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# Gene Section

## Review

## DLX2 (distal-less homeobox 2)

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### Abstract

DLX2 belongs to the six-member family of DLX genes characterized by a homeobox related to that found in the insect Distal-less (Dll) gene. It was the first human homologue to be discovered (Selski et al., 1993; McGuinness et al., 1996).

The six DLX genes are organized as three bigenic pairs with a tail-to-tail orientation (Zerucha et al., 2000) and located on chromosomes where HOX clusters are also found (DLX5/DLX6; 7q21.3, syntenic to the HOXA cluster), (DLX1/DLX2; 2q32 syntenic to the HOXD cluster; Simeone et al., 1994; Zerucha et al., 2000) and (DLX3/DLX4; 17q21.33 syntenic to the HOXB cluster).

During embryonic development DLX genes are involved in the control of appendage and craniofacial morphogenesis and in the differentiation of reproductive organs; in the adult they play a role in bone homeostasis and in the maintenance of tissue

integrity (Kraus and Lufkin, 2006).

### Identity

**Other names:** TES-1, TES1

**HGNC (Hugo):** DLX2

**Location:** 2q31.1

#### Local order

Reverse strand of human chromosome 2, from 172964167 to 172967628 - see Figure 1 below. DLX2 forms a bigenic cluster with DLX1 at 2q31.

### DNA/RNA

#### Note

DLX2 is in an inverted convergent orientation from DLX1, with both exons 3 separated by 10.7 kb where two enhancers have been identified and functionally characterized (Zerucha et al., 2000; Sumiyama et al., 2002; Ghanem et al., 2003; Park et al., 2004).

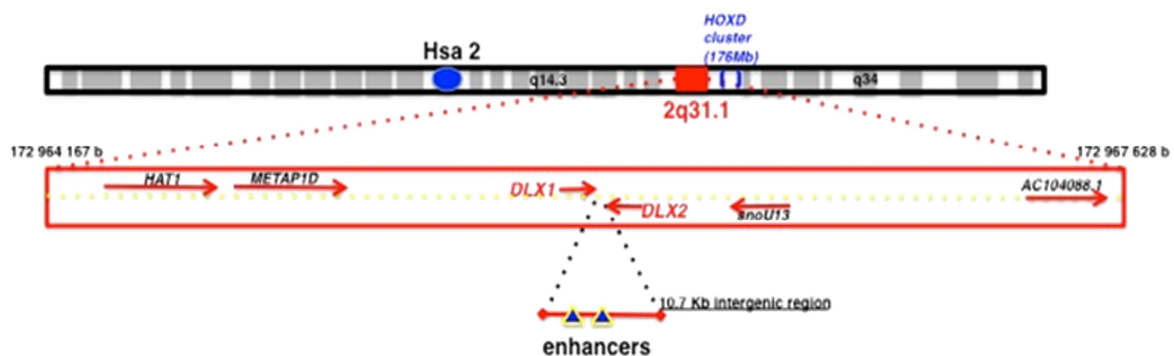


Figure 1. Genomic context of the human DLX1/DLX2 bigenic locus.

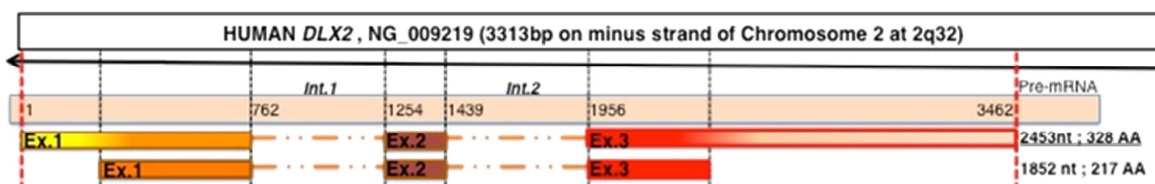


Figure 2. The two known human DLX2 transcripts.

While one regulatory element is enough and sufficient to drive proper and full expression of Dlx1/Dlx2 genes based upon mouse reporter assays, other, extragenic elements are involved in the dual regulation of Dlx1 and Dlx2.

