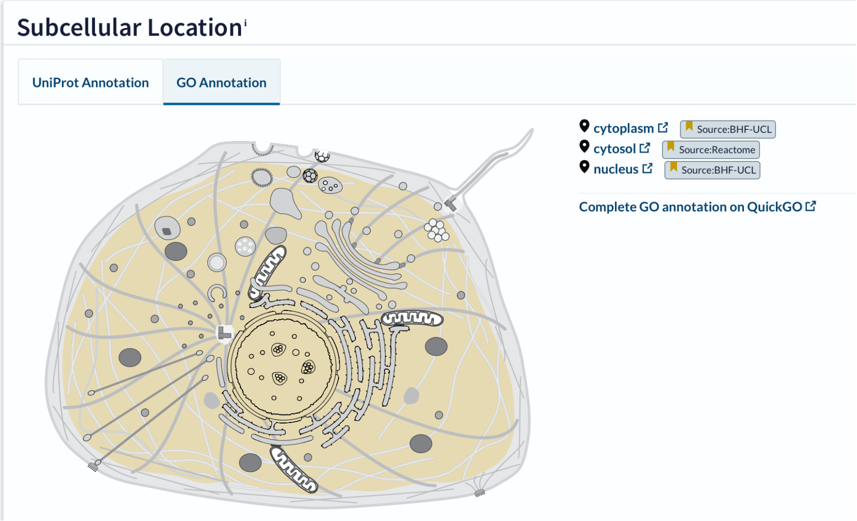
S01 - REŠITVE

1) Če v PubMed vnesemo vse zahtevane filtre, se nam izpišejo 4 članki. Iz med njih ima najbolj zanimiv naslov članek: *"Oh, Dear We Are in Tribble": An Overview of the Oncogenic Functions of Tribbles 1*

2) S tem iskanjem najdemo 4 članke.

3) Tribble 1 spada med psevdokinaze. Gre za za kinaze, ki nimajo katalitične domene in posledično ne morejo fosforilirati substratov.

4) Nahaja se v citosolu in jedru (Slika 1).



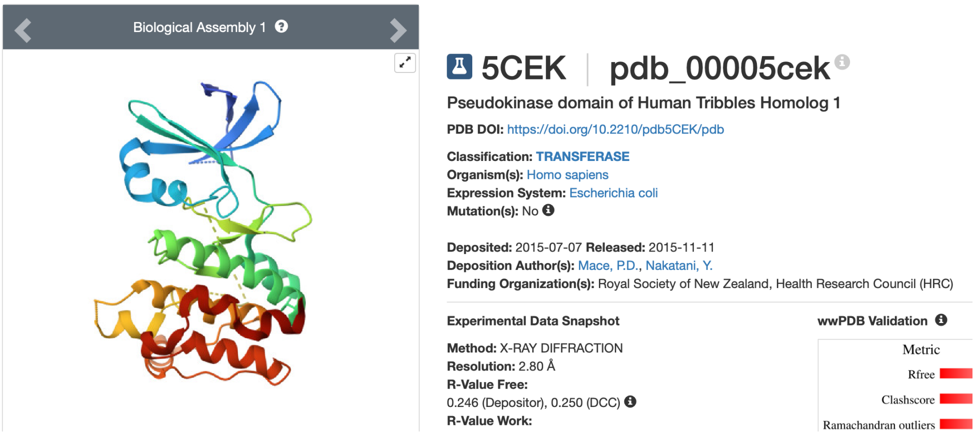
Subcellular Location

cytoplasm Source:BHF-UCL
cytosol Source:Reactome
nucleus Source:BHF-UCL

Complete GO annotation on QuickGO

Slika1: Odgovor se skriva v UniProtu (ID: Q96RU8), pod zavihkom »Subcellular Location«.

5) Izražen je bil v E. Coli (Slika 2).



