Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL INIST-CNRS

# Gene Section
## Short Communication

# TALDO1 (transaldolase 1)

**Zachary Oaks, Andras Perl**

Departments of Medicine, Microbiology, and Immunology, Biochemistry and Molecular Biology, Neuroscience and Physiology, and Pathology, SUNY Upstate Medical University, Syracuse, New York, USA (ZO, AP)

Published in Atlas Database: July 2013

Online updated version : http://AtlasGeneticsOncology.org/Genes/TALDO1ID50613ch11p15.html
DOI: 10.4267/2042/53086



## Abstract

Short communication on TALDO1, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

## Identity

**Other names:** TAL, TAL-H, TALDOR, TALH

**HGNC (Hugo):** TALDO1

**Location:** 11p15.5

## DNA/RNA

**Note**

Starts at 747432 bp from pter and ends at 765024 bp from pter according to hg19-Feb_2009.

Size: 17593 bases; Orientation: TALDO1 is on the plus strand.

### Description

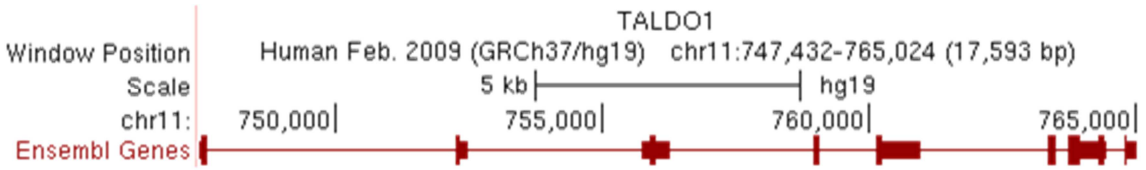
Exons 2 and 3 of TALDO1 contain retrotransposable elements (Banki et al., 1994).

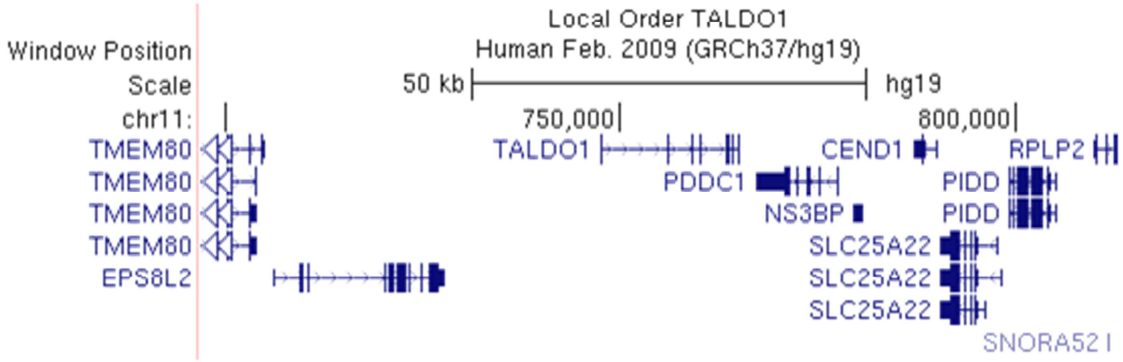
### Transcription

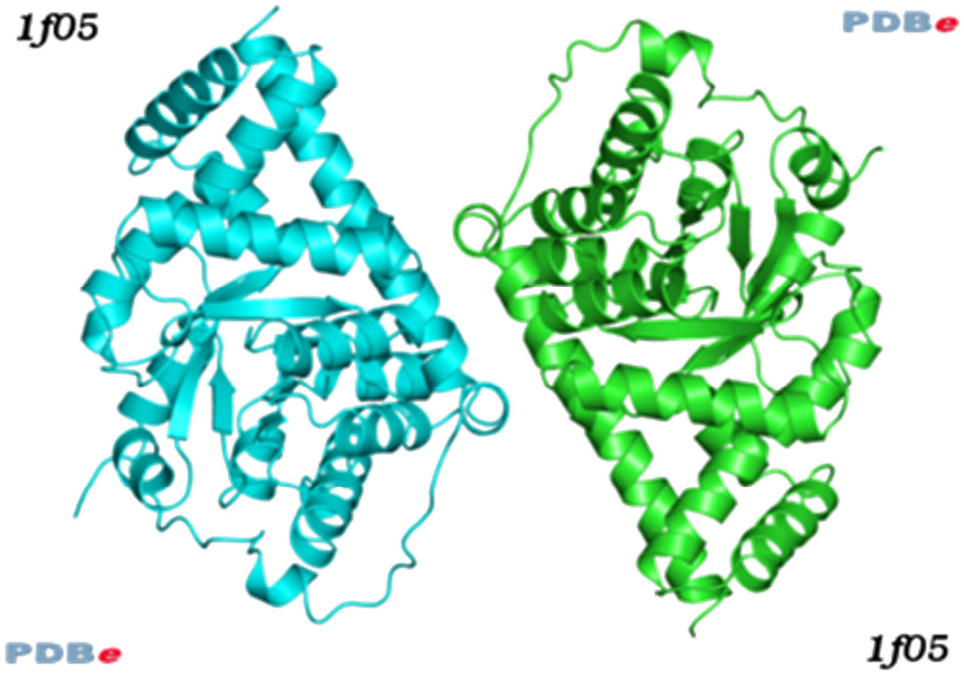
TALDO1 has 8 exons and its mRNA is composed of 1319 bp.