The imprinting status of the DLX1/DLX2 locus has received much less attention than that of their DLX5/DLX6 paralogs (see their respective cards). However, an epigenetic mechanism linking Dlx2 function with neural stem cell maintenance has been demonstrated in adult mice (Lim et al., 2009). Chromatin immunoprecipitation assays differentiating subventricular zone neural stem cells has shown that the Dlx2 locus is a direct bivalent target of the histone methyltransferase Mll1 (mixed-lineage leukemia 1). Whether such methylation process has a clinical relevance remains to be determined, as altered methylation of DLX2 has been observed in pathogenic conditions, including in primary cells from brain astrocytomas, where hypermethylation of DLX2 CpG island has been observed (Wu et al., 2010).

### Transcription

Transcription from DLX2 yields two splice variants which share the first two exons, the homeodomain and the N-terminal DLL domain (see Figure 2). The major, mature isoform encodes a 328 AA long transcription factor (34.2 kDa and pI 9.25). Sense isoforms have not been reported for this gene.

## Protein

### Description

The major DLX2 isoform is a 328 AA helix-turn-helix homeodomain transcription factor (34.2 kDa and pI 9.5). The ultraconserved homeobox domain spans exons 1 and 2 at 153-211. A second N-terminal DNA binding domain, specific to the DLX2/3/5 clade within the distal-less family, is encoded by exon 1 at AA 51-132. Local composition biases include three poly-glycine and one poly-histidine stretches, and a phosphorylation target serine at 232 (see Figure 3 below).

### Expression

DLX2 is a predominantly nuclear transcription factor, from the helix-turn-helix group. It transactivates target gene expression in heterodimeric association with other DLX and MSX transcription factors. Its consensus binding site is TTA(G/A)TTGA. Chromatin immunoprecipitation assays have shown that during mouse forebrain development, Dlx2 (along with Dlx1) specifically binds an intergenic enhancer within the Dlx5/Dlx6 locus (see their respective cards), and transactivates their expression (Zerucha et al., 2000; Zhou et al., 2004). Interestingly, regulation of the Dlx5/Dlx6 locus in the developing retina occurs through transactivation by Dlx2 but not Dlx1.

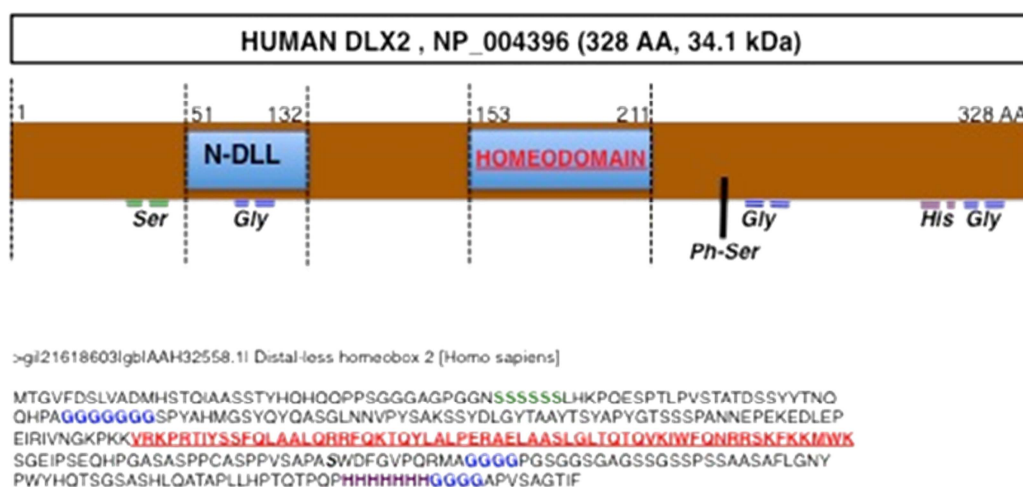


Figure 3. Structure of the major DLX2 protein isoform. Note the N- and C-terminal poly-glycine stretches, and the N-terminal DLL-like domain.