5CEK | pdb_00005cek

Pseudokinase domain of Human Tribbles Homolog 1

PDB DOI: https://doi.org/10.2210/pdb5CEK/pdb

Classification: TRANSFERASE
Organism(s): Homo sapiens
Expression System: Escherichia coli
Mutation(s): No

Deposited: 2015-07-07 **Released:** 2015-11-11
Deposition Author(s): Mace, P.D., Nakatani, Y.
Funding Organization(s): Royal Society of New Zealand, Health Research Council (HRC)

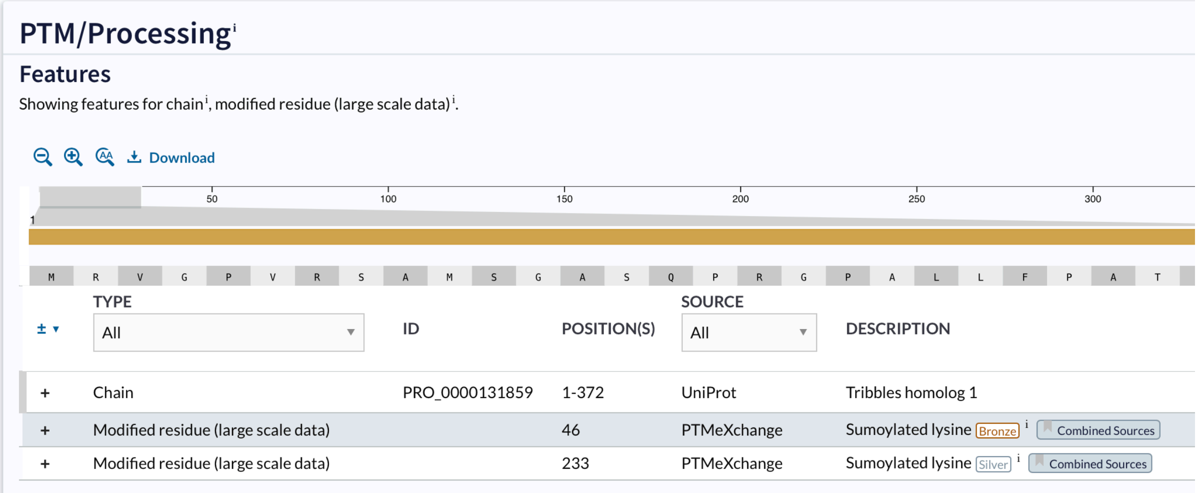
Experimental Data Snapshot

Method: X-RAY DIFFRACTION
Resolution: 2.80 Å
R-Value Free:
0.246 (Depositor), 0.250 (DCC)
R-Value Work:

wwPDB Validation

Slika 2: Prek UniProt-a lahko po zavihkom »structure« dostopamo do PDB struktur. Tam lahko najdemo podatek »expression system«.

6) Imenuje se sumoilacija (lizina). Nahaja se na 46. in 233. aminokislinskem ostanku (Slika 3). Gre za posttranslacijsko modifikacijo, kjer se posebna družina SUMO proteinov (**S**mall **U**biquitin-like **Mo**difier) prek glicinskega ostanka veže na lizin.



