**Atlas of Genetics and Cytogenetics in Oncology and Haematology**

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# Gene Section

## Review

# MAZ (MYC Associated Zinc Finger Protein)

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## Abstract

Myc-associated zinc finger protein (MAZ), also known as serum amyloid A-activating factor 1 (SAF1), Pur-1 or Zif87, is ubiquitously expressed in various tissues. MAZ is a transcription factor with six Cys2His2-type zinc finger motifs at the carboxyl-terminus that interact with a permutation of the GGGAGGG sequence motif present in GC-rich promoter regions of target genes, likely through DNA unfolding of G-quadruplex structures to modulate gene expressions. MAZ is also suggested to participate in transcription termination and polyadenylation. Deregulated expression of MAZ is reported to correlate with various tissue malignancies that include the breast, thyroid, hepatocellular and urothelial cancers.

**Keywords**

MAZ; transcription factor; Zinc finger; DNA binding; Purine binding; breast cancer; thyroid cancer; hepatocellular cancer; urothelial cancer.

## Identity

**Other names**

PUR1 (Purine-Binding Transcription Factor), SAF-1 (Serum Amyloid A Activating Factor 1), SAF-2 (Serum Amyloid A Activating Factor 2), SAF-3 (Serum Amyloid A Activating Factor 3), ZF87 (Transcription Factor Zif87), ZNF801 (Zinc Finger Protein 801)

**HGNC (Hugo)**

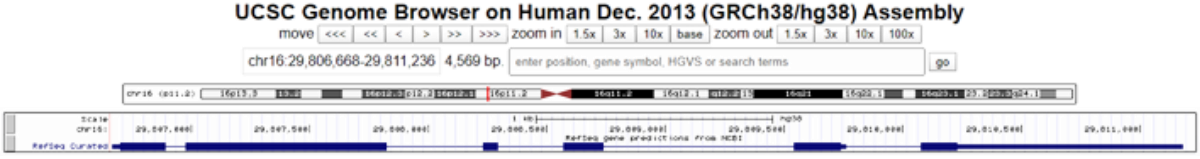
MAZ

**Location**

16p11.2

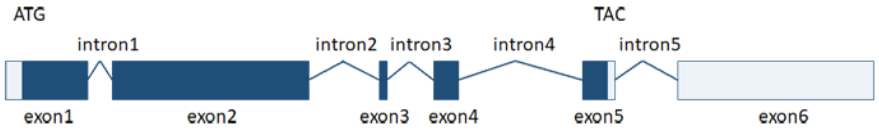
**Location (base pair)**

chr16:29,817,858-29,822,504; 4,647 bp.




UCSC representation of the gene on chromosome 16. RefSeq sequence shows introns as lines, exons as boxes and encoding exons as thicker boxes. Retrieved from: http://genome.ucsc.edu on November 6, 2017.

## DNA/RNA




The human MAZ consists of six exons, the first five of which are encoding exons; total exon length is 4.57 kb (Song et al., 1998).

## Description

The human MAZ contains six exons; the encoding sequence consists of 1431 bases (Song et al., 1998).

