

## Gene Section

### Mini Review

# E2F6 (E2F transcription factor 6)

Matthew Oberley

McArdle Laboratory for Cancer Research, University of Wisconsin - Madison, 1400 University Ave.  
Madison, WI 53706, USA (MO)

Published in Atlas Database: March 2004

Online updated version: <http://AtlasGeneticsOncology.org/Genes/E2F6ID521.html>

DOI: 10.4267/2042/38063

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.  
© 2004 Atlas of Genetics and Cytogenetics in Oncology and Haematology

## Identity

**Other names:** E2F-6; E2F transcription factor 6;

E2 Binding Factor 6

**HGNC (Hugo):** E2F6

**Location:** 2p25.1

## DNA/RNA

### Description

In humans, E2F6 has 8 exons that span 20881 bp of genomic sequence. It has an ORF of 843 nt.

### Transcription

There have been 5 mRNA splice variants identified in humans.

Transcript variant 1 is the predominant transcript, and it encodes the longest mRNA isoform (a), which is 2342 bp.

Transcript variant 2 contains an additional segment (2413 bp mRNA), compared to variant 1, that causes a frameshift leading to an early stop codon. This transcript may function in a regulatory role with no protein translated. The predicted protein (isoform b) is much shorter than isoform a. Transcript variants 2 and 4 encode isoform b.

Transcript variant 3 lacks a segment (2287 bp mRNA), compared to variant 1, that causes a frameshift leading to an early stop codon. This transcript may function in a regulatory role with no protein translated. The predicted protein (isoform c) is much shorter than isoform a.

Transcript variant 4 contains two additional segments (2546 bp mRNA), compared to variant 1, that cause a frameshift leading to an early stop

codon. This transcript may function in a regulatory role with no protein translated. The predicted protein (isoform b) is much shorter than isoform a.

Transcript variant 5 contains an additional segment (2475 bp mRNA), compared to variant 1, that causes a frameshift leading to an early stop codon. This transcript may function in a regulatory role with no protein translated. The predicted protein (isoform d) is much shorter than isoform a.

### Pseudogene

There is an E2F6 pseudogene located on chromosome 22q11.2 (LOC376818) containing 2144 bp of the E2F6 gene with no introns.

## Protein

### Description

The predominately expressed isoform is 282 amino acids. The DNA binding domain is thought to be between aa 50 and 129. It has a DEF box between aa 95 to 195. The dimerization domain is thought to reside between aa 130 and 222. There is a leucine zipper domain between aa 143 and 164. The transcriptional repression domain is located on the C terminus from aa 173 to 281. The N-terminal 1-75 aa are missing in isoform B which is predicted to be 206 AA.

### Expression

Ubiquitous, though more highly expressed in the placenta, skeletal muscle, heart, ovary, kidney, small intestine and spleen.

### Localisation

Nuclear.

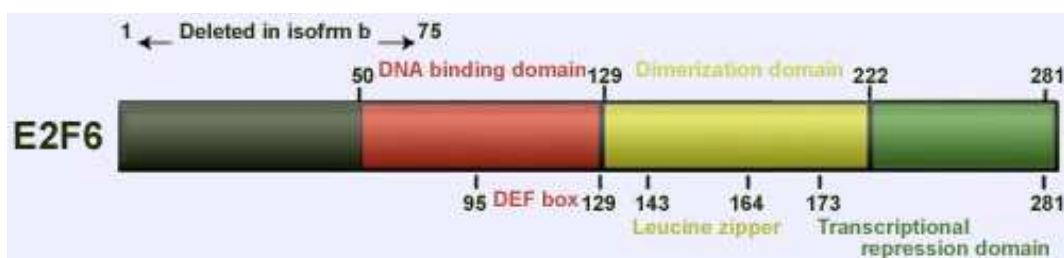


Diagram created by M. Oberley.