PTM/Processing

Features

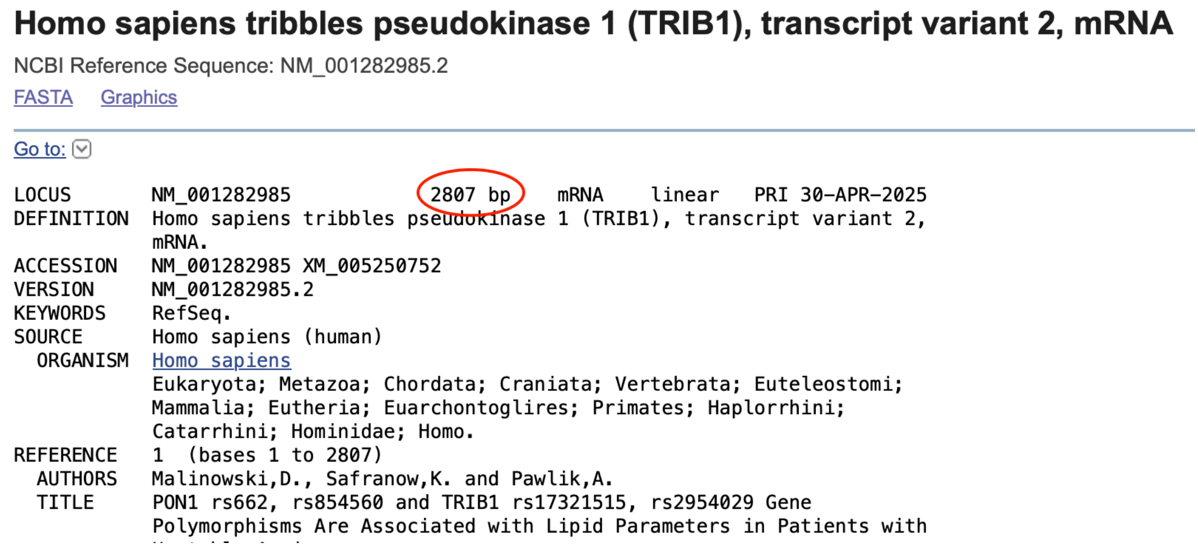
Showing features for chain, modified residue (large scale data).

	TYPE	ID	POSITION(S)	SOURCE	DESCRIPTION
±	All			All	
+	Chain	PRO_0000131859	1-372	UniProt	Tribbles homolog 1
+	Modified residue (large scale data)		46	PTMeXchange	Sumoylated lysine Bronze Combined Sources
+	Modified residue (large scale data)		233	PTMeXchange	Sumoylated lysine Silver Combined Sources

Modifikacija ima več vlog, med drugim stabilizira proteine, sodeluje pri jedrnem transportu in transkripcijski regulaciji.

Slika 3: Na UniProt pod zavihkom »PTM/Processing« najdemo podatke o modifikacijah ter indormacijo o tem, na katerem mestu se nahajajo. Sam mehanizem sumoilacije lahko poiščemo na spletu.

7) mRNA, ki kodira za tribble 1 je dolga 2807 bp (Slika 4).



Homo sapiens tribbles pseudokinase 1 (TRIB1), transcript variant 2, mRNA

NCBI Reference Sequence: NM_001282985.2

```
LOCUS       NM_001282985            2807 bp    mRNA    linear   PRI 30-APR-2025
DEFINITION  Homo sapiens tribbles pseudokinase 1 (TRIB1), transcript variant 2,
            mRNA.
ACCESSION   NM_001282985 XM_005250752
VERSION     NM_001282985.2
KEYWORDS    RefSeq.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 2807)
  AUTHORS   Malinowski,D., Safranow,K. and Pawlik,A.
  TITLE     PON1 rs662, rs854560 and TRIB1 rs17321515, rs2954029 Gene
            Polymorphisms Are Associated with Lipid Parameters in Patients with
```