## NCBI/COBALT alignment of DLX homeoproteins; clades 1/4/6 and 2/3/5

DLX1.1	NP_835221	1	--mt.MTTMPESLNSPVSQKAVFMEFG	FPNQMSPPSMHSHGYSMHCLHSAGESQPDgAYSSAS--SFSRPLGY	69		
DLX6.3	NP_005213	1	mmt.MTTMADGLEQDSSKSAFMEFG(29)	PHSQSSSPA-MAGAHYPLHCLHSAAAAAagSHHHHh--QHHRHGS	98		
DLX1.2	NP_001033582	1	--mt.MTTMPESLNSPVSQKAVFMEFG	FPNQMSPPSMHSHGYSMHCLHSAGESQPDgAYSSAS--SFSRPLGY	69		
DLX4.a	NP_612138	1	---MTSLPCPLPGRDASKAVFDLA	-----PVPVAAAAYPLGLSPPTAASP--NLSYSR--PYGHLLSY	57		
DLX4.b	NP_001925	1	-----	-----	-----		
DLX5	NP_005212	1	---MTGVFDRRVPDIRSGDFQAPF--	----QTSAAHHPSQESPTLPESATDSD-YYs----pTGGAPRgy[13]	71		
DLX3	NP_005211	1	---MSGSFDRKLSILT-----	---DISSLSCHAGSKDPTLPESVTDLG-YYSAPO-----HDY[11]	61		
DLX2	NP_004396	1	---MTGVFDSLVDHSTQIAASST[14]	PGGNSSSSSLHkp-QESPTLPVSTATDSS-YTTNQQhpAGGGGG-[8]	88		
				N DLL			
DLX1.1	NP_835221	70	PYV---NSVS--SHASSFYISS-----VQSYF--GSASLAQSRLEDPGAD--[3]	STVVEGGEVRFNGKGRKIRKPR	132		
DLX6.3	NP_005213	99	PYASGCGNSYNhr5LAAYPYMHB5QHSPYLQSYH--NBSAAAQTRGDDTDQQRK	-TVIENGEIRFNGKGRKIRKPR	171		
DLX1.2	NP_001033582	70	PYV---NSVS--SHASSFYISS-----VQSYF--GSASLAQSRLEDPGQDLV[4]	IQVQEADEAGWGGSGG-----	129		
DLX4.a	NP_612138	58	PYTEPANPGDS-----YLSCQPAALSQP--lcGPAEHPQLEADSEKPRL	--SPEPSERRPQAPAKKLRKPR	121		
DLX4.b	NP_001925	1	-----M-----KLSVLPPRSLAPYTVlcCFF-----DSEKPRL	--SPEPSERRPQAPAKKLRKPR	49		
DLX5	NP_005212	72	PYQYQH-GVN--GSAGSYPAKAYADYSASSYH--QYGAYNRVPSATNQR	KEVTEPEVRMVGKPKKVRKPR	141		
DLX3	NP_005211	62	PYYTHHQNLN--GLAGTGAYSPKSEYTYGASYSR--QYGAYREQPLPAQDFVSV	KEEPEAEVRMVGKPKKVRKPR	133		
DLX2	NP_004396	89	SYOQAS-GLN--NVP--YSAKSYDLGYTAAYT--SYAPYGTSSSPANPE	KEDLEPEIRIVNGKPKKVRKPR	156		
			N DLL	N DLL	HOMEODOMAIN		
DLX1.1	NP_835221	133	TIYSSLQLQALNRRFQOTQYLALPERAEALASLGLTQTQVQKIMFONKRSKFKKLMKQGGAALEGSALANGRALSAGSPP-		211		
DLX6.3	NP_005213	172	TIYSSLQLQALNRRFQOTQYLALPERAEALASLGLTQTQVQKIMFONKRSKFKKLLKQGSNPHESDPLQGSAAALSFRSPA-		250		
DLX1.2	NP_001033582	1	-----	-----	-----		
DLX4.a	NP_612138	122	TIYSSLQLQHLNQRFOHTQYLALPERAQLAAQLGLTQTQVQKIMFONKRSKYKLLKQNSGGQGGDFPGRTFVSVSPCPP-		200		
DLX4.b	NP_001925	50	TIYSSLQLQHLNQRFOHTQYLALPERAQLAAQLGLTQTQVQKIMFONKRSKYKLLKQNSGGQGGDFPGRTFVSVSPCPP-		128		
DLX5	NP_005212	142	TIYSSFLAALQRRFQKTQYLALPERAEALASLGLTQTQVQKIMFONKRSKIKKIMKNGEMPPEHS-PSSSDPMACNSP--		218		
DLX3	NP_005211	134	TIYSSYQLAALQRRFQKAQYLALPERAEALAAQLGLTQTQVQKIMFONKRSKFKKLYKNGEVPLEHS-PNNSDSMACNSPP-		211		
DLX2	NP_004396	157	TIYSSFLAALQRRFQKTQYLALPERAEALASLGLTQTQVQKIMFONKRSKFKKQKSGEIPSEQH-PGASASPPCASPPV		235		
			Helix1	HOMEODOMAIN	Helix2	Helix3	Q50
DLX1.1	NP_835221	212	-VPPGWN	PNSSSGKSGGNAGSYIPSYTSMWYSAHQEA	MQQPQLM		255
DLX6.3	NP_005213	251	-LPPVWD[1]	--SASAKGVSMKPPNSYMPGYSHWYSSPHQDT	NQRPMKM		293
DLX1.2	NP_001033582	1	-----	-----	-----		-----
DLX4.a	NP_612138	201	-LPSLWD	L----PKAGTLPTSVCYCNFPGAMYQHSSDV	LASPQKM		240
DLX4.b	NP_001925	129	-LPSLWD	L----PKAGTLPTSVCYCNFPGAMYQHSSDV	LASPQKM		168
DLX5	NP_005212	219	qSPAVWE[11]	PHAHPPTSNQSPASSYLSNASWYTSAASSI[9]	LQHPLA-[7]		289
DLX3	NP_005211	212	-SPALWD[11]	SQLPPLPYSASPSYLDPTNSMYHAQNLG[8]	--QPATL[15]		287
DLX2	NP_004396	236	hAPASWD[17]	SGAGSSGSSPSSAASAFIGNYPMYHQTSGSA[8]	LLHPTQT[23]		328

