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Gene Section
Mini Review

CBX7 (chromobox homolog 7)

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Identity

HGNC (Hugo): CBX7

Location: 22q13.1

Note
Orientation: minus strand. Size: 32508 bases.

DNA/RNA

Description

DNA size is 4081 bp with 6 exons. CBX7 is a highly conserved gene in chimpanzee, dog, cow, rat and mouse.

Transcription

mRNA size: 3964 bp.

Protein

Note

251 amino acids. Isoelectric point: 10,0228. Molecular weight of the protein: 28209 Da.

Description

CBX7 has a chromodomain region which is commonly found in proteins associated with the remodelling and manipulation of chromatin. In mammals, chromodomain-containing proteins are responsible for aspects of gene regulation related to chromatin remodelling and formation of heterochromatin regions. Chromodomain-containing proteins also bind methylated histones and appear in the RNA-induced transcriptional silencing complex. Specifically, CBX7 is involved in maintaining the transcriptionally repressive state of its target genes. The better characterized target of CBX7 is the INK4a/ARF locus, which is repressed by CBX7 in order to overcome the senescent phenotype in several mouse and human cell lines. Repression of other targets like E-cadherin has been also suggested.

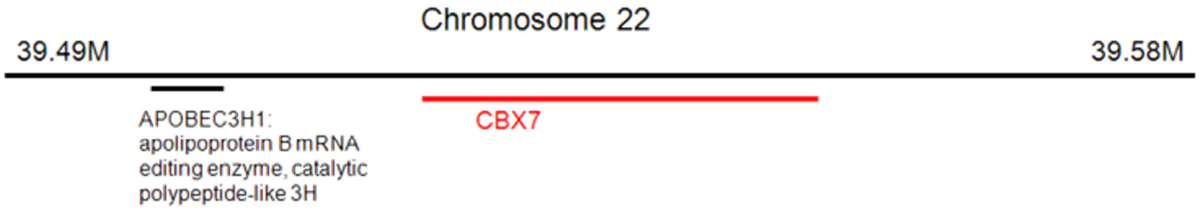

Figure 1. Location of Cbx7 within Chromosome 22.

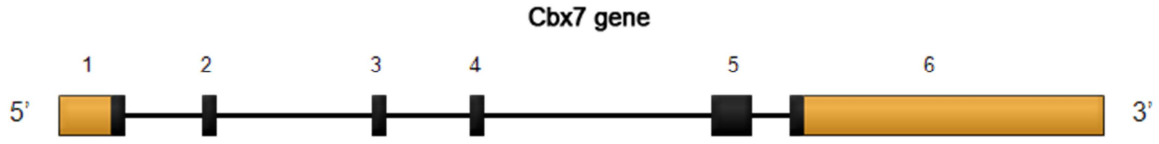

Figure 2. Diagram of Cbx7 transcript. Cbx7 has 6 exons. The black boxes indicate the consensus coding sequences (CCDS).

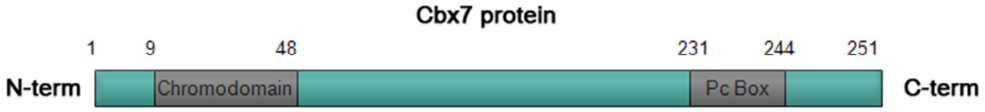

Figure 3. Structure of Cbx7 protein. Cbx7 has a chromodomain motif and a Polycomb (Pc) box which are indicated in grey.

Expression

CBX7 is expressed ubiquitously, but at higher levels in the nervous system, thyroid gland, prostate, fallopian tubes and bladder in normal tissue. CBX7 expression is also high in ES cells.

Localisation

In the nucleus.

Function

CBX7 is a member of the Polycomb group (PcG) genes, which are transcriptional repressors that play an essential role in development, cancer progression and stem cell maintenance. Mainly two different PcG complexes have been described: Polycomb Repressive Complex 1 (PRC1) and PRC2. PRC2 is the complex implicated in initiating the silencing of its target genes by methylating histone H3 on lysines 9 and 27. PRC1 is implicated in stabilizing this repressive state by recognizing the methylation marks through the Polycomb proteins and by ubiquitinating the histone H2A on Lys119. CBX7 belongs to the PRC1 complex and has been described to be a regulator of cellular lifespan by repressing the INK4a/ARF locus in several mouse and human cell lines. On the other hand, depletion of CBX7 from the cell induces a senescent phenotype by increasing the expression of the cell cycle regulators p16/ARF.

X chromosome inactivation

CBX7 has high affinity for binding H3K9me3 and H3K27me3. It associates with heterochromatin, binds RNA and it's enriched in the X chromosome, giving CBX7 a role in maintaining the repression of genes in the X chromosome.