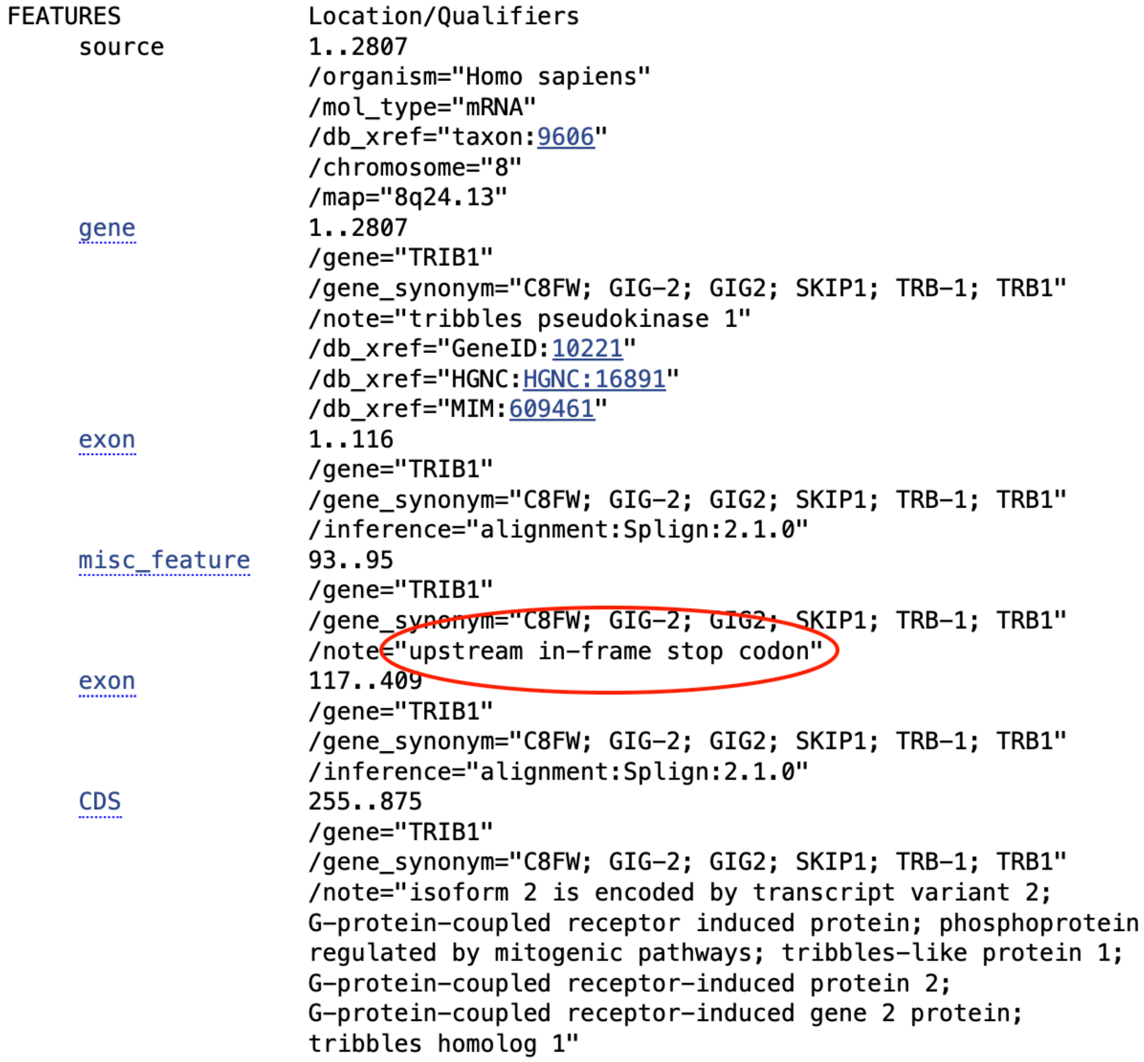
Slika 4: Iskanje po GenBank za TRIB1 (NM_001282985.2).