**Figure 4. NCBI/COBALT alignment of DLX homeoproteins.** Note the disposition according to the DLX 1/4/6 versus DLX 2/3/5 clades. Indicated by a yellow box is the ultraconserved glutamine featured by most homeoproteins at position 50 of the homeodomain.

## Function

A particularity of Dlx2 is its ability to cooperate with a nuclear non-coding RNA (sense and single-stranded, 440 b), Evf-2, transcribed from the Dlx5/Dlx6 locus, to form a stable complex which binds and transactivates both Dlx5/6 intergenic enhancers (Feng et al., 2006).

While such an RNA/homeoprotein cooperativity has been demonstrated for other factors (Dubnau and Struhl, 1996), it has not been reported so far for other Dlx family members.

On the other hand, Dlx2 has been shown to autorepress its expression during mouse tooth formation when expressed alone, while autoactivating it when expressed in combination with PitX2 (Venugopalan et al., 2011).

This observation lends support to the notion that the transcriptional activity of DLX factors often depends upon cooperative binding with other homeoproteins, including from the PTX and MSX families (Zhang et al., 1997; Vieux-Rochas et al., 2013).

## Homology

With regards to other members of the DLX family, DLX2 belongs to the DLX2/3/5 clade based on sequence homology (see Figure 4). It shares an N-terminal DLL-like domain specific to this clade. The homeodomain sequence remains close to the other DLX proteins.

## Implicated in

### Breast tumors and their metastases to bone and lung tissues

#### Note

Neoplastic processes often result from combinatorial activity of developmental genes (Abate-Shen, 2002). Dysregulated expression of homeobox-containing genes of the distal-less family, arranged as three bigenic pairs in mammals (DLX1/2, DLX3/4 and DLX5/6; Kraus and Lufkin, 2006), has been reported to correlate with distinct oncogenic mechanisms.

DLX2 is expressed and necessary but insufficient to initiate metabolic stress-induced necrosis within several solid human high-grade tumors (Lee et al., 2011). DLX2 is strongly expressed in human primary breast tumors, its expression is associated with better prognosis and fewer relapses (Morini et al., 2010). In contrast, DLX2 expression is lost by breast tumor-derived metastatic cells found in lung or bone tissues - a poor prognosis marker (Morini et al., 2010). The combined downregulation of DLX2 and upregulation of DLX5 might thus prove a valuable prognostic marker.

