

# Gene Section

## Short Communication

# CASZ1 (castor zinc finger 1)

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Published in Atlas Database: January 2013

Online updated version : <http://AtlasGeneticsOncology.org/Genes/CASZ1ID45989ch1p36.html>

DOI: 10.4267/2042/50193

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## Identity

**Other names:** CAS11, CST, SRG, ZNF693, dJ734G22.1

**HGNC (Hugo):** CASZ1

**Location:** 1p36.22

## DNA/RNA

### Description

DNA of CASZ1a contains 160072 bp composed of 21 exons with 11 zinc fingers, alternative splicing at exon 16 of CASZ1a can result in CASZ1b (16 exons with 5 zinc fingers) (Liu et al., 2006).

### Transcription

CASZ1 mRNA transcribed in centromeric to telomeric orientation. The CASZ1a cDNA sequence spans 7964 bp, with a 5' UTR of 346 bp, an open reading frame of 5280 bp, and a 3' UTR of

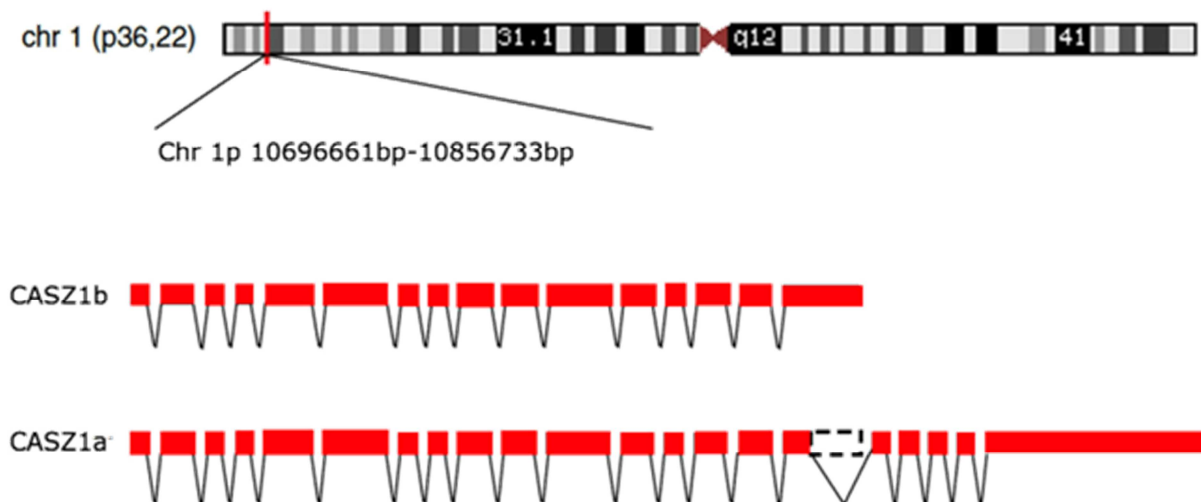
2339 bp; the CASZ1b cDNA sequence spans 4438 bp, with a 5' UTR of 346 bp, an open reading frame of 3501 bp, and a 3' UTR of 592 bp (Liu et al., 2006; with updated information from NCBI database).

## Protein

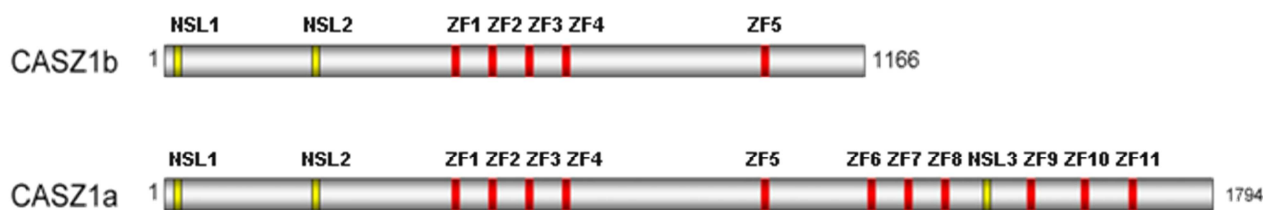
### Description

The 5' of CASZ1 contains 2 nuclear localization signals, which tag proteins for import into the cell nucleus, followed by 5 zinc fingers of C2H2 type (Cys<sub>2</sub>His<sub>2</sub>).