8) Gen vsebuje 3 eksone, nahaja se na kromosomu 8 (Slika 5).

```
FEATURES             Location/Qualifiers
     source          1..2807
                     /organism="Homo sapiens"
                     /mol_type="mRNA"
                     /db_xref="taxon:9606"
                     /chromosome="8"
                     /map="8q24.13"
     gene            1..2807
                     /gene="TRIB1"
                     /gene_synonym="C8FW; GIG-2; GIG2; SKIP1; TRB-1; TRB1"
                     /note="tribbles pseudokinase 1"
                     /db_xref="GeneID:10221"
                     /db_xref="HGNC:HGNC:16891"
                     /db_xref="MIM:609461"
     exon            1..116
                     /gene="TRIB1"
                     /gene_synonym="C8FW; GIG-2; GIG2; SKIP1; TRB-1; TRB1"
                     /inference="alignment:Splign:2.1.0"
     misc_feature    93..95
                     /gene="TRIB1"
                     /gene_synonym="C8FW; GIG-2; GIG2; SKIP1; TRB-1; TRB1"
                     /note="upstream in-frame stop codon"
     exon            117..409
                     /gene="TRIB1"
                     /gene_synonym="C8FW; GIG-2; GIG2; SKIP1; TRB-1; TRB1"
                     /inference="alignment:Splign:2.1.0"
     CDS             255..875
                     /gene="TRIB1"
                     /gene_synonym="C8FW; GIG-2; GIG2; SKIP1; TRB-1; TRB1"
                     /note="isoform 2 is encoded by transcript variant 2;
                     G-protein-coupled receptor induced protein; phosphoprotein
                     regulated by mitogenic pathways; tribbles-like protein 1;
                     G-protein-coupled receptor-induced protein 2;
                     G-protein-coupled receptor-induced gene 2 protein;
                     tribbles homolog 1"
                     /codon_start=1
                     /product="tribbles homolog 1 isoform 2"
                     /protein_id="NP_001269914.1"
                     /db_xref="CCDS:CCDS64971.1"
                     /db_xref="GeneID:10221"
                     /db_xref="HGNC:HGNC:16891"
                     /db_xref="MIM:609461"
                     /translation="MHSYVRSRKRLREEEAARLFKQIVSAVAHCHQSAIVLGDLKLRK
                     FVFSTEERTQLRLESLEDTHIMKGEDDALSDKHGCPAYVSPEILNTTGTYSGKAADVW
                     SLGVMLYTLLVGRYPFHDSDPSALFSKIRRGQFCIPEHISPKARCLIRSLLRREPSER
                     LTAPEILLHPWFESVLEPGYIDSEIGTSDQIVPEYQEDSDISSFFC"
     exon            410..2807
                     /gene="TRIB1"
```

Slika 5: GenBank zadetek za TRIB1, gledamo FEATURES.

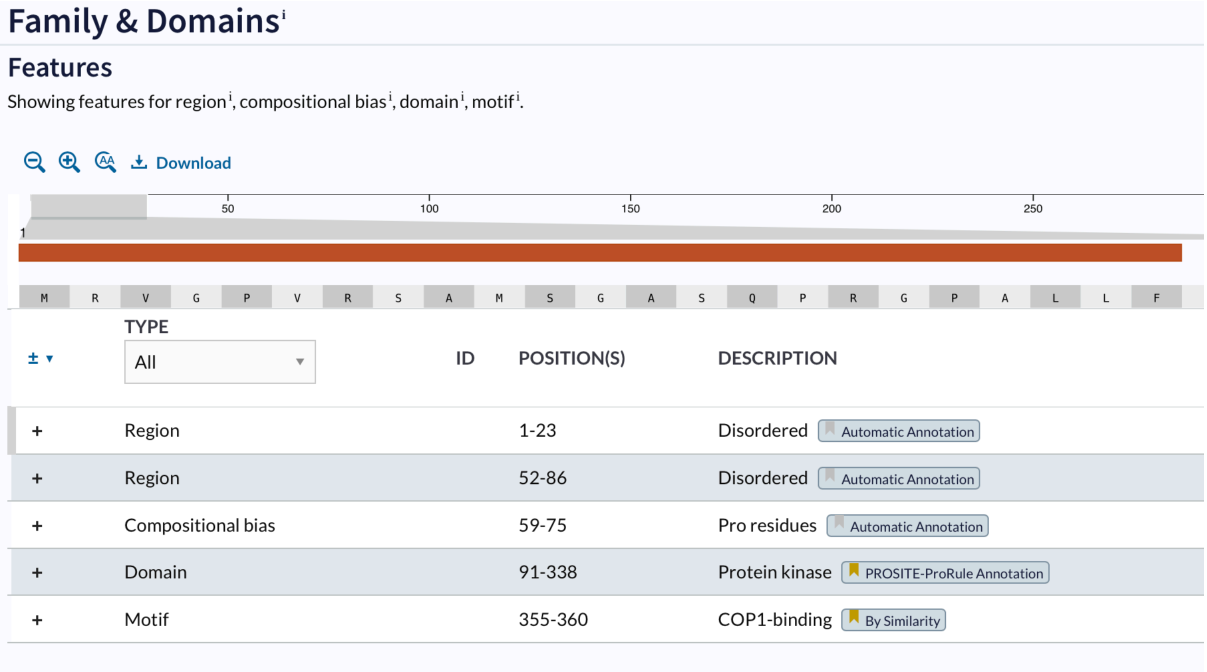
9) *(misc-feature* - (Slika 6)*)* Gre za »upstream in-frame stop codon« oz. zgoraj-ležeči stop kodon znotraj okvirja, ki se nahaja na mestu 93-95 (Slika 5). Stop kodon se nahaja pred start kodonom kodirajočega zaporedja. Preprečuje, da bi ribosom s prevajanjem začel »previsoko« na genu. Npr. če se pred start kodonom kodirajočega zaporedja nahaja še kakšen dodaten start kodon in ribosom tam začne s prevajanjem, se bo translacija zaradi prisotnosti zgoraj-ležečega stop kodona ustavila.



```
FEATURES             Location/Qualifiers
     source          1..2807
                     /organism="Homo sapiens"
                     /mol_type="mRNA"
                     /db_xref="taxon:9606"
                     /chromosome="8"
                     /map="8q24.13"
     gene            1..2807
                     /gene="TRIB1"
                     /gene_synonym="C8FW; GIG-2; GIG2; SKIP1; TRB-1; TRB1"
                     /note="tribbles pseudokinase 1"
                     /db_xref="GeneID:10221"
                     /db_xref="HGNC:HGNC:16891"
                     /db_xref="MIM:609461"
     exon            1..116
                     /gene="TRIB1"
                     /gene_synonym="C8FW; GIG-2; GIG2; SKIP1; TRB-1; TRB1"
                     /inference="alignment:Splign:2.1.0"
     misc_feature    93..95
                     /gene="TRIB1"
                     /gene_synonym="C8FW; GIG-2; GIG2; SKIP1; TRB-1; TRB1"
                     /note="upstream in-frame stop codon"
     exon            117..409
                     /gene="TRIB1"
                     /gene_synonym="C8FW; GIG-2; GIG2; SKIP1; TRB-1; TRB1"
                     /inference="alignment:Splign:2.1.0"
     CDS             255..875
                     /gene="TRIB1"
                     /gene_synonym="C8FW; GIG-2; GIG2; SKIP1; TRB-1; TRB1"
                     /note="isoform 2 is encoded by transcript variant 2;
                     G-protein-coupled receptor induced protein; phosphoprotein
                     regulated by mitogenic pathways; tribbles-like protein 1;
                     G-protein-coupled receptor-induced protein 2;
                     G-protein-coupled receptor-induced gene 2 protein;
                     tribbles homolog 1"
```

