

## Gene Section

### Mini Review

# SOX4 (SRY (sex determining region Y)-box 4)

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## Identity

**Other names:** EVI16

**HGNC (Hugo):** SOX4

**Location:** 6p22.3

## DNA/RNA

### Description

This intronless gene encompasses 4789 base pairs.

### Transcription

The mRNA transcript is 4789 base pairs.

## Protein

### Description

The mRNA encodes a 47.3 kDa protein consisting of 474 amino acids.

### Expression

SOX4 appears to be fairly ubiquitously expressed at low levels in most adult tissues, with high levels found mostly in T lymphocytes. Its expression is up-regulated in many cancer types relative to benign tissue of origin (Rhodes et al., 2004).

### Localisation

Nucleus.

### Function

SOX4 is a member of the class I SRY-related HMG-box family of transcription factors. It has been shown to be involved in determination of cell fate and the regulation of embryonic development of many organ systems including heart (Restivo et al., 2006; Schilham et al., 1996), pancreas

(Lioubinski et al., 2003; Wilson et al., 2005) and brain (Cheung et al., 2000; Hong and Saint-Jeannet, 2005). SOX4 has been shown to be a transcriptional activator in lymphocytes (van de Wetering et al., 1993) and facilitates B and T cell differentiation (Schilham et al., 1996; Schilham et al., 1997). SOX4 gene expression is up-regulated in many tumor types, with experimental evidence suggesting that this contributes to cellular transformation (Liu et al., 2006; Shin et al., 2004), control of apoptosis (Liu et al., 2006; Pramoongjago et al., 2006; Aaboe et al., 2006; Ahn et al., 2002) and/or a metastatic phenotype (Liao et al., 2008; Tavazzo et al., 2008).

### Homology

SOX4 is part of a family of Sox transcription factors that share significant homology. SOX4 is in the Group C Sox homology group that includes SOX11, SOX22 and SOX24. SOX4 shares the highest degree of homology with SOX11 (Bowles et al., 2000).

## Implicated in

### Adenoid cystic carcinoma (ACC)

#### Note

Gene expression profiling using micro arrays has shown SOX4 is one of the most up-regulated genes in ACC, relative to non-neoplastic tissue of origin (Frierson et al., 2002). Immunohistochemistry analysis confirms the up-regulation of SOX4 in primary ACC tumors compared to normal tissue (Pramoongjago et al., 2006).

#### Disease

ACC is the second most common malignant salivary gland tumor, representing 28% of malignant submandibular gland tumors.

## Bladder cancer

### Note

Whole genome expression profiling of 166 bladder tumors and 27 normal samples showed SOX4 up-regulated 5 fold in the tumors. When over-expressed in the bladder cell line HU609, SOX4 strongly impaired cell viability and promoted apoptosis (Aaboe et al., 2006).

### Prognosis

A correlation was found between strong SOX4 expression levels and increased patient survival.

## Breast cancer

### Note

MicroRNA miR335 has been shown to regulate Sox4 levels and is frequently found lost in primary tumors of breast cancer patients who relapse (Tavazoie et al., 2008). In experimental model systems, it appears that SOX4 is a primary gene product associated with metastasis and migration.

## Leukemia

### Note

SOX4 transcript is found in high levels in B-ALL and T-ALL, but not in AML, CML, CLL, Sezary syndrome, or T cell prolymphocytic leukemia (Mallampati et al., 2008). Retroviral tagging in mouse models suggests a functional role for SOX4 in hematologic malignancies (Shin et al., 2004; Suzuki et al., 2002; Lund et al., 2002).

## Lung cancer

### Note

SOX4 is upregulated in a significant percentage of lung cancers (Bangur et al., 2002; Friedman et al., 2004) and antibodies to this protein can be found in the serum of lung cancer patients (Friedman et al., 2004).

## Hepatocellular carcinoma

### Note

Experimental manipulation of SOX4 in hepatocellular carcinoma cell line models suggests that SOX4 is pro-apoptotic in this tumor type (Ahn et al., 2002). Paradoxically, another group found that knocking down SOX4 expression in a hepatocellular carcinoma cell line decreased tumorigenicity (Liao et al., 2008).

## Medulloblastoma

### Note

SOX4 is significantly overexpressed in medulloblastoma compared to normal cerebellum and ependymoma (de Bont et al., 2008; Yokota et al., 2004).

### Prognosis

A trend was found towards increased survival with increased levels of expression of SOX4.

## Prostate Cancer

### Note

SOX4 has been shown to be over-expressed in prostate tumor samples by microarray analysis, real-time PCR and immunohistochemistry. Additionally, stable transfection of Sox4 into non-transformed prostate cells form colonies in soft agar, suggesting SOX4 can be a transforming oncogene.

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