C2H2 zinc fingers are thought to have DNA binding and protein-protein mediation roles. For CASZ1a, six other zinc fingers (ZF) are present along with a third nuclear localization signal between ZF8 and ZF9. CASZ1b totals 1166 amino acids and CASZ1a totals 1794 amino acids (Liu et al., 2006; Virden et al., 2012).



Location of DNA of CASZ1 and two forms of the gene due to alternative splicing.



Functional domains of CASZ1.

## Expression

Increased expression when cells of neural and mesenchymal origin are induced to differentiation *in vitro*. CASZ1 is highly expressed in eye, heart, lung, skeletal muscle, pancreas, testis, small intestine and stomach (Liu et al., 2006; Liu et al., 2011a). CASZ1 is dynamically expressed in the development heart and during neurogenesis (Vacalla and Theil, 2002).

## Localisation

Nucleus, cytoplasm.

## Function

CASZ1 is a crucial zinc finger transcription factor that controls the differentiation of neural (Cui and Doe, 1992) and cardiac muscle cells (Christine and Conlon, 2008), eye development (Vacalla and Theil, 2002) and has tumor suppressor properties (Liu et al., 2011b). There is monoallelic loss of CASZ1 in neuroblastoma (NB) tumors through loss of heterozygosity (LOH) and epigenetic silencing (Wang et al., 2012). Restoration of CASZ1 in NB cells induces cell differentiation, inhibits cell migration and suppresses NB growth (Liu et al., 2011a; Liu et al., 2011b). Structural and functional studies show that either deletion of the N-terminus or mutation in any of the first four zinc fingers of CASZ1b results in a drastic loss in transcriptional activity, which also leads to a decreased tumor suppression activity (Viriden et al., 2012). Additionally, single nucleotide polymorphisms in this gene are associated with blood pressure variations in East Asian populations (Takeuchi et al., 2010).

## Homology

Unknown.

## Mutations

### Note

Unknown.

## Implicated in

### Neuroblastoma

#### Note

Neuroblastomas (NB) are pediatric cancers arising from cells of the sympathoadrenal lineage of neural crest cells (Brodeur, 2003; Maris, 2010). CASZ1 maps

to 1p36.22, part of the most commonly deleted regions of chromosome 1p that occur in 35% of NB cases (Brodeur, 2003).

A recent study in 184 primary NB showed that 1p36.3 is the shortest region of overlap for loss of heterozygosity (LOH) (White et al., 2005), although 98% of these 1p36.3 LOH NB tumors also have lost the region encompassing CASZ1 (Liu et al., 2011b). Additionally, CASZ1 is epigenetically silenced in NB by EZH2, a methyltransferase (Wang et al., 2012). HDAC inhibitor treatment of NB cells increases CASZ1 expression (Carén et al., 2007; Fransson et al., 2007).

Consistent with CASZ1 being epigenetically regulated, a bivalent mark was found in CASZ1 promoter region in ES cells (Bernstein et al., 2006). CASZ1 is upregulated when NB cells are induced to differentiate by retinoic acid, and restoration of CASZ1 in NB cells up-regulates differentiation genes such as NGFR and TrkA, and suppresses tumor growth (Liu et al., 2011a; Liu et al., 2011b). In NB patients, low CASZ1 expression in NB tumors is associated with poor prognosis and an undifferentiated histology, which suggests loss of CASZ1 may contribute to NB tumorigenesis.

### Cervical carcinoma

#### Note

Human papillomavirus (HPV) genome integration into host chromatin enables expression of oncogenes E6 and E7 leading to cervical carcinogenesis.

HPV integration may affect transcriptionally active sites. In one reported case of cervical cancer, HPV was found to functionally delete CASZ1 (Schmitz et al., 2012).

### Blood hypertension

#### Note

Hypertension, increases in blood pressure, can lead to cardiovascular disease including stroke and ischemic heart disease. CASZ1 has been found to be one of seven loci associated with hypertension in East Asian populations (Takeuchi et al., 2010). CASZ1 could be linked to heart malfunction through inflammatory responses.

CASZ1 had been found to have associations in European ancestry but Japanese loci effect size was significantly larger (Takeuchi et al., 2010).

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*This article should be referenced as such:*

Liu Z, Ding N, Thiele CJ. CASZ1 (castor zinc finger 1). *Atlas Genet Cytogenet Oncol Haematol*. 2013; 17(6):421-423.

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