DLX2 has been observed to be one of several homeogenes whose CpG islands were hypermethylated in luminal breast cancer cells, at 1 kb from the transcription start site (Kamalakaran et al., 2011). This status has been found to correlate significantly with higher expression level of DLX2, which lends support to the notion that DLX2 may serve as a candidate prognosis marker in breast cancer (Morini et al., 2010).

### **Solid tumors involving other organs**

#### **Note**

Induction of DLX2 expression has been further reported in other solid tumors, including promoting advanced gastric adenocarcinoma (Tang et al., 2013), promoting growth from lung, prostate and glioma tumors, and correlates with melanoma malignancy (Yilmaz et al., 2011; Yan et al., 2013). It appears that at least one member of each DLX bigenic pair (DLX2, DLX5 and DLX4 : see Hara et al., 2007) is closely implicated with solid tumorigenicity.

### **Acute lymphoblastic leukemia**

#### **Note**

Conversely, DLX2 expression is lost along with DLX3 and DLX4 in samples from patients afflicted by acute lymphoblastic leukemia with t(4;11)(q21;q23) chromosomal abnormality (Ferrari et al., 2003). In the same paper it is also shown that Dlx genes participate to the regulatory cascade initiated by acute lymphoblastic leukemia (ALL)-1, a recurring partner of translocations involving chromosome band 11q23 in human biphenotypic leukemias.

### **Autism spectrum disorder**

#### **Note**

Autism has been recognized as a condition which may result from an imbalance between inhibitory and excitatory processes in the developing and mature brain. Dlx1 and Dlx2 control the specification, fate and metabolic function of a subset of neurons known to exert an inhibitory role in the brain. As part of a cascade of homeobox-containing genes controlling neuronal specification in the brain, the DLX1/2 locus has thus been

examined for association with autism spectrum disorder. Extensive coverage of both coding and intergenic sequences among a large cohort of autistic probands has uncovered only a handful of non-synonymous variants - which nevertheless provides a strong set of functional candidates to assess whether disrupted DLX2 expression might play a role in autism (Hamilton et al., 2005). More recently, a large cohort study has pinpointed stronger candidate sites of polymorphism correlated with increased susceptibility to develop the neurologic condition (Liu et al., 2009) - however a direct functional impact remains to be evidenced. Interestingly, DLX2 was found to harbour trinucleotide repeats but as for its DLX6 paralog, family-based association analysis ruled out this polymorphism as a risk variant, in either autism or schizophrenia patients (Laroche et al., 2008).

### **Dysmorphogenesis**

#### **Note**

Although mouse embryos invalidated for Dlx1 and/or Dlx2 display craniofacial abnormalities, a direct involvement of DLX1/DLX2 mutation in human malformations remains to be demonstrated. For instance, while synpolydactyly has been tightly linked to DLX2 (Sarfarazi et al., 1995), it is the lack of induction of its promoter by defective PITX2 which has been demonstrated to directly cause Axenfeld-Rieger syndrome (ARS, OMIM #180500) - an autosomal dominant condition featuring a wide range of tooth anomalies, maxillary hypoplasia, and eye malformation (Espinoza et al., 2002).

## **References**

- Selski DJ, Thomas NE, Coleman PD, Rogers KE. The human brain homeogene, DLX-2: cDNA sequence and alignment with the murine homologue. *Gene*. 1993 Oct 15;132(2):301-3
- Simeone A, Acampora D, Pannese M, D'Esposito M, Stornaiuolo A, Gulisano M, Mallamaci A, Kastury K, Druck T, Huebner K. Cloning and characterization of two members of the vertebrate Dlx gene family. *Proc Natl Acad Sci U S A*. 1994 Mar 15;91(6):2250-4
- Sarfarazi M, Akarsu AN, Sayli BS. Localization of the syndactyly type II (synpolydactyly) locus to 2q31 region and identification of tight linkage to HOXD8 intragenic marker. *Hum Mol Genet*. 1995 Aug;4(8):1453-8
- Dubnau J, Struhl G. RNA recognition and translational regulation by a homeodomain protein. *Nature*. 1996 Feb 22;379(6567):694-9
- McGuinness T, Porteus MH, Smiga S, Bulfone A, Kingsley C, Qiu M, Liu JK, Long JE, Xu D, Rubenstein JL. Sequence, organization, and transcription of the Dlx-1 and Dlx-2 locus. *Genomics*. 1996 Aug 1;35(3):473-85
- Zhang H, Hu G, Wang H, Scivolino P, Iler N, Shen MM, Abate-Shen C. Heterodimerization of Msx and Dlx homeoproteins results in functional antagonism. *Mol Cell Biol*. 1997 May;17(5):2920-32