### Pseudogene

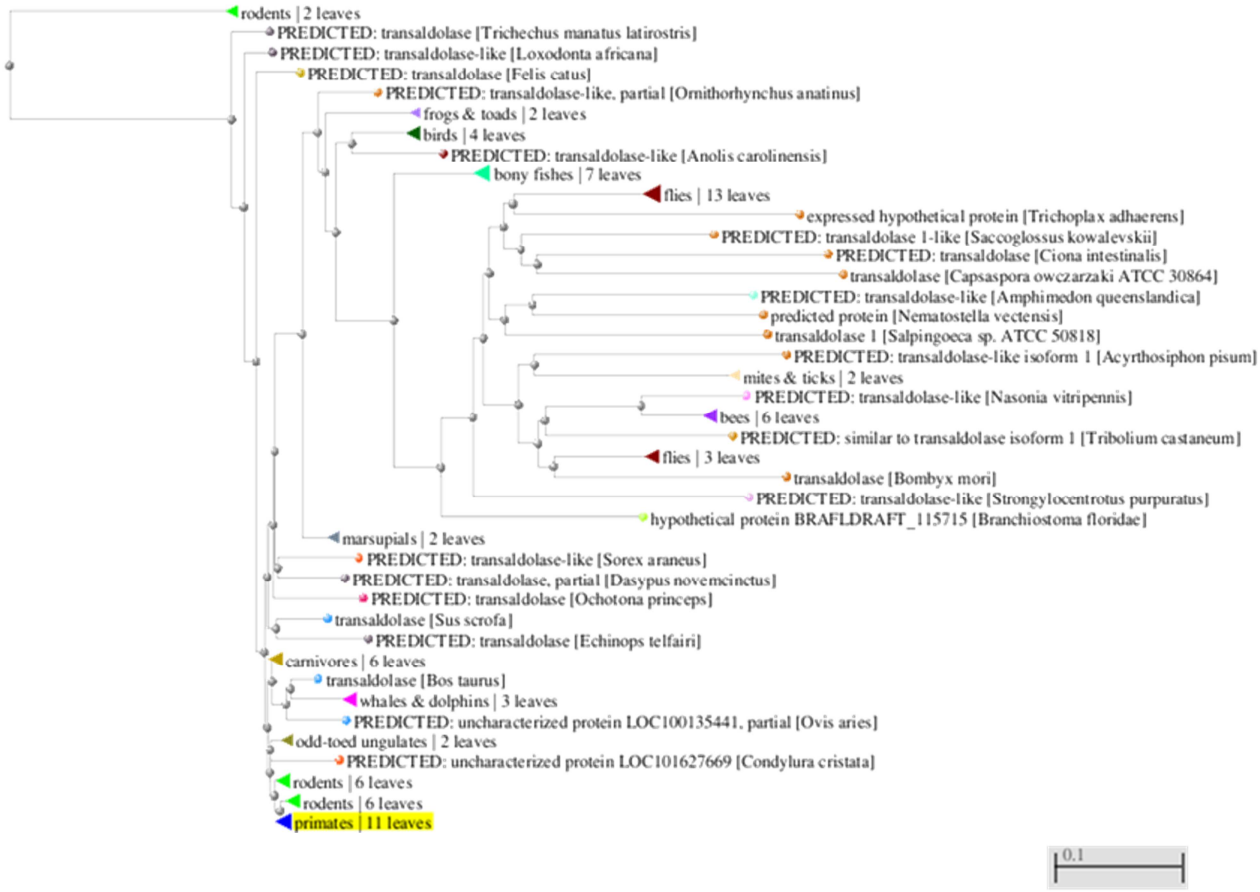
TALDO1P1 (Transaldolase 1 pseudogene 1).






**The 3-dimensional structure of transaldolase from Thorell et al., 2000.** Image downloaded from http://www.ebi.ac.uk.




From blast of reference proteins (Refseq) against human Transaldolase (NP_006746.1).