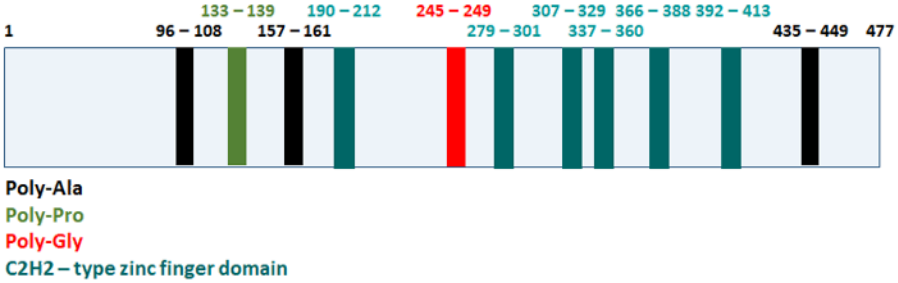
## Transcription

The human gene encoding for MAZ is located on chromosome 16p11.2 and is transcribed as an mRNA of 2.7 kilobases (kb). The primary transcript encodes a 477 amino-acid long MAZ-1 protein with a 60-kDa molecular mass that contains six C2H2-type zinc-finger domains responsible for DNA binding. MAZ protein has two additional isoforms: MAZ-2 and MAZ-3. The MAZ-2 transcript is generated by an alternative splicing that results in the insertion of a new exon originating from the non-coding sequences of the intron 4. This transcript gives rise to the MAZ-2 isoform, which is a 493 amino-acids long protein with distinct carboxyl-terminus which contains two additional zinc-finger domains (Ray et al., 2002). The MAZ-2 isoform is reported to have a higher DNA-binding activity and to act as a negative regulator of MAZ-1 function (Ray et al., 2002). The MAZ-3 transcript is expressed at very low levels under normal physiological condition in various tissues, but is highly expressed during inflammation. The MAZ-3 transcript is transcribed from a distinct upstream promoter and is processed with alternative splicing. The MAZ-3 transcript is translated from a different starting codon that gives rise to the MAZ-3 isoform of 455 amino-acids (Ray et al., 2009).

## Pseudogene

No reported pseudogenes are found.

# Protein

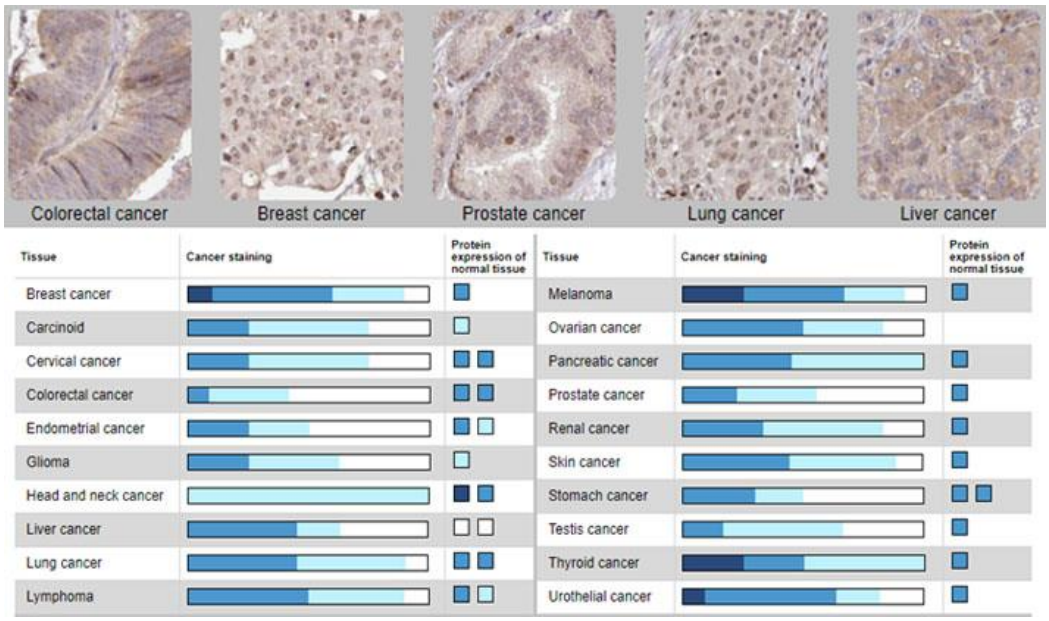



Domains of MAZ are depicted with vertical colored lines; Blacks are Poly-Alanine repeats; Green is Poly-Proline tract; Red column is Poly-Glycine repeat. C2H2-type zinc finger domains of MAZ-1 are represented in dark blue-green vertical lines

.