Epigenetic regulation

CBX7, as part of the PRC1 complex, has a role in maintaining the repressive state of its target genes. CBX7 binds to the long non-coding RNA ANRIL in order to represses the INK4a/ARF locus and this interaction is essential for CBX7's function. Both CBX7 and ANRIL have been found to have high levels in prostate cancer tissues.

Stem cells self-renewal

CBX7 has been recently implicated to be essential for maintaining the pluripotency state of stem cells (ES cells). Overexpression of CBX7 in ESC impairs cell differentation. On the other hand, depletion of CBX7 from ESC induces spontaneous differentiation. Two different miR families (miR-125 and miR-181) were identified in a screening for CBX7 regulators and have been described to have a role in ESC differentiation by targeting the 3'UTR of CBX7.

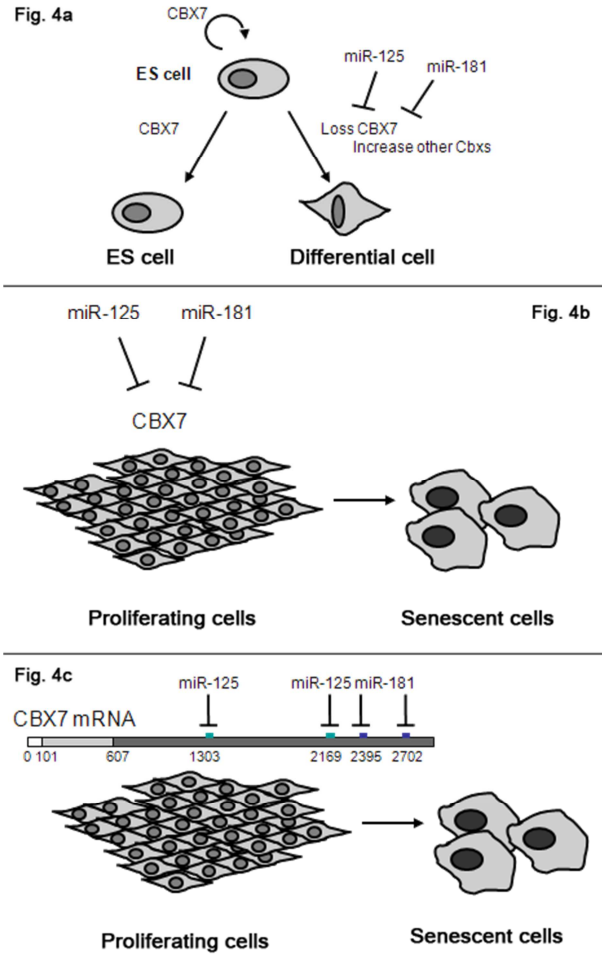

Figure 4. 4a: Summary of Cbx7's mechanism in embryonic stem cells (ESC). Cbx7 is essential for ESC self-renewal. Loss of Cbx7, either by differentiating ESC or by an exogenous/endogenous induction of the microRNA (miR) families miR-125 and miR-181, induces ESC differentiation. This is accompanied by an increase in other Cbxs as they are targets of Cbx7. On the other hand, overexpression of Cbx7 in ESC reinforces pluripotency and keeps the cells in an ESC-like state when forced to differentiate. **4b and 4c: Summary of Cbx7's mechanism in human primary fibroblasts (IMR-90).** Ectopic expression of the miR families miR-125 and miR-181 induces a degradation of Cbx7 mRNA in IMR-90. Depletion of Cbx7 induces the cells to senesce. Thus, overexpression of miR-125 and miR-181 induces senescence through downregulation of Cbx7.

Mutations

Note

Expression of CBX7 without the Pc box or with point mutations in the chromodomain region (F11A, K31A, W32A, W35A) does not extend the life span of human

or mouse cells. The mutant R17Q, which affects the binding of CBX7 to RNA,
extended the lifespan of cells, but to a lesser extent than CBX7 wt. Point mutations in the Pc box as F234D or F244D result in loss or reduced interaction of CBX7 with RNF2.

Implicated in

Various cancers

Disease

CBX7 has been implicated in several tumors such as gastric cancer, follicular lymphoma, breast cancer, colon carcinoma, pancreatic cancer, tyroid cancer, glioma.

Prognosis

There is a controversy in the role of CBX7 in cancer, as some papers associate CBX7 overexpression with poor prognosis and advanced estate of the tumor and aggressiveness, while others state that depletion of CBX7 from certain cancers indicates the state of malignancy of the tumor. The ability of CBX7 to regulate multiple targets and the relevance of those targets in different tumor types and stages probably explain those paradoxical findings.

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