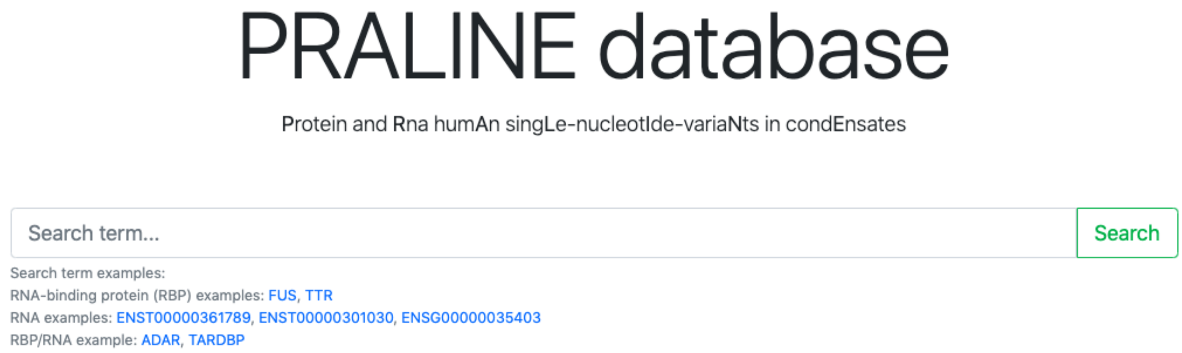
The PRALINE database

Tutorial

PRALINE database allows the study of proteins and RNAs found in assemblies associated with liquid-liquid phase separation and liquid-to-solid phase transition. PRALINE contains information about calculations and experimentally-validated macromolecular interactions as well as predictions of RNA secondary structure content, liquid-liquid phase-separation and liquid–to-solid phase transition propensities, with a focus on disease-related single-nucleotide variants (SNVs) contained in the molecules sequences.

PRALINE can be accessed using either protein or RNA names that can be provided as Gene Name, Ensembl Gene / Transcript ID or UniprotKB ID, as shown in the examples above.



PRALINE database

Protein and Rna humAn singLe-nucleotIde-variaNts in condEnsates

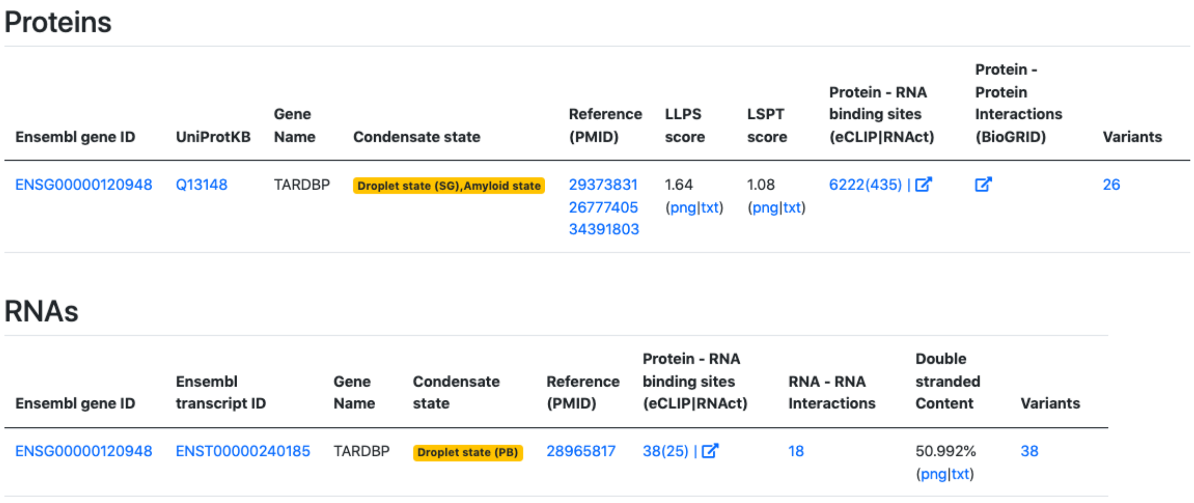
Search term examples:

RNA-binding protein (RBP) examples: FUS, TTR

RNA examples: ENST00000361789, ENST00000301030, ENSG00000035403

RBP/RNA example: ADAR, TARDBP

If a molecule (i.e TARDBP) is available both as a protein and as RNA, both types of information are shown, otherwise only one of them will be presented.