# Protein

## Description

Transaldolase (TAL) is a 337 amino acid protein in the non-oxidative phase of the pentose phosphate pathway (PPP) with a predicted mass of 37.55kDa. TAL has an α/β barrel and that includes lysine 142 which is responsible for generating the Schiff base intermediate during sugar phosphate metabolism (Thorell et al.,200). A mass spectrometry based investigation of the acetylome identified TAL acetylation at lysines 286, 269, 321, 219 (Choudhary et al., 2009).
It has also been proposed that TAL activity may be affected by phosphorylation (Lachaise et al., 2001).

## Expression

TALDO1 is ubiquitously expressed, except in erythrocytes.

## Localisation

Cytosol and nucleus (Colombo et al., 1997).

## Function

The reversible reaction carried out by TAL is: erythros-4-phosphate+fructose-6-phophateglyceraldehydes-3-phosphate+sedoheptulose-7-phosphate. TAL has been proposed as the rate limiting enzyme in the non-oxidative PPP (Banki et al., 1996; Heinrich et al., 1976; Perl, 2007; Wood, 1985).

## Homology

Using the blastp function within Homo sapiens, the only protein to share homology within humans (a paralog) was sorting nexin 32 (SNX32) with an identity of 36%.

# Mutations

## Germinal

Homozygous deletion of Serine 171 due to the loss of 3bp in the TALDO1 sequence results in liver cirrhosis and subsequent carcinogenesis.

# Implicated in

## Hepatocellular carcinoma

**Cytogenetics**

Deletion of nucleotides 512-514 in TALDO1 resulted in the loss of serine 171 in the TAL protein and subsequent TAL deficiency (Verhoeven et al., 2001; Valayannopoulos et al., 2006). TAL deficiency results in the accumulation of sedoheptulose-7-phosphate and polyols. Further studies into TAL deficiency determined that the deletion of S171 resulted in a complete loss of enzymatic activity and rapid degradation in the proteasome (Grossman et al., 2004). Missense mutations at arginine 192, in which the arginine is mutated to either a histidine or cysteine, also results in loss of TAL activity and liver damage in patients (Verhoeven et al., 2005; Wamelink at al., 2008). In addition to liver damage, renal and cardiac complications are also present in these patients (Verhoeven et al., 2001; Valayannopoulos et al., 2006; Verhoeven et al., 2005; Wamelink et al., 2008).
In a mouse model of TAL deficiency, sperm dysmotility and subsequent male infertility are present (Perl et al., 2006). Furthermore, TAL deficiency results in the development of hepatosteatosis, cirrhosis, and hepatocellular carcinoma in both homozygous TAL knockouts and heterozygous mice relative to C57Bl/6 wild type mice (Hanczko et al., 2009).
The pathogenic mechanism of liver damage in TAL deficiency is linked to depletion of NADPH, oxidative stress, and mitochondrial dysfunction (Perl et al., 2011).
In TAL deficiency, it has been proposed that oxidative stress is exacerbated by increased aldose reductase activity which generates polyols and depletes NADPH (Perl et al., 2011). Low NADPH diminishes the cells ability to regulate cellular redox and polyols can induce proliferation through JNK/c-Jun (Perl et al., 2011). Thus, TAL deficiency and insufficiency predispose to oxidative stress which promotes liver damage, increased proliferation, and hepatocellular carcinoma.

## Squamous cell carcinoma of the head and neck

**Cytogenetics**

3 SNPs in the TALDO1 gene have been associated with different squamous cell carcinoma of the head and neck risk.
The conversion of cytosine to either guanine or thymine at 490bp upstream of the origin of replication (rs10794338) was protective against tumorigenesis (Basta et al., 2008).
In contrast, the mutation of thymine to adenine at position 1874 (rs3901233) and adenine to cytosine at position 2187 (rs4963163) increase the risk of squamous cell cancer of the head and neck (Basta et al., 2008).


From blastp of NP_006746.1 against all non-redundant protein sequences.

# References


Heinrich PC, Morris HP, Weber G. Behavior of transaldolase (EC 2.2.1.2) and transketolase (EC 2.2.1.1) Activities in normal, neoplastic, differentiating, and regenerating liver. Cancer Res. 1976 Sep;36(9 pt.1):3189-97

Wood T.. The pentose phosphate pathway. New York: Academic Press. 1985.

Banki K, Halladay D, Perl A.. Cloning and expression of the human gene for transaldolase. A novel highly repetitive element constitutes an integral part of the coding sequence. J Biol Chem. 1994 Jan 28;269(4):2847-51.

Banki K, Hutter E, Colombo E, Gonchoroff NJ, Perl A.. Glutathione levels and sensitivity to apoptosis are regulated by changes in transaldolase expression. J Biol Chem. 1996 Dec 20;271(51):32994-3001.

