

## Gene Section

### Mini Review

# CLIC4 (chloride intracellular channel 4)

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### Identity

**Other names:** MTCLIC; P64H1; CLIC4L; H1; huH1

**HGNC (Hugo):** CLIC4

**Location:** 1p36.11

### DNA/RNA

#### Description

CLIC4 gene comprises of 6 exons spanning a region of about 99 kb on human chromosome 1p36.

#### Transcription

CLIC4 gene codes for a protein of 253 amino acids length corresponding to molecular weight of about 29 kDa. No alternative isoforms of CLIC4 has been reported.

### Protein

#### Description

CLIC4 is a putative chloride channel for intracellular organelles. The human protein consists of 253 amino acids with an N-terminal transmembrane domain and C-terminal nuclear localisation signal.

#### Expression

Ubiquitous and induced by p53, TNF-alpha and c-myc.

#### Localisation

It is localised in cytoplasm and mitochondria in primary keratinocytes and translocated to nucleus upon cellular stress.

#### Function

CLIC4 has been shown to regulate TGF-beta signaling. It has been shown to translocate to the nucleus in a Schnurri-2 dependent manner and nuclear CLIC4 has been shown to subsequently stabilise phospho- Smad2 and Smad3.

CLIC4 has been implicated in angiogenesis. It has been shown to be involved in acidification of vacuoles along the cell hollowing tubulogenic pathway.

CLIC4 has been shown to be expressed in myofibroblasts and inhibit motility of MEF/3T3 cells.

CLIC4 has been implicated in Myc-induced apoptosis. It was identified as a candidate gene after protein expression analysis during Myc-induced apoptosis. Myc has been shown to bind to CLIC4 promotor and activate its transcription.



CLIC4 gene consists of 6 exons. The number between the exons indicate the length in kilo bases of intervening introns.



Domain organisation of CLIC4. TM indicates transmembrane domain and NLS represents nuclear localisation signal.

## Homology

CLIC1, CLIC2, CLIC3, CLIC5 and CLIC6.

## Implicated in

### Various cancer

#### Note

Expression analysis on a human tumour array has shown that CLIC4 expression is diminished in several tumour types including breast, ovary and kidney. CLIC4 expression has also been shown to be upregulated in some tumours.

In matched tissue arrays, CLIC4 was predominantly nuclear in normal epithelial tissues but not cancers. As tumours progressed CLIC4 expression became undetectable in tumour cells but increased in stromal cells.

Sequence analysis of CLIC4 cDNA of 60 human cancer cell lines (NCI60) and EST database analysis failed to reveal mutations in CLIC4 gene.

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