

## TBX2 (T-box 2)

### Identity

**Note** T-box proteins contain a T-domain that has roles in dimerization and DNA binding. TBX2 belongs to the Tbx2 subfamily of T-box transcription factors. Other subfamilies of T-box genes are Brachyury, T-brain1, Tbx1 and Tbx6. TBX2, TBX3, TBX4 and TBX5 belong to the Tbx2 subfamily. TBX2 and TBX3 are the only mammalian T-box factors with reported transcriptional repressor functions.

**Other names** **FLJ10169**

**Hugo** **TBX2**

**Location** 17q23

Genes flanking TBX2 in centromere to telomere direction on 17q23 are: APPBP2, 17q21-q23, amyloid beta precursor protein (cytoplasmic tail) binding protein 2

TBX2, 17q23, T-box2

PPM1D, 17q23, protein phosphatase 1D magnesium-dependent, delta isoform

LOC440450, 17q23.2 LOC440450

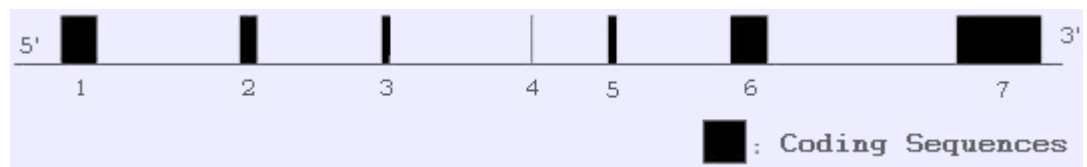
LOC388407, 17q23.2, hypothetical gene supported by BC046200

LOC388406, 17q23.2, hypothetical LOC388406

MGC71999, 17q23.2, alpha-NAC protein

### DNA/RNA

**Note** Genes of the same T-box subfamily are thought to have arisen from duplication and recombination of a single ancestor gene. TBX2 is most closely related to TBX3 (12q24), whereas the other members of the subfamily, TBX4 and TBX5, are more closely related to one another. It is postulated that genes of the same subfamily may have redundant expression patterns and thus potential functional redundancy.



The alignment of TBX2 mRNA (3396 bp) to its genomic sequence.

**Description** TBX2 gene spans 9,5kb. TBX2 gene has 7 exons and the sizes of the exons 1 to 7 are 676, 268, 147, 77, 164, 635, 1413 bps. Exon/intron boundaries of TBX2 and a polymorphism within intron 2 of the gene have

also been reported.

**Transcription** TBX2 mRNA is 3396 bp. TBX2 mRNA is expressed in a wide variety of tissues including fetal kidney and fetal lung as well as multiple adult tissues, kidney, lung, placenta, ovary, prostate, spleen, testis and breast. Relatively reduced expression of TBX2 can be detected in heart, white blood cells, small intestine and thymus. Transcript size heterogeneity has been detected for TBX2, possibly due to alternative polyadenylation. Increased TBX2 mRNA is observed within 2 hours after addition of retinoic acid in B16 mouse melanoma cells due to the presence of a degenerate retinoic acid response element (RARE) between -186 and -163 in the promoter region of the TBX2 gene.

**Transcript localisation:** Human and mouse TBX2, TBX3, and TBX5 transcripts detected by riboprobes are found asymmetrically across the embryonic neural retina, with highest levels of transcripts within dorsal and peripheral retina. The dorsoventral gradient of TBX2 expression cannot be detected before the ganglion cell layer (GCL) forms and expression is found to be restricted to the inner neuroblastic retina and later to the GCL and inner nuclear layer.

TBX2 transcript is also detected in the optic and otic vesicles at 9.5 dpc, and in the naso-facial mesenchyme, and later in the developing limbs and other internal organ primordia (of lungs and genitalia).

Later at around 8 and 10 dpc, TBX2 is detected in allantois, inflow tract (IFT), outflow tract (OFT) and atrio-ventricular canal (AVC) of the developing mouse heart. Chick heart development is also consistent in terms of similar TBX2 expression patterns.

During mammary development, TBX2 expression is detected at 11.5 dpc in the mesodermal milk lines.

**Pseudogene** No pseudogenes have been reported for TBX2.

## Protein

**Description** Protein consists of 702 amino acids and is 74.2 kDa. Protein has the T-box DNA binding domain (corresponds to amino acids 96-279) of the T-box family of transcriptional regulators.