Colombo E, Banki K, Tatum AH, Daucher J, Ferrante P, Murray RS, Phillips PE, Perl A.. Comparative analysis of antibody and cell-mediated autoimmunity to transaldolase and myelin basic protein in patients with multiple sclerosis. J Clin Invest. 1997 Mar 15;99(6):1238-50.

Thorell S, Gergely P Jr, Banki K, Perl A, Schneider G.. The three-dimensional structure of human transaldolase. FEBS Lett. 2000 Jun 23;475(3):205-8.

Lachaise F, Martin G, Drougard C, Perl A, Vuillaume M, Wegnez M, Sarasin A, Daya-Grosjean L.. Relationship between posttranslational modification of transaldolase and catalase deficiency in UV-sensitive repair-deficient xeroderma pigmentosum fibroblasts and SV40-transformed human cells. Free Radic Biol Med. 2001 Jun 15;30(12):1365-73.

Verhoeven NM, Huck JH, Roos B, Struys EA, Salomons GS, Douwes AC, van der Knaap MS, Jakobs C.. Transaldolase deficiency: liver cirrhosis associated with a new inborn error in the pentose phosphate pathway. Am J Hum Genet. 2001 May;68(5):1086-92. Epub 2001 Mar 27.

Grossman CE, Niland B, Stancato C, Verhoeven NM, Van Der Knaap MS, Jakobs C, Brown LM, Vajda S, Banki K, Perl A.. Deletion of Ser-171 causes inactivation, proteasome-mediated degradation and complete deficiency of human transaldolase. Biochem J. 2004 Sep 1;382(Pt 2):725-31.

Verhoeven NM, Wallot M, Huck JH, Dirsch O, Ballauf A, Neudorf U, Salomons GS, van der Knaap MS, Voit T, Jakobs C.. A newborn with severe liver failure, cardiomyopathy and transaldolase deficiency. J Inherit Metab Dis. 2005;28(2):169-79.

Perl A, Qian Y, Chohan KR, Shirley CR, Amidon W, Banerjee S, Middleton FA, Conkrite KL, Barcza M, Gonchoroff N, Suarez SS, Banki K.. Transaldolase is essential for maintenance of the mitochondrial transmembrane potential and fertility of spermatozoa. Proc Natl Acad Sci U S A. 2006 Oct 3;103(40):14813-8. Epub 2006 Sep 26.

Valayannopoulos V, Verhoeven NM, Mention K, Salomons GS, Sommelet D, Gonzales M, Touati G, de Lonlay P, Jakobs C, Saudubray JM.. Transaldolase deficiency: a new cause of hydrops fetalis and neonatal multi-organ disease. J Pediatr. 2006 Nov;149(5):713-7.

Perl A.. The pathogenesis of transaldolase deficiency. IUBMB Life. 2007 Jun;59(6):365-73. (REVIEW)

Basta PV, Bensen JT, Tse CK, Perou CM, Sullivan PF, Olshan AF.. Genetic variation in Transaldolase 1 and risk of squamous cell carcinoma of the head and neck. Cancer Detect Prev. 2008;32(3):200-8. doi: 10.1016/j.cdp.2008.08.008. Epub 2008 Sep 20.

Wamelink MM, Struys EA, Salomons GS, Fowler D, Jakobs C, Clayton PT.. Transaldolase deficiency in a two-year-old boy with cirrhosis. Mol Genet Metab. 2008 Jun;94(2):255-8. doi: 10.1016/j.ymgme.2008.01.011. Epub 2008 Mar 10.

Choudhary C, Kumar C, Gnad F, Nielsen ML, Rehman M, Walther TC, Olsen JV, Mann M.. Lysine acetylation targets protein complexes and co-regulates major cellular functions. Science. 2009 Aug 14;325(5942):834-40. doi: 10.1126/science.1175371. Epub 2009 Jul 16.

Hanczko R, Fernandez DR, Doherty E, Qian Y, Vas G, Niland B, Telarico T, Garba A, Banerjee S, Middleton FA, Barrett D, Barcza M, Banki K, Landas SK, Perl A.. Prevention of hepatocarcinogenesis and increased susceptibility to acetaminophen-induced liver failure in transaldolase-deficient mice by N-acetylcysteine. J Clin Invest. 2009 Jun;119(6):1546-57. doi: 10.1172/JCI35722. Epub 2009 May 11.

Perl A, Hanczko R, Telarico T, Oaks Z, Landas S.. Oxidative stress, inflammation and carcinogenesis are controlled through the pentose phosphate pathway by transaldolase. Trends Mol Med. 2011 Jul;17(7):395-403. doi: 10.1016/j.molmed.2011.01.014. Epub 2011 Mar 2. (REVIEW)



*This article should be referenced as such:*

Oaks Z, Perl A. TALDO1 (transaldolase 1). Atlas Genet Cytogenet Oncol Haematol. 2014; 18(2):117-121.