Proteins

Ensembl gene ID	UniProtKB	Gene Name	Condensate state	Reference (PMID)	LLPS score	LSPT score	Protein - RNA binding sites (eCLIP|RNAct)	Protein - Protein Interactions (BioGRID)	Variants
ENSG00000120948	Q13148	TARDBP	Droplet state (SG),Amyloid state	29373831 26777405 34391803	1.64 (png|txt)	1.08 (png|txt)	6222(435) | ↗	↗	26

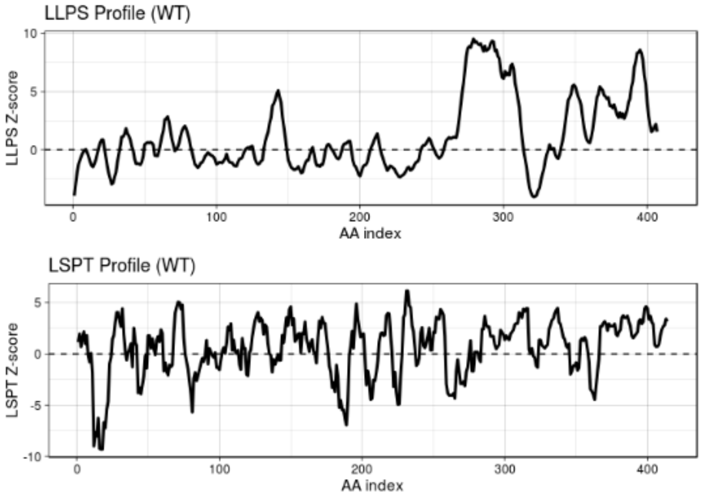
RNAs

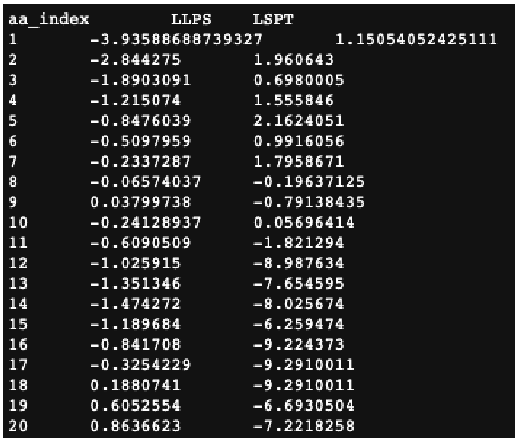
Ensembl gene ID	Ensembl transcript ID	Gene Name	Condensate state	Reference (PMID)	Protein - RNA binding sites (eCLIP|RNAct)	RNA - RNA Interactions	Double stranded Content	Variants
ENSG00000120948	ENST00000240185	TARDBP	Droplet state (PB)	28965817	38(25) | ↗	18	50.992% (png|txt)	38

In the query page the user can find information about the condensate state in which the protein / RNA has been observed (Droplet, Amyloid), with a further SG/PB label if the molecule has been seen in stress granules (SGs) or processing bodies (PBs), respectively. The references of the studies reporting the molecule are shown as PMID. Indeed, by hovering over the column's name, each label is explained and relevant links to literature are provided.

Protein search

Searching for a protein, the user can retrieve the liquid-liquid phase separation (LLPS) and liquid-to-solid phase transition (LSPT) propensities, as predicted by catGRANULE and Zyggregator algorithms respectively. The scores are Z-normalised and displayed at single amino acid resolution (see About section for more information). Both profile graph and a table are available for the download.