**Function** In an evolutionarily diverse group of organisms including chick, *Xenopus*, mouse, and human, TBX2 is involved during development of widely diverse organs and tissues including limbs, kidneys, lungs, mammary glands, heart and craniofacial structures. In order to identify genes that may be regulated by Tbx2, mouse cDNA microarrays were used to analyze differential gene expression profiles, comparing stably transfected NIH3T3 cells overexpressing Tbx2 with vector-transfected controls. 107 genes were up-regulated (more than or equal to 2-fold) and 66 genes were down-regulated (more than or equal to 2-fold). Among the upregulated genes in the Tbx2-overexpressing cells were: Caveolin, Pleiotrophin, Osteoblast-specific factor-2 and Collagen Type I alpha. Cadherin 3, Tenascin C, and Insulin-like Growth Factor Binding Protein 10/CYR61 (IBP10) were among the genes that

are downregulated.

In vitro reporter assays and transgenic mice studies suggest that TBX2 represses the transcription of certain cardiac genes (e.g. Connexin 40, Connexin 43, and Natriuretic Peptide Precursor A) during heart development. TBX2 and TBX3 are also thought to be regulating one another in Hedgehog related signaling pathways during chick limb development.

In addition to developmental functions, evidence suggest that TBX2 also has important roles in cell cycle regulation through repressing the expression of [CDKN1A](#) (p21, cyclin-dependent kinase inhibitor) and [CDKN2A](#) (p19ARF). In BMI oncogene deficient murine embryonic fibroblasts, TBX2 is shown to repress the CDKN2A promoter and also attenuate the induction of CDKN2A by E2F1, [MYC](#), and [HRAS](#), providing senescence bypass and suggesting TBX2 as a potent immortalizing gene.

**Homology** C.familiaris: Tbx2, T-box 2 transcription factor  
M.musculus: Tbx2, T-box 2  
R.norvegicus: Tbx2\_predicted, T-box 2 (predicted)  
D.melanogaster: bi, bifid  
A.gambiae: 1280927, Anopheles gambiae str. PEST ENSANGG00000011542 gene.  
C.elegans: tbx-2, T-box family member (47.0 kD)

## Mutations

**Germinal** Despite the high frequency T-box family gene mutations identified as causes of congenital developmental disorders, there have been no mutations reported for TBX2 that cause congenital anomalies. Germline segregation of TBX2 mutations with human diseases has not been identified.

**Somatic** CGH (comparative genomic hybridization), Southern blot, FISH, PCR based techniques and microarray analyses suggest amplification and overexpression of TBX2 in certain cancer cells.

## Implicated in

**Entity** [Breast cancer](#)

**Note** TBX2 has been found to be amplified and overexpressed in breast cancer cell lines and primary tumors. TBX2 resides on the chromosomal band 17q23 that is frequently amplified in breast cancer cells. Evidence suggests presence of distinct proximal and distal amplicons on 17q23 with defined boundaries. TBX2 seems to be at the center of the distal amplicon. In addition to breast cancer cell line data, a study of tissue microarray of 372 primary tumors found TBX2 amplification in 8.6% of the cases. Moreover, preferential amplification and overexpression of TBX2 have been detected in BRCA1 and BRCA2 mutated breast tumors compared to sporadic controls.

**Entity** Pancreatic Cancer

**Note** TBX2 amplification has been detected in 50% of 20 pancreatic cancer cell lines detected by interphase FISH.

**Entity** Melanomas

**Note** TBX2 overexpression in melanoma cell lines is thought to target histone deacetylase 1 to the CDKN1A initiator. Expression of a dominant-negative Tbx2 leads to displacement of histone deacetylase 1 with up-regulation of CDKN1A expression, and the induction of replicative senescence in CDKN2A-null B16 melanoma cells. In human melanoma cells, expression of the same dominant negative TBX2 results with reduced growth and induction of senescence-associated heterochromatin foci.

**Note** Analysis of TBX2 in other tumor types has not been widely reported.

## External links

### Nomenclature

[Hugo](#) [TBX2](#)  
[GDB](#) [TBX2](#)  
[Entrez\\_Gene](#) [TBX2\\_6909](#) T-box 2

### Cards

[Atlas](#) [TBX2ID42485ch17q23](#)  
[GeneCards](#) [TBX2](#)  
[Ensembl](#) [TBX2](#)  
[CancerGene](#) [TBX2](#)  
[Genatlas](#) [TBX2](#)  
[GeneLynx](#) [TBX2](#)  
[eGenome](#) [TBX2](#)  
[euGene](#) [6909](#)