Slika 6: GenBank zadetek za TRIB1, gledamo FEATURES.

10) Tribble 1 vsebuje protein kinazno domeno (91-338) in COP1-vezavni motiv (355-360) (Slika 7). Prek protein kinazne domene se veže na CEBPA, prek COP1-vezavnega motiva pa na COP1 (Slika 8).



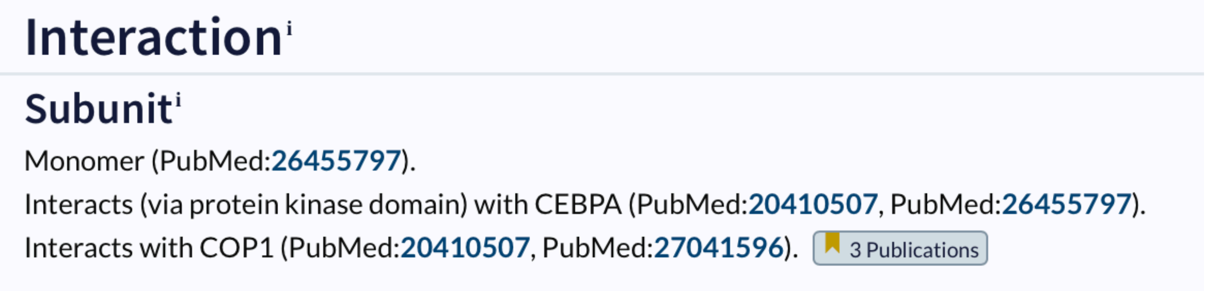
Family & Domains[i]

Features

Showing features for region[i], compositional bias[i], domain[i], motif[i].

