Atlas of Genetics and Cytogenetics in Oncology and Haematology

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# Gene Section
## Short Communication

# CXXC5 (CXXC finger protein 5)

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## Abstract

Review on CXXC5, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

## Identity

**Other names:** CF5, RINF, WID

**HGNC (Hugo):** CXXC5

**Location:** 5q31.2

**Local order:** From centromere to telomere: SPATA24-DNAJC18-ECSCR-TMEM173-UBE2D2-**CXXC5**-PSD2-NRG2.

**Note:** Orientation on forward strand.

## DNA/RNA

### Description

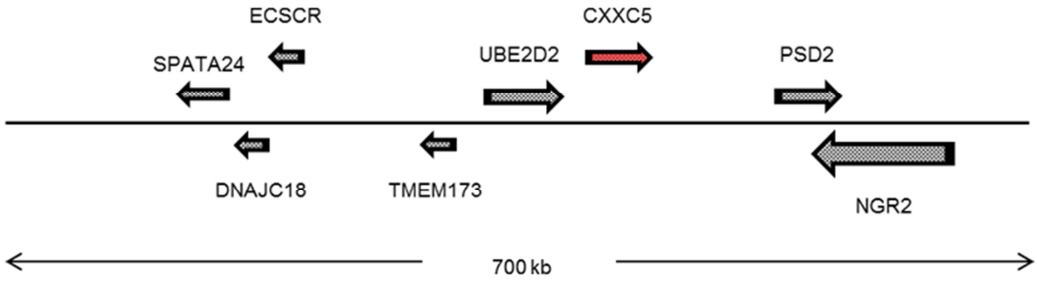
The gene is on the plus strand and encompasses 35 kb of DNA.
The exon number of gene is 3 and parts of the second and third exons encode the protein (ENSP00000302543).

### Transcription

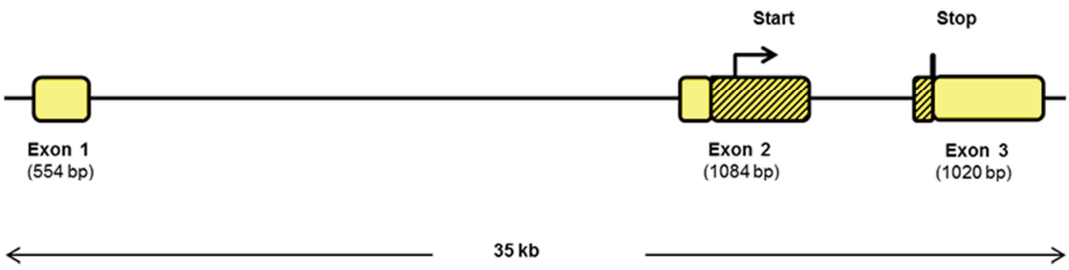
1447 bp long mRNA; 969 bp long open reading frame.

### Pseudogene

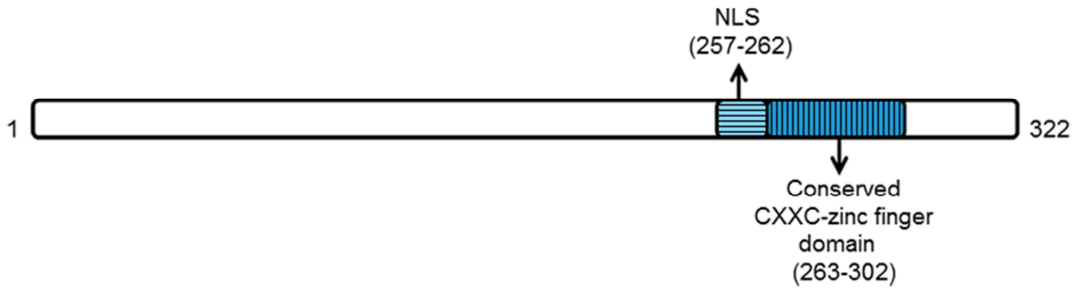
No reported pseudogenes.




Local order of CXXC5 is shown together with leading and subsequent genes on chromosome 5. The direction of arrows indicates transcriptional directions on the chromosome and arrow sizes approximate gene sizes.



Boxes are exons. The lines are introns. Shaded parts of the exon boxes are coding regions. Unshaded parts are noncoding regions.




CXXC5 contains a nuclear localization signal adjacent to the CXXC-zinc finger domain.

# Protein

## Description

CXXC5 encodes a 322 amino-acid protein with a molecular mass of 33 kDa. Amino-acid sequence suggests that CXXC5 contains a number of phosphorylation and acetylation sites.
By homology, CXXC5 is considered to be a member of CXXC-type zinc finger protein family, which binds to non-methylated CpG dinuclotide containing DNA.

## Expression

CXXC5 is expressed in various tissues.

## Localisation

CXXC5 protein is mainly in the nucleus. CXXC5 protein may also be localized in the cytoplasm coupled with Dishevelled (Dvl) protein (Andersson et al., 2009).

## Function

CXXC5 can be induced by retinoid signaling and is required for myelopoiesis (Pendino et al., 2009). CXXC5 protein is involved in the DNA-damage induced p53 activation as well as in the regulation of cell cycle and apoptosis (Zhang et al., 2009). CXXC5 protein participates in the TNF-a-induced apoptosis through association with SMAD (Wang et al., 2013).
CXXC5 protein is a critical modulator of BMP4-regulated Wnt-signaling in neural stem cells (Andersson et al., 2009).
CXXC5 protein is shown to repress TET2 gene expression (Ko et al., 2013).

## Homology

CXXC domain is a highly conserved domain of a class of proteins that interact with non-methylated CpG dinucleotides (CpGs). The CXXC domain of CXXC5 displays a significant homology to CXXC domains of CXXC4 and TET3 proteins (Ko et al., 2013).

# Mutations

**Note**

Not defined yet.

# Implicated in

## Acute myeloid leukemia (AML) and Myelodysplastic syndrome (MDS)

**Disease**

Acute myeloid leukemia (AML) is a disease manifested by cytogenetic anomalies affecting cell proliferation, death and differentiation (Renneville et al., 2008). Myelodysplastic syndrome (MDS) defines a hematological condition with insufficient hematopoiesis. MDS results from chromosomal deletions, inversions and translocations giving rise to trilineage dysplasia (Mhawech and Saleem, 2001).

**Oncogenesis**

The region on the chromosome 5 which also contains CXXC5 gene (5q31.2) is often deleted in AML and MDS (Treppendahl et al., 2013). Low survival rate has been observed in intensive chemotherapy treated patients with AML who show a high level of CXXC5 gene expression (Astori et al., 2013).

## Acute promyelocytic leukemia (APL)

**Disease**

APL, which is characterized by the translocation event of the retinoic acid receptor alpha gene, is a rare subtype of AML in which leukemia cells are sensitive to anthracyclines (Tallman and Altman, 2008).

**Oncogenesis**

Terminal maturation of premyelocytic leukemia cells requires the expression of CXXC5 (Pendino et al., 2009).

## Breast cancer

**Disease**

Breast cancer is a disease which is mainly originated in the lining of the milk ducts and/or the lobules.

**Oncogenesis**

It has been shown that CXXC5 is transcriptionally upregulated in some solid tumors including

melanoma, thyroid and breast cancer. In addition, overexpression of CXXC5 in breast cancer is suggested to be associated with poor prognosis (Knappskog et al., 2011).

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