### Genomic and cartography

[GoldenPath](#) [TBX2 - 17q23](#) [chr17:56832039-56841607 + 17q23.2](#) (hg17-May\_2004)  
[Ensembl](#) [TBX2 - 17q23.2 \[CytoView\]](#)  
[NCBI](#) [Genes Cyto](#) [Gene Seq](#) [Map View - NCBI]  
[OMIM](#) [Disease map \[OMIM\]](#)  
[HomoloGene](#) [TBX2](#)

### Gene and transcription

[Genbank](#) [AK001031](#) [SRS] [AK001031](#) [ENTREZ]  
[Genbank](#) [AL832900](#) [SRS] [AL832900](#) [ENTREZ]  
[Genbank](#) [BC052566](#) [SRS] [BC052566](#) [ENTREZ]

<a href="#">Genbank</a>	<a href="#">BC070054</a> [SRS] <a href="#">BC070054</a> [ENTREZ]
<a href="#">Genbank</a>	<a href="#">BM985069</a> [SRS] <a href="#">BM985069</a> [ENTREZ]
<a href="#">RefSeq</a>	<a href="#">NM_005994</a> [SRS] <a href="#">NM_005994</a> [ENTREZ]
<a href="#">RefSeq</a>	<a href="#">NT_086883</a> [SRS] <a href="#">NT_086883</a> [ENTREZ]
<a href="#">AceView</a>	<a href="#">TBX2</a> AceView - NCBI
<a href="#">TRASER</a>	<a href="#">TBX2</a> Traser - Stanford
<a href="#">Unigene</a>	<a href="#">Hs.531085</a> [SRS] <a href="#">Hs.531085</a> [NCBI] <a href="#">HS531085</a> [spliceNest]
<b>Protein : pattern, domain, 3D structure</b>	
<a href="#">SwissProt</a>	<a href="#">Q13207</a> [SRS] <a href="#">Q13207</a> [EXPASY] <a href="#">Q13207</a> [INTERPRO]
<a href="#">Prosite</a>	<a href="#">PS01283 TBOX_1</a> [SRS] <a href="#">PS01283 TBOX_1</a> [Expasy]
<a href="#">Prosite</a>	<a href="#">PS01264 TBOX_2</a> [SRS] <a href="#">PS01264 TBOX_2</a> [Expasy]
<a href="#">Prosite</a>	<a href="#">PS50252 TBOX_3</a> [SRS] <a href="#">PS50252 TBOX_3</a> [Expasy]
<a href="#">Interpro</a>	<a href="#">IPR008967 P53_like_DNA_bnd</a> [SRS] <a href="#">IPR008967 P53_like_DNA_bnd</a> [EBI]
<a href="#">Interpro</a>	<a href="#">IPR002070 TF_Brachyury</a> [SRS] <a href="#">IPR002070 TF_Brachyury</a> [EBI]
<a href="#">Interpro</a>	<a href="#">IPR001699 TF_T-box</a> [SRS] <a href="#">IPR001699 TF_T-box</a> [EBI]
<a href="#">CluSTr</a>	<a href="#">Q13207</a>
<a href="#">Pfam</a>	<a href="#">PF00907 T-box</a> [SRS] <a href="#">PF00907 T-box</a> [Sanger] <a href="#">pfam00907</a> [NCBI-CDD]
<a href="#">Smart</a>	<a href="#">SM00425 TBOX</a> [EMBL]
<a href="#">Blocks</a>	<a href="#">Q13207</a>
<b>Polymorphism : SNP, mutations, diseases</b>	
<a href="#">OMIM</a>	<a href="#">600747</a> [map]
<a href="#">GENECLINICS</a>	<a href="#">600747</a>
<a href="#">SNP</a>	<a href="#">TBX2</a> [dbSNP-NCBI]
<a href="#">SNP</a>	<a href="#">NM_005994</a> [SNP-NCI]
<a href="#">SNP</a>	<a href="#">TBX2</a> [GeneSNPs - Utah] <a href="#">TBX2</a> [SNP - CSHL] <a href="#">TBX2</a> [HGBASE - SRS]
<b>General knowledge</b>	
<a href="#">Family Browser</a>	<a href="#">TBX2</a> [UCSC Family Browser]
<a href="#">SOURCE</a>	<a href="#">NM_005994</a>
<a href="#">SMD</a>	<a href="#">Hs.531085</a>
<a href="#">SAGE</a>	<a href="#">Hs.531085</a>
<a href="#">Amigo</a>	<a href="#">process development</a>
<a href="#">Amigo</a>	<a href="#">component nucleus</a>
<a href="#">Amigo</a>	<a href="#">process regulation of transcription, DNA-dependent</a>
<a href="#">Amigo</a>	<a href="#">function transcription factor activity</a>
<a href="#">BIOCARTA</a>	<a href="#">Tumor Suppressor Arf Inhibits Ribosomal Biogenesis</a>
<a href="#">PubGene</a>	<a href="#">TBX2</a>