## Description

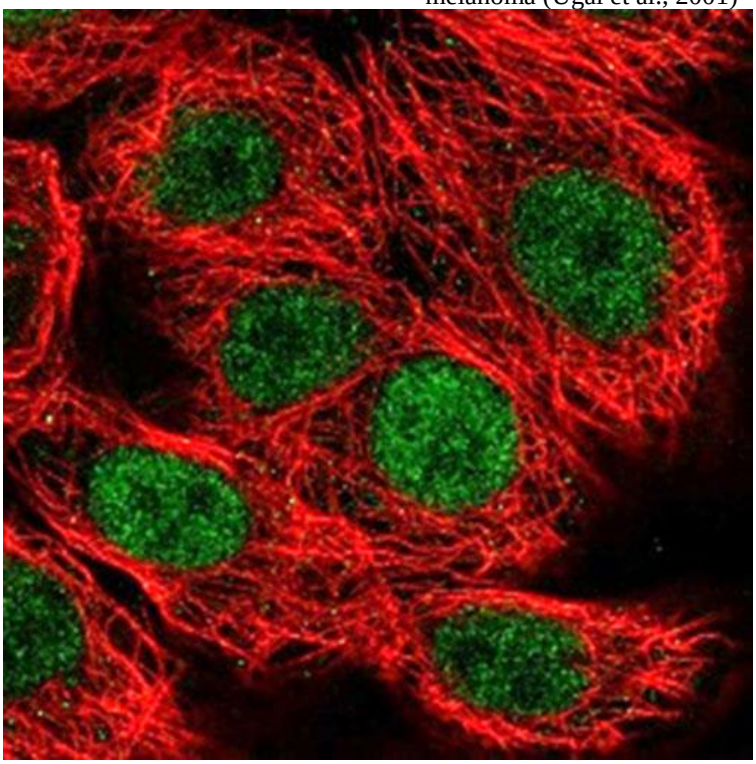
The human MAZ protein contains three Poly alanine, one poly-proline and one poly-glycine domains (Song et al., 1998). Poly-alanine repeats considered to have role in cellular localization of the protein; the alteration in the intracellular distribution may contribute to diseases, including muscular dystrophy (OPMD) (Oma et al., 2004). Similarly, poly-glycine repeats are responsible in protein targeting (Uthayakumar et al., 2012). Poly-proline tracks, on the other hand, generates structures that are predicted to have important roles in protein-protein interactions (Williamson, 1994). The human MAZ-1 contains six C2H2-type zinc finger domains (Song et al., 1998), which are frequently occurring in proteins involved in transcriptional regulation.




Expression and synthesis of MAZ in various cancerous tissues. Retrieved from: http://www.proteinatlas.org/ENSG00000103495-MAZ/cancer on November 2, 2017.

## *Expression*

MAZ is expressed in the human heart, brain, lungs, liver, skeletal muscle, pancreas, and prostate (Jiao et al., 2013; Dudas et al., 2008). The synthesis of MAZ protein is observed to occur at high levels in breast, thyroid and urothelial cancers as well as in melanoma (Ugai et al., 2001)



Immunofluorescent staining of human cell line MCF7. Retrieved from: http://www.proteinatlas.org/ENSG00000103495-MAZ/cell on November 2, 2017. Immunofluorescent staining of MCF7 cells derived from breast adenocarcinoma shows that MAZ localizes to the nucleus.

## *Localisation*

MAZ is located in the nucleus (Jordan-Sciutto et al, 2000).

## *Function*

MAZ as a transcription factor interacts with a permutation of the GGGAGGG sequence motif

present in GC-rich promoter regions of target genes by unfolding of G-quadruplex structures of DNA (Cogoi et al., 2014) to activate or repress transcription. MAZ is also suggested to participate in transcription termination and polyadenylation. Several oncogenes, including MYC, HRAS, PPARG, TSG101, VEGFA, CAV1, PTHR1, NOS3, MYB, and hTER, are transcriptionally regulated by MAZ (Jun Song et al., 2001; Lee et al., 2016; Ray et al., 2002). Deregulated expression of MAZ appears to participate in the development and/or progress various tissue malignancies including the breast, thyroid, hepatocellular and urothelial cancers (Jiao et al., 2013; Dudas et al., 2008; Yu et al., 2017; Ray, 2011; Zhu et al., 2016)

### Homology

The human MAZ protein is conserved 100% in chimpanzee (P.troglodytes), 98.4% in mouse (M.musculus), and 98.4% in rat (R.norvegicus); with conserved DNA of 99.8%, 93.2%, and 92.7%, respectively (Retrieved from: https://blast.ncbi.nlm.nih.gov/Blast.cgi. November 2, 2017).

