ZFX (zinc finger protein, X-linked)

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Identity

Other names: ZNF926
HGNC (Hugo): ZFX
Location: Xp22.11

DNA/RNA

Note
Differential splicing of a single ZFX transcript results in five variants. Variants 1, 2 and 3 result in isoform I, variant 4 results in isoform II and variant 5 results in isoform III.

Description
ZFX gene is a human X- chromosome gene that escapes X inactivation (Schneider-Gadicke et al.,1989a) and is composed of 10 exons, ranging in size from 57 to 6062 nt.
Exons 1 to 5 in isoform 2 and exons 1 to 6 in isoform 1 comprise the 5' UTR and encodes N-terminal acidic domain.
Exon 10 contains 3' UTR and AATAAA polyadenylation signal and encodes C-terminal zinc-finger domain for isoforms 1 and 2 (Schneider-Gadicke et al.,1989a).

Transcription
Transcription initiation sites were not exactly identified, but there is some ORF with the first ATG codon at nucleotide 1 in cDNAs (Schneider-Gadicke et al.,1989b).

Pseudogene
Pseudogenes were not exactly identified.

Protein

Description
The ZFX isoform I, the longest isoform, contains 805 amino acids (130 kDa). Isoforms II (91 kDa) and III contain 576 and 432 amino acids, respectively. Isoform II binds to the AGGCCCCCA and AGGCCCGGA sequences located at HLA-A11 promoter (LHaridon et al.,1996) and in accompanying with isoform I could play a role as co-activators in HIV-1 LTR induction (Nikpour et al., 2012). Isoforms I and II contain three domains: acidic domain (transcription activation region), nuclear localization signal (NLS) and 13 zinc finger domains, that differ in the length of their N-terminal (acidic) domain resulting in qualitatively and quantitatively different regulatory properties (Schneider-Gadicke et al.,1989b).

Expression
ZFX gene escapes X inactivation in humans (Schneider-Gadicke et al.,1989a) and is expressed in a wide range of human tissues (Schneider-Gadicke et al.,1989b).

Localisation
It was shown that ZFX isoform I is concentrated in the nucleus of glioma cell line, while ZFX isoform II is found in the cytoplasm (Zhu et al., 2013).
**Function**

ZFX gene is differentially expressed in tissues and may have separate functions in gonadal and somatic tissues (Lau and Chan, 1989). It may play a role as a sex determination factor in mammals (Zhu et al., 2013). ZFX acts as a transcriptional regulator in self renewal and differentiation mechanisms in human embryonic and hematopoietic stem cells (Galan-Caridad et al., 2007; Harel et al., 2012). ZFX has an important role in cell cycle progression and cell growth control (Jiang et al., 2012b).

**Homology**

In mammals, ZFX gene is highly conserved (Ashworth et al., 1990; Lau and Chan, 1989; Palmer et al., 1990). Zinc finger protein X linked is one of the members of ZFY family comprised of three members: ZFX, ZFY and ZFA (Palmer et al., 1990).

**Mutations**

A novel Xp22.11 deletion causing a syndrome of craniosynostosis and periventricular nodular heterotopias affecting all or part of three annotated genes, ZFX, PDK3, and PCY71B has recently been reported in a male subject (van Kogelenberg et al., 2011). Furthermore, Zfx mutation results in small animal size and reduced germ cell number in male and female mice (Luoh et al., 1997). Moreover, molecular cytogenetic analysis of a male infant with severe mental retardation and autism shows that there is a duplication in Xp in this subject (Rao et al., 1994).

**Implicated in**

**Glioma cell and cell lines**

In human glioma cell lines, knocking down of ZFX expression by lentivirus-mediated RNA interference (RNAi) shows that ZFX plays an important role in glioma cell proliferation, survival and growth potential in both subcutaneous and intracranial models in mice (Zhu et al., 2013). Furthermore, Zhou et al. detected ZFX expression in U251 cells using semi-quantitative PCR. They showed that expression of ZFX is significantly higher in glioma tissues compared to non glioma tissues using real-time RT-PCR. In the same vein, Knocking down of ZFX gene expression in U251 cells results in disturbed cell proliferation and increased apoptosis and arrested cells in S phase (Zhou et al., 2011).

**Gastric cancer tissues and cells**

ZFX expression was examined by quantitative real-time RT-PCR in 30 paired gastric tissue samples. Result shows that ZFX gene has differential expression in gastric tissues. There is a statistically significant association between the ZFX expression and different tumour types and grades (Nikpour et al., 2012). Furthermore, ZFX silencing inhibits gastric cancer cell growth in both in vitro and in vivo via modulating extracellular signal-regulated kinase/mitogen-activated protein kinase (ERK-MAPK) pathway (Wu et al., 2013).

**Non - small cell lung cancer (NSCLC)**

ZFX overexpresses in NSCLC and its expression is correlated with lymph node metastasis. Knocking down of ZFX gene by short hairpin RNA interference (shRNA) in NSCLC cell line reduces cell viability and colony formation and causes cell cycle arrest (Jiang et al., 2012b).

**Laryngeal squamous cell carcinoma (LSCC)**

ZFX expression up-regulates in LSCC tissues compared to the non-tumoral tissues. Knock-down of ZFX by shRNA results in suppression of proliferation and colony-forming potential of infected Hep-2 human LSCC cells and induces enhancing of cell apoptosis. Furthermore, high expression of ZFX associates with LSCC progression and its decreased expression associates with declined tumor cell growth (Fang et al., 2012).

**Osteosarcoma cells**

Inhibition of ZFX expression by siRNA results in decreased proliferation, colony formation and invasion of Saos-2 cells. Silencing of ZFX gene
expression causes cell cycle arrest in which greater portion of the cells existed in G1 phase and minor portion in S and G2/M phases (Jiang et al., 2013; Jiang et al., 2012a).

**Prostate cancer**

Prostate cancer tissues show higher expression of ZFX than that observed in normal adjacent tissues and BPH tissues. Furthermore, silencing the expression of ZFX in the prostate cancer cells effectively abolishes the cellular proliferation and colony-formation ability, and results in G1 phase cell cycle arrest. Moreover, inhibition of ZFX induces apoptosis by activating caspase-1, caspase-3 and caspase-9. (Jiang et al., 2012c).

**Childhood B lineage acute lymphoblastic leukemia**

ZFX protein expresses in human leukemia cell lines REH, HL-60, NB(4) and K562. Furthermore, ZFX mRNA expression in the newly-diagnosed ALL group while in the ALL complete remission group was significantly reduces. Moreover, ZFX mRNA level is significantly higher in Children with a poor prognosis than those with a good prognosis at diagnosis (Wang et al., 2013).

### References

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