## Other databases

### Probes

[Probe](#) [TBX2 Related clones \(RZPD - Berlin\)](#)

### PubMed

[PubMed](#) [8 Pubmed reference\(s\) in LocusLink](#)

## Bibliography

### **Cloning and mapping of a human gene (TBX2) sharing a highly conserved protein motif with the Drosophila omb gene.**

Campbell C, Goodrich K, Casey G, Beatty B.

Genomics 1995; 28: 255-260.

Medline [8530034](#)

### **Identification, characterization, and localization to chromosome 17q21-22 of the human TBX2 homolog, member of a conserved developmental gene family.**

Law DJ, Gebuhr T, Garvey N, Agulnik SI, Silver LM.

Mamm Genome 1995; 6: 793-797.

Medline [8597636](#)

### **Expression of the T-box family genes, Tbx1-Tbx5, during early mouse development.**

Chapman DL, Garvey N, Hancock S, Alexiou M, Agulnik SI, Gibson-Brown JJ, Cebra-Thomas J, Bollag RJ, Silver LM, Papaioannou VE.

Dev Dyn 1996; 206: 379-390.

Medline [8853987](#)

### **Evidence of a role for T-box genes in the evolution of limb morphogenesis and the specification of forelimb/hindlimb identity.**

Gibson-Brown JJ, Agulnik SI, Chapman DL, Alexiou M, Garvey N, Silver LM, Papaioannou VE.

Mech Dev 1996; 56: 93-101.

Medline [8798150](#)

### **Genomic structure of TBX2 indicates conservation with distantly related T-box genes.**

Campbell CE, Casey G, Goodrich K.

Mamm Genome 1998; 9: 70-73.

Medline [9434949](#)

### **Expression of T-box genes Tbx2-Tbx5 during chick organogenesis.**

Gibson-Brown JJ, Agulnik S, Silver LM, Papaioannou VE.

Mech Dev 1998; 74: 165-169.

Medline [9651516](#)

### **Multiple genes at 17q23 undergo amplification and overexpression in breast cancer.**

Barlund M, Monni O, Kononen J, Cornelison R, Torhorst J, Sauter G, Kallioniemi OLLI-P, Kallioniemi A.  
Cancer Res 2000; 60: 5340-5344.  
Medline [11034067](#)

**Expression of chick Tbx-2, Tbx-3, and Tbx-5 genes during early heart development: evidence for BMP2 induction of Tbx2.**

Yamada M, Revelli JP, Eichele G, Barron M, Schwartz RJ.  
Dev Biol 2000; 228: 95-105.  
Medline [11087629](#)

**Microarray analysis of Tbx2-directed gene expression: a possible role in osteogenesis.**

Chen J, Zhong Q, Wang J, Cameron RS, Borke JL, Isales CM, Bollag RJ.  
Mol Cell Endocrinol 2001; 25: 177: 43-54.  
Medline [11377819](#)

**Overexpressed genes/ESTs and characterization of distinct amplicons on 17q23 in breast cancer cells.**

Erson AE, Niell BL, DeMers SK, Rouillard JM, Hanash SM, Petty EM.  
Neoplasia 2001; 3: 521-526.  
Medline [11774034](#)

**Virtual genome scan: a tool for restriction landmark-based scanning of the human genome.**

Rouillard JM, Erson AE, Kuick R, Asakawa J, Wimmer K, Muleris M, Petty EM, Hanash S.  
Genome Res 2001; 11: 1453-1459  
Medline [11483587](#)

**Expression of Drosophila omb-related T-box genes in the developing human and mouse neural retina.**

Sowden JC, Holt JKL, Meins M, Smith HK, Bhattacharya SS.  
Invest Ophthal Vis Sci 2001; 42: 3095-3102.  
Medline [11726608](#)

**Cooperative action of Tbx2 and Nkx2.5 inhibits ANF expression in the atrioventricular canal: implications for cardiac chamber formation.**

Habets PE, Moorman AF, Clout DE, van Roon MA, Lingbeek M, van Lohuizen M, Campione M, Christoffels VM.  
Genes Dev 2002; 16: 1234-1246.  
Medline [12023302](#)

**Frequent amplification of 8q24, 11q, 17q, and 20q-specific genes in pancreatic cancer.**

Mahlamaki EH, Barlund M, Tanner M, Gorunova L, Hoglund M, Karhu R, Kallioniemi

A.