- Zerucha T, Stühmer T, Hatch G, Park BK, Long Q, Yu G, Gambarotta A, Schultz JR, Rubenstein JL, Ekker M. A highly conserved enhancer in the Dlx5/Dlx6 intergenic region is the site of cross-regulatory interactions between Dlx genes in the embryonic forebrain. *J Neurosci*. 2000 Jan 15;20(2):709-21
- Abate-Shen C. Deregulated homeobox gene expression in cancer: cause or consequence? *Nat Rev Cancer*. 2002 Oct;2(10):777-85
- Espinoza HM, Cox CJ, Semina EV, Amendt BA. A molecular basis for differential developmental anomalies in Axenfeld-Rieger syndrome. *Hum Mol Genet*. 2002 Apr 1;11(7):743-53
- Sumiyama K, Irvine SQ, Stock DW, Weiss KM, Kawasaki K, Shimizu N, Shashikant CS, Miller W, Ruddle FH. Genomic structure and functional control of the Dlx3-7 bigene cluster. *Proc Natl Acad Sci U S A*. 2002 Jan 22;99(2):780-5
- Ferrari N, Palmisano GL, Paleari L, Basso G, Mangioni M, Fidanza V, Albini A, Croce CM, Levi G, Brigati C. DLX genes as targets of ALL-1: DLX 2,3,4 down-regulation in t(4;11) acute lymphoblastic leukemias. *J Leukoc Biol*. 2003 Aug;74(2):302-5
- Ghanem N, Jarinova O, Amores A, Long Q, Hatch G, Park BK, Rubenstein JL, Ekker M. Regulatory roles of conserved intergenic domains in vertebrate Dlx bigene clusters. *Genome Res*. 2003 Apr;13(4):533-43
- Park BK, Sperber SM, Choudhury A, Ghanem N, Hatch GT, Sharpe PT, Thomas BL, Ekker M. Intergenic enhancers with distinct activities regulate Dlx gene expression in the mesenchyme of the branchial arches. *Dev Biol*. 2004 Apr 15;268(2):532-45
- Zhou QP, Le TN, Qiu X, Spencer V, de Melo J, Du G, Plews M, Fonseca M, Sun JM, Davie JR, Eisenstat DD. Identification of a direct Dlx homeodomain target in the developing mouse forebrain and retina by optimization of chromatin immunoprecipitation. *Nucleic Acids Res*. 2004;32(3):884-92
- Hamilton SP, Woo JM, Carlson EJ, Ghanem N, Ekker M, Rubenstein JL. Analysis of four DLX homeobox genes in autistic probands. *BMC Genet*. 2005 Nov 2;6:52
- Feng J, Bi C, Clark BS, Mady R, Shah P, Kohtz JD. The Evf-2 noncoding RNA is transcribed from the Dlx-5/6 ultraconserved region and functions as a Dlx-2 transcriptional coactivator. *Genes Dev*. 2006 Jun 1;20(11):1470-84
- Kraus P, Lufkin T. Dlx homeobox gene control of mammalian limb and craniofacial development. *Am J Med Genet A*. 2006 Jul 1;140(13):1366-74
- Hara F, Samuel S, Liu J, Rosen D, Langley RR, Naora H. A homeobox gene related to *Drosophila* distal-less promotes ovarian tumorigenicity by inducing expression of vascular endothelial growth factor and fibroblast growth factor-2. *Am J Pathol*. 2007 May;170(5):1594-606
- Laroche F, Ramoz N, Leroy S, Fortin C, Rousselot-Paillet B, Philippe A, Colleaux L, Bresson JL, Mogenet A, Golse B, Mouren-Simeoni MC, Gorwood P, Galli T, Simonneau M, Krebs MO, Robel L. Polymorphisms of coding trinucleotide repeats of homeogenes in neurodevelopmental psychiatric disorders. *Psychiatr Genet*. 2008 Dec;18(6):295-301