± ▾	TYPE All ▾	ID	POSITION(S)	DESCRIPTION
+	Region		1-23	Disordered Automatic Annotation
+	Region		52-86	Disordered Automatic Annotation
+	Compositional bias		59-75	Pro residues Automatic Annotation
+	Domain		91-338	Protein kinase PROSITE-ProRule Annotation
+	Motif		355-360	COP1-binding By Similarity

Slika 7: Na UniProtu lahko pod zavihkom »Family & Domains« najdemo podatke o različnih domenah, regijah in motivih našega proteina. Najdemo tudi podatke o poziciji.



Interaction[i]

Subunit[i]

Monomer (PubMed:26455797).

Interacts (via protein kinase domain) with CEBPA (PubMed:20410507, PubMed:26455797).

Interacts with COP1 (PubMed:20410507, PubMed:27041596). 3 Publications

Slika 8: Podatek o interakcijah s temi domenami pa nademo po zavihkom »Interaction«.

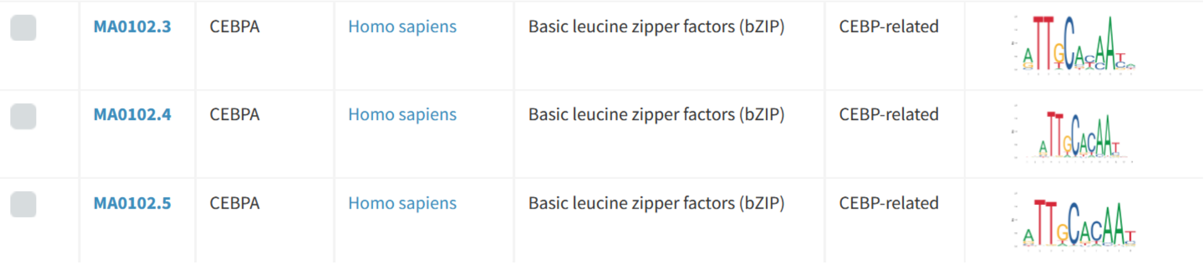
→ od tu naprej se vprašanja nanašajo na CEBPA:

11) Primer:

Narejeno v UniProtu iz štirih organizmov, katerih CEBPA je anotiran.
Rezultati so smiselni, saj lahko opazimo, da sta si proteina iz miši in podgane bolj sorodna med sabo kot s proteinoma iz drugih dveh organizmov. Prav tako sta si protein iz človeka in goveda sorodnejša.

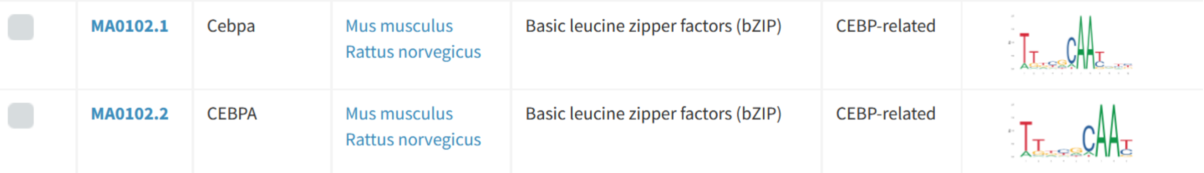
12) Levcinska zadrga. 8K8C

13)



☐	MA0102.3	CEBPA	Homo sapiens	Basic leucine zipper factors (bZIP)	CEBP-related	
☐	MA0102.4	CEBPA	Homo sapiens	Basic leucine zipper factors (bZIP)	CEBP-related	
☐	MA0102.5	CEBPA	Homo sapiens	Basic leucine zipper factors (bZIP)	CEBP-related	