Genes Chromosomes Cancer 2002; 35: 353-358.

Medline [12378529](#)

**TBX2 is preferentially amplified in BRCA1- and BRCA2-related breast tumors.**

Sinclair CS, Adem C, Naderi A, Soderberg CL, Johnson M, Wu K, Wadum L, Couch VL, Sellers TA, Schaid D, Slezak J, Fredericksen Z, Ingle JN, Hartmann L, Jenkins RB, Couch FJ.

Cancer Res 2002; 62: 3587-3591.

Medline [12097257](#)

**The T-box family.**

Wilson V, Conlon FL

Genome Biol 2002; 3: REVIEWS3008.

Medline [12093383](#)

**Tension-induced reduction in connexin 43 expression in cranial sutures is linked to transcriptional regulation by TBX2.**

Borke JL, Yu JC, Isales CM, Wagle N, Do NN, Chen JR, Bollag RJ.

Ann Plast Surg 2003; 51: 499-504.

Medline [14595187](#)

**T-box genes in human disorders.**

Packham EA, Brook JD.

Hum Mol Genet 2003; 12 Spec No 1: R37-44. Review.

Medline [12668595](#)

**T-box binding protein type two (TBX2) is an immediate early gene target in retinoic-acid-treated B16 murine melanoma cells.**

Boskovic G, Niles RM.

Exp Cell Res 2004; 295: 281-289.

Medline [15093729](#)

**Tbx2 represses expression of Connexin43 in osteoblastic-like cells.**

Chen JR, Chatterjee B, Meyer R, Yu JC, Borke JL, Isales CM, Kirby ML, Lo CW, Bollag RJ.

Calcif Tissue Int 2004; 74: 561-573.

Medline [15354864](#)

**T-box transcription factor Tbx2 represses differentiation and formation of the cardiac chambers.**

Christoffels VM, Hoogaars WM, Tessari A, Clout DE, Moorman AF, Campione M.

Dev Dyn 2004; 229: 763-770.

Medline [15042700](#)

**Tbx2 directly represses the expression of the p21(WAF1) cyclin-dependent**

**kinase inhibitor.**

Prince S, Carreira S, Vance KW, Abrahams A, Goding CR.  
Cancer Res 2004; 64: 1669-1674.  
Medline [14996726](#)

**The role of Tbx2 and Tbx3 in mammary development and tumorigenesis.**

Rowley M, Grothey E, Couch FJ.  
J Mammary Gland Biol Neoplasia 2004; 9: 109-118.  
Medline [15300007](#)

**Tbx Genes Specify Posterior Digit Identity through Shh and BMP Signaling.**

Suzuki T, Takeuchi J, Koshiba-Takeuchi K, Ogura T.  
Dev Cell 2004; 6: 43-53. Erratum in: Dev Cell. 2005; 8: 971-972.  
Medline [14723846](#)

**T-box genes and heart development: putting the "T" in heart.**

Plageman TF Jr, Yutzey KE.  
Dev Dyn 2005; 232: 11-20.  
Medline [15580613](#)

**Murine T-box transcription factor Tbx20 acts as a repressor during heart development, and is essential for adult heart integrity, function and adaptation.**

Stennard FA, Costa MW, Lai D, Biben C, Furtado MB, Solloway MJ, McCulley DJ, Leimena C, Preis JI, Dunwoodie SL, Elliott DE, Prall OW, Black BL, Fatkin D, Harvey RP.  
Development 2005; 132: 2451-2462.  
Medline [15843414](#)

**Tbx2 is overexpressed and plays an important role in maintaining proliferation and suppression of senescence in melanomas.**

Vance KW, Carreira S, Brosch G, Goding CR.  
Cancer Res 2005; 65: 2260-2268.  
Medline [15781639](#)

[REVIEW articles](#)      *automatic search in PubMed*

[Last year publications](#)      *automatic search in PubMed*

[BiblioGene - INIST](#)

**Contributor(s)**

Written      07-2005      Ayse Elif Erson, Elizabeth M. Petty

**Citation**

*This paper should be referenced as such :*

**Erson AE, Pettv EM . TBX2 (T-box 2). Atlas Genet Cytogenet Oncol Haematol. Julv**

2005 .

URL :

<http://www.infobiogen.fr/services/chromcancer/Genes/TBX2ID42485ch17q23.html>

© *Atlas of Genetics and Cytogenetics in Oncology and Haematology*

---