## Function

Heterodimerization with DP1 or 2 creates a sequence specific transcriptional repressor. Overexpression of E2F6 can delay the exit of cells from S-phase, indicating a role for E2F6 in cell-cycle control. E2F6 has been shown via yeast two hybrid and co-IPs to interact with members of the polycomb repressive complex 1, such as Bmi1, RYBP, RING1, MEL-18, and Mph1. The functional outcomes of these interactions are as of yet unclear. E2F6 has been biochemically purified in a complex containing polycomb group members h-1(3) mbt like protein, RING1, RING2, hMBLR, as well as YAF and HP1g; this complex also contained a novel euchromatic histone methyl-transferase (Eu-HMTase1). This finding led to speculation that E2F6 controlled cellular entry into quiescence, but E2F6 nullizygous MEFs had no kinetic changes or defects in their ability to enter quiescence, or to re-enter into the cell-cycle. However, these animals had homeotic transformations of the axial skeleton, a phenotype that resembled Bmi1 nullizygous mice. This implicated E2F6 in regulation of normal development.

## Homology

E2F6 has homology with E2Fs1-5 in the DNA-binding domain, the dimerization domain, and the marked box domain located between aa 231 and 239.

## Mutations

### Note

A synthetic mutation in aa 68; L->E: reduced E2F6 transcriptional repressor activity by abrogating DNA binding, but had little effect on S-phase entry.

## Implicated in

### Development

#### Note

E2F6 is required for normal homeotic development in murine models as mice nullizygous for E2F6 display transformations in the axial skeleton.

#### Disease

None known.

## References

- Morkel M, Wenkel J, Bannister AJ, Kouzarides T, Hagemeier C. An E2F-like repressor of transcription. *Nature*. 1997 Dec 11;390(6660):567-8
- Cartwright P, Müller H, Wagener C, Holm K, Helin K. E2F-6: a novel member of the E2F family is an inhibitor of E2F-dependent transcription. *Oncogene*. 1998 Aug 6;17(5):611-23
- Gaubatz S, Wood JG, Livingston DM. Unusual proliferation arrest and transcriptional control properties of a newly discovered E2F family member, E2F-6. *Proc Natl Acad Sci U S A*. 1998 Aug 4;95(16):9190-5
- Trimarchi JM, Fairchild B, Verona R, Moberg K, Andon N, Lees JA. E2F-6, a member of the E2F family that can behave as a transcriptional repressor. *Proc Natl Acad Sci U S A*. 1998 Mar 17;95(6):2850-5
- Kherrouche Z, Begue A, Stehelin D, Monté D. Molecular cloning and characterization of the mouse E2F6 gene. *Biochem Biophys Res Commun*. 2001 Oct 19;288(1):22-33
- Trimarchi JM, Fairchild B, Wen J, Lees JA. The E2F6 transcription factor is a component of the mammalian Bmi1-containing polycomb complex. *Proc Natl Acad Sci U S A*. 2001 Feb 13;98(4):1519-24
- Dahme T, Wood J, Livingston DM, Gaubatz S. Two different E2F6 proteins generated by alternative splicing and internal translation initiation. *Eur J Biochem*. 2002 Oct;269(20):5030-6
- Ogawa H, Ishiguro K, Gaubatz S, Livingston DM, Nakatani Y. A complex with chromatin modifiers that occupies E2F- and Myc-responsive genes in G0 cells. *Science*. 2002 May 10;296(5570):1132-6
- Storre J, Elsässer HP, Fuchs M, Ullmann D, Livingston DM, Gaubatz S. Homeotic transformations of the axial skeleton that accompany a targeted deletion of E2f6. *EMBO Rep*. 2002 Jul;3(7):695-700
- Trimarchi JM, Lees JA. Sibling rivalry in the E2F family. *Nat Rev Mol Cell Biol*. 2002 Jan;3(1):11-20
- Caretti G, Salsi V, Vecchi C, Imbriano C, Mantovani R. Dynamic recruitment of NF-Y and histone acetyltransferases on cell-cycle promoters. *J Biol Chem*. 2003 Aug 15;278(33):30435-40
- Oberley MJ, Inman DR, Farnham PJ. E2F6 negatively regulates BRCA1 in human cancer cells without methylation of histone H3 on lysine 9. *J Biol Chem*. 2003 Oct 24;278(43):42466-76

*This article should be referenced as such:*

Oberley M. E2F6 (E2F transcription factor 6). *Atlas Genet Cytogenet Oncol Haematol*. 2004; 8(2):67-68.