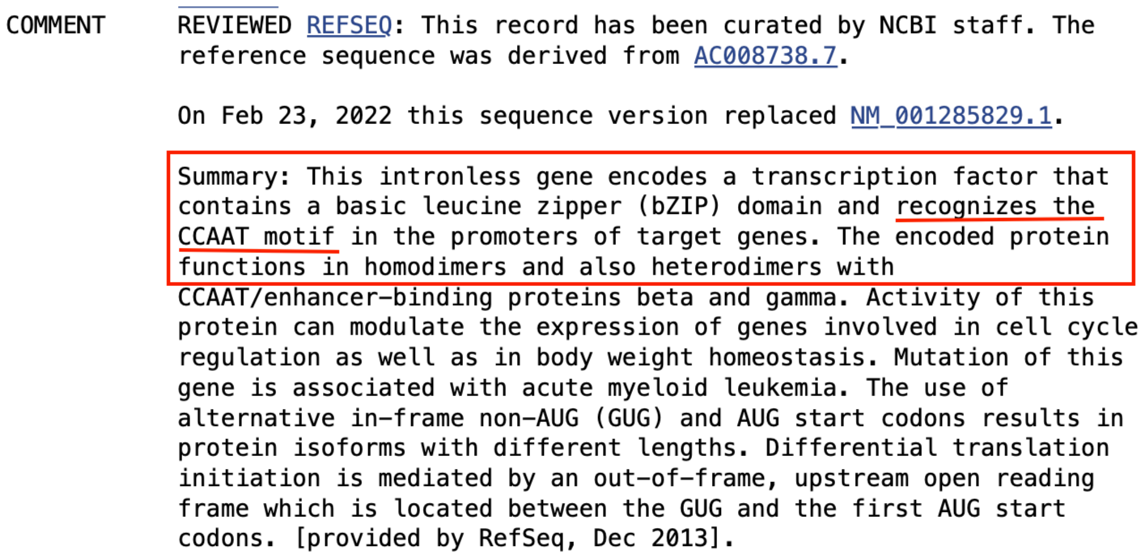
Pri iskanju lahko opazimo, da je najbolj ohranjeno nukleotidno zaporedje TTGCACAAT. Pri miših je zaporedje le nekoliko drugačno, zadetki pokažejo tako:



☐	MA0102.1	Cebpa	Mus musculus Rattus norvegicus	Basic leucine zipper factors (bZIP)	CEBP-related	
☐	MA0102.2	CEBPA	Mus musculus Rattus norvegicus	Basic leucine zipper factors (bZIP)	CEBP-related	

Opazimo lahko bolj ohranjene CAAT, ki jih najdemo tudi pri človeku, torej je osnovni motiv ohranjen, kar kaže na evolucijsko ohranjenost funkcije CEBPA.

14) Na GenBank (NM_001285829.2) lahko v komentarju preberemo, da je prepoznavni motiv CCAAT (Slika 9), ki se malo razlikuje od zgoraj pridobljenih zaporedjih iz orodja JASPAR. Razliko je možno pripisati dejstvu, da JASPAR oblikuje matrike na podlagi več eksperimentalnih podatkov. Vezava CEBPA ni strogo omejena na nukleotidno zaporedje CCAAT, ampak je pomemben le prepoznavni motiv, ki je podoben temu zaporedju.



```
COMMENT     REVIEWED REFSEQ: This record has been curated by NCBI staff. The
            reference sequence was derived from AC008738.7.

            On Feb 23, 2022 this sequence version replaced NM_001285829.1.

            Summary: This intronless gene encodes a transcription factor that
            contains a basic leucine zipper (bZIP) domain and recognizes the
            CCAAT motif in the promoters of target genes. The encoded protein
            functions in homodimers and also heterodimers with
            CCAAT/enhancer-binding proteins beta and gamma. Activity of this
            protein can modulate the expression of genes involved in cell cycle
            regulation as well as in body weight homeostasis. Mutation of this
            gene is associated with acute myeloid leukemia. The use of
            alternative in-frame non-AUG (GUG) and AUG start codons results in
            protein isoforms with different lengths. Differential translation
            initiation is mediated by an out-of-frame, upstream open reading
            frame which is located between the GUG and the first AUG start
            codons. [provided by RefSeq, Dec 2013].
```

Slika 9: GenBank zadetek za CEBPA, gledamo COMMENT.