## Mutations

**Note**

Genetic mutations are not described for MAZ.

## Implicated in

### Prostate cancer

It was reported that the MAZ expression is higher in clinical prostate cancer (PCa) specimens than in benign prostatic hyperplasia (BPH) and adjacent normal tissues (Jiao et al., 2013). Moreover, the MAZ expression appears to be positively correlated with the expression of androgen receptor ( AR), which is critical for the initiation and development of androgen-dependent PCa (Jiao et al., 2013). Extending these findings, experimental studies in cell models derived from PCa indicated that MAZ is involved in the phenotypic manifestation of PCa cell models as siRNA knockdown of MAZ levels reduces cell proliferation, migration, and invasion through mechanisms involve the expression of AR (Jiao et al., 2013).

### Hepatocellular carcinoma

The expression of MAZ was reported to be upregulated in the majority (78.94%) of hepatocellular carcinoma (HCC) samples compared to normal liver samples (Dudas et al., 2008). Experimental studies using cell lines derived from HCC further suggest that MAZ-mediated regulation of PROX1, which is a transcription factor critical for the expression of a number of genes involved in hepatic metabolic functions, contributes to the progression of HCC (Dudas et al., 2008).

### Breast cancer

Based on data sets in Gene expression-based Outcome for Breast Cancer Online (GOBO, http://co.bmc.lu.se/gobo/), the expression of MAZ is found to be correlated with distant metastasis-free survival (DMFS) in basal-like breast cancer (BLBC) patients and that the under-expression of MAZ is involved in the metastatic spread of BLBC (Yu et al., 2017). Based on these finding, it was suggested that MAZ plays dual roles in basal-like breast cancer (BLBC): it suppresses cancer progression but promotes cellular proliferation (Yu et al., 2017). Experimental studies using model cell lines derived from breast cancer indeed suggest that MAZ promotes cell proliferation yet it suppresses the aggressiveness of BLBC by controlling the transition toward a more mesenchymal phenotype (Yu et al., 2017; Ray, 2011).

### Pancreatic carcinoma

Based on samples from pancreatic carcinoma patients, it was reported that the expression of MAZ is significantly higher in PC tissue compared to the adjacent non-tumor tissues (Zhu et al., 2016). Moreover, it appears that the over-expression of MAZ is associated with poor prognosis of PC patients (Zhu et al., 2016).

### Hodgkin's Disease and Paraneoplastic Cerebellar Dysfunction

In neuronal cells, MAZ interacts with the Deleted in Colorectal Cancer product ( DCC), the receptor for NTN1 netrin-1 which plays a central role in axonal guidance and neuronal migration as well as survival during development. Analyses of sera from patients with HD and PCD Hodgkin's disease and paraneoplastic cerebellar degeneration indicated that patient sera contain auto-antigens directed against the MAZ-DCC complex. Based on these observations, it was speculated that auto-antigens could interfere with neuronal function resulting in neuronal degeneration (Bataller and Wade, 2002).

## To be noted

Expression of the MAZ gene is found to be regulated by MIR-125B, which is suggested to affect VEGF-induced angiogenesis in glioblastoma (Vandertop et al., 2017).

MIR449A targets MAZ transcripts, the down-regulation of which is reported to contribute to glioblastoma (Chen et al., 2015; Zhao et al., 2014; Yao et al., 2015).

MIR34C is also reported to target MAZ. Decrease levels of MAZ by miR-34c are suggested to impair the integrity and increased the permeability of blood-tumor barrier (Zhao et al., 2014).

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