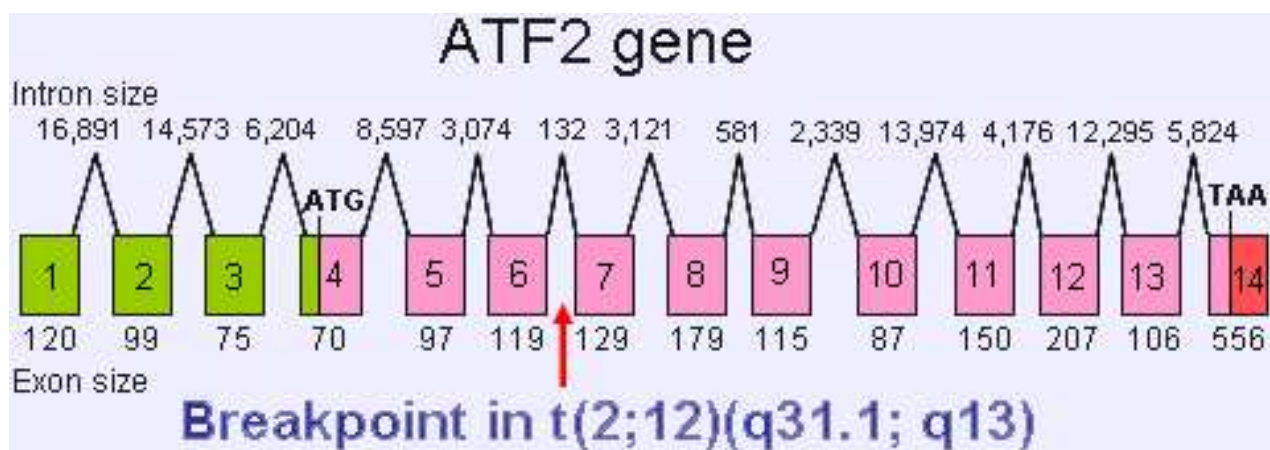
G to A transition in exon 10. Val258Ile Substitution.

## Implicated in

### Clear cell sarcoma

### Cytogenetics

t(2;12)(q31.1;q13)



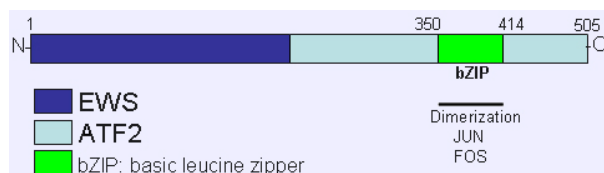
The arrow indicates the location of the breakpoint in chromosome 2. The ATF2 gene breaks within intron 6. In the translocation partner EWS the breakpoint occurs in intron 7. The transcript resulting from the hybrid gene fuses exon 7 of EWS to exon 7 of ATF2.

### Hybrid/Mutated Gene

EWS -ATF2 fusion transcript.

### Abnormal Protein

The EWS-ATF2 fusion protein retains the ATF2 C-terminal region that contains the bZIP dimerization domain. But the fusion protein has lost the N-terminal domain of ATF2 that is kinase inducible. The N-terminal region of EWS is retained in the fusion protein but has lost both its RNA binding domain and its Zinc-finger Ran binding domain.



Structure of the EWS-ATF2 fusion protein.

### Oncogenesis

EWS-ATF2 may define a novel subset of clear cell sarcoma that occurs preferentially in the gastrointestinal tract and presents little or no melanocytic differentiation.

## References

Livingstone C, Patel G, Jones N. ATF-2 contains a phosphorylation-dependent transcriptional activation domain. *Embo J* 1995;14:1785-1797.

Fuchs SY, Tappin I, Ronai Z. Stability of the ATF2 transcription factor is regulated by phosphorylation and dephosphorylation. *J Biol Chem* 2000;275:12560-12564.

Bhounik A, Ivanov V, Ronai Z. Activating transcription factor 2-derived peptides alter resistance of human tumor cell lines to ultraviolet irradiation and chemical treatment. *Clin Cancer Res* 2001;7:331-342.

Mayr BM, Canettieri G, Montminy MR. Distinct effects of cAMP and mitogenic signals on CREB-binding protein recruitment impart specificity to target gene activation via CREB. *Proc Natl Acad Sci USA* 2001;98:10936-10941.

van Dam H, Castellazzi M. Distinct roles of Jun: Fos and Jun: ATF dimers in oncogenesis. *Oncogene* 2001;20:2453-2464.

Woo IS, Kohno T, Inoue K, Ishii S, Yokota J. Infrequent mutations of the activating transcription factor-2 gene in human lung cancer, neuroblastoma and breast cancer. *Int J Oncol* 2002;20:527-531.

Przybylski GK, Dik WA, Wanzeck J, Grabarczyk P, Majunke S, Martin-Subero JI, Siebert R, Dölken G, Ludwig WD, Verhaaf B, van Dongen JJ, Schmidt CA, Langerak AW. Disruption of the BCL11B gene through inv(14)(q11.2q32.31) results in the expression of BCL11B-TRDC fusion transcripts and is associated with the absence of wild-type BCL11B transcripts in T-ALL. *Leukemia* 2005;19:201-208.

Antonescu CR, Nafa K, Segal NH, Dal Cin P, Ladanyi M. EWS-CREB1: a recurrent variant fusion in clear cell sarcoma--association with gastrointestinal location and absence of melanocytic differentiation. *Clin Cancer Res* 2006;12:5356-5362.

Liu H, Deng X, Shyu YJ, Li JJ, Taparowsky EJ, Hu CD. Mutual regulation of c-Jun and ATF2 by transcriptional activation and subcellular localization. *Embo J* 2006;25:1058-1069.

Ryan CM, Harries JC, Kindle KB, Collins HM, Heery DM. Functional interaction of CREB binding protein (CBP) with nuclear transport proteins and modulation by HDAC inhibitors. *Cell Cycle* 2006;5:2146-2152.

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