- Lim DA, Huang YC, Swigut T, Mirick AL, Garcia-Verdugo JM, Wysocka J, Ernst P, Alvarez-Buylla A. Chromatin remodelling factor Mll1 is essential for neurogenesis from postnatal neural stem cells. *Nature*. 2009 Mar 26;458(7237):529-33
- Liu X, Novosedlik N, Wang A, Hudson ML, Cohen IL, Chudley AE, Forster-Gibson CJ, Lewis SM, Holden JJ. The DLX1 and DLX2 genes and susceptibility to autism spectrum disorders. *Eur J Hum Genet*. 2009 Feb;17(2):228-35
- Morini M, Astigiano S, Gitton Y, Emionite L, Mirisola V, Levi G, Barbieri O. Mutually exclusive expression of DLX2 and DLX5/6 is associated with the metastatic potential of the human breast cancer cell line MDA-MB-231. *BMC Cancer*. 2010 Nov 25;10:649
- Wu X, Rauch TA, Zhong X, Bennett WP, Latif F, Krex D, Pfeifer GP. CpG island hypermethylation in human astrocytomas. *Cancer Res*. 2010 Apr 1;70(7):2718-27
- Kamalakaran S, Varadan V, Giercksky Russnes HE, Levy D, Kendall J, Janevski A, Riggs M, Banerjee N, Synnestvedt M, Schlichting E, Kåresen R, Shama Prasada K, Rotti H, Rao R, Rao L, Eric Tang MH, Satyamoorthy K, Lucito R, Wigler M, Dimitrova N, Naume B, Borresen-Dale AL, Hicks JB. DNA methylation patterns in luminal breast cancers differ from non-luminal subtypes and can identify relapse risk independent of other clinical variables. *Mol Oncol*. 2011 Feb;5(1):77-92
- Lee SY, Jeon HM, Kim CH, Ju MK, Bae HS, Park HG, Lim SC, Han SI, Kang HS. Homeobox gene Dlx-2 is implicated in metabolic stress-induced necrosis. *Mol Cancer*. 2011 Sep 14;10:113
- Venugopalan SR, Li X, Amen MA, Florez S, Gutierrez D, Cao H, Wang J, Amendt BA. Hierarchical interactions of homeodomain and forkhead transcription factors in regulating odontogenic gene expression. *J Biol Chem*. 2011 Jun 17;286(24):21372-83
- Yilmaz M, Maass D, Tiwari N, Waldmeier L, Schmidt P, Lehembre F, Christofori G. Transcription factor Dlx2 protects from TGFβ-induced cell-cycle arrest and apoptosis. *EMBO J*. 2011 Sep 6;30(21):4489-99
- Tang P, Huang H, Chang J, Zhao GF, Lu ML, Wang Y. Increased expression of DLX2 correlates with advanced stage of gastric adenocarcinoma. *World J Gastroenterol*. 2013 May 7;19(17):2697-703
- Vieux-Rochas M, Bouhali K, Mantero S, Garaffo G, Provero P, Astigiano S, Barbieri O, Caratozzolo MF, Tullo A, Guerrini L, Lallemand Y, Robert B, Levi G, Merlo GR. BMP-mediated functional cooperation between Dlx5/Dlx6 and Msx1/Msx2 during mammalian limb development. *PLoS One*. 2013;8(1):e51700
- Yan ZH, Bao ZS, Yan W, Liu YW, Zhang CB, Wang HJ, Feng Y, Wang YZ, Zhang W, You G, Zhang QG, Jiang T. Upregulation of DLX2 confers a poor prognosis in glioblastoma patients by inducing a proliferative phenotype. *Curr Mol Med*. 2013 Mar;13(3):438-45

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