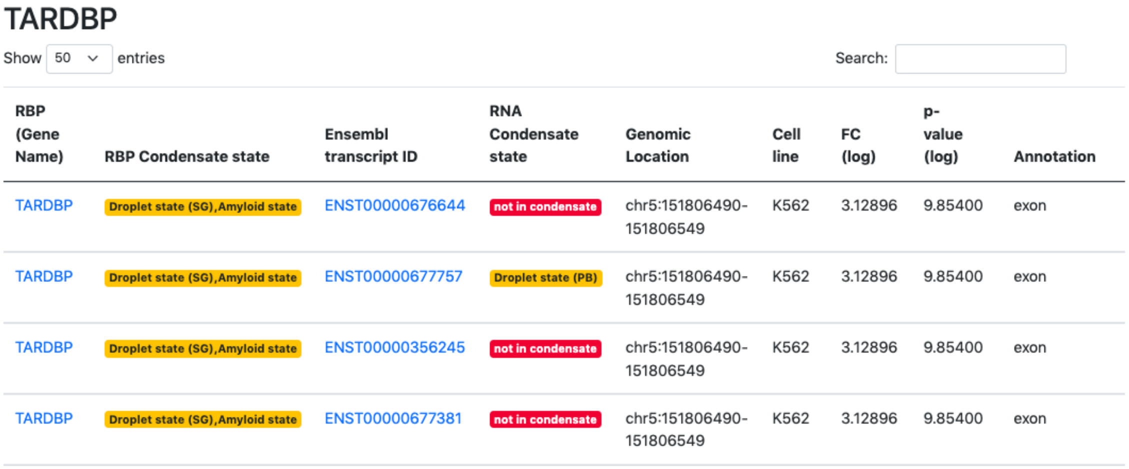




```
aa_index         LLPS     LSPT
1       -3.93588688739327       1.15054052425111
2       -2.844275       1.960643
3       -1.8903091      0.6980005
4       -1.215074       1.555846
5       -0.8476039      2.1624051
6       -0.5097959      0.9916056
7       -0.2337287      1.7958671
8       -0.06574037     -0.19637125
9       0.03799738      -0.79138435
10      -0.24128937     0.05696414
11      -0.6090509      -1.821294
12      -1.025915       -8.987634
13      -1.351346       -7.654595
14      -1.474272       -8.025674
15      -1.189684       -6.259474
16      -0.841708       -9.224373
17      -0.3254229      -9.2910011
18      0.1880741       -9.2910011
19      0.6052554       -6.6930504
20      0.8636623       -7.2218258
```

Information about experimentally validated protein-protein interactions is available through an external link to BioGRID database (33070389). BioGRID was not integrated in PRALINE because protein binding sites are not yet provided and the database is updated regularly.

The user can retrieve protein-RNA interactions predicted with catRAPID algorithm and available externally in the RNAct database, or experimentally validated interactions collected from eCLIP experiments (32728246). The user can visualize the total number of different interactions in which the protein is involved and between parentheses the number of contacts involving condensates RNAs.



TARDBP

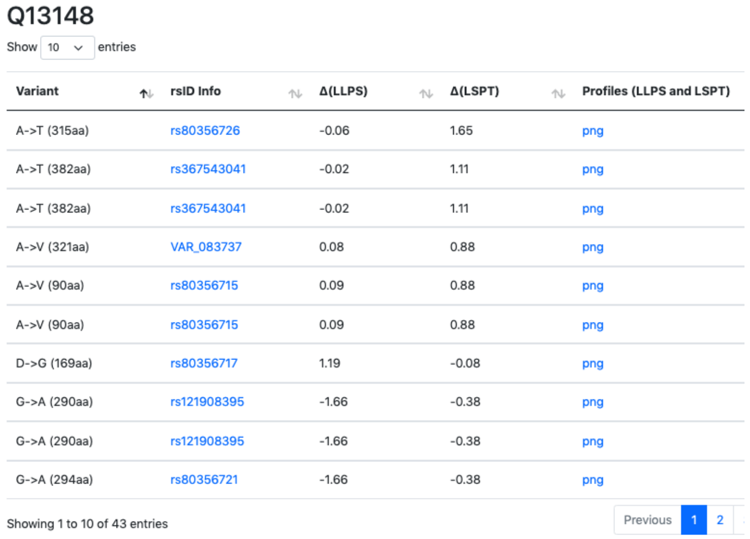
Show 50 entries Search:

RBP (Gene Name)	RBP Condensate state	Ensembl transcript ID	RNA Condensate state	Genomic Location	Cell line	FC (log)	p-value (log)	Annotation
TARDBP	Droplet state (SG),Amyloid state	ENST00000676644	not in condensate	chr5:151806490-151806549	K562	3.12896	9.85400	exon
TARDBP	Droplet state (SG),Amyloid state	ENST00000677757	Droplet state (PB)	chr5:151806490-151806549	K562	3.12896	9.85400	exon
TARDBP	Droplet state (SG),Amyloid state	ENST00000356245	not in condensate	chr5:151806490-151806549	K562	3.12896	9.85400	exon
TARDBP	Droplet state (SG),Amyloid state	ENST00000677381	not in condensate	chr5:151806490-151806549	K562	3.12896	9.85400	exon

As in the other sections, by hovering over the column's name, the labels are explained and relevant links to literature are provided.

For each protein, a list of RNA partners is given, together with additional information, including the condensate state of both protein and RNA molecules, and chromosomal coordinates of the binding site and its annotation in the gene, as well as the cell line in which the analysis was done. Both the fold-change and P-value of the interactions are provided (27018577).

In the variants section, the SNVs (in rs format) collected from DisGeNet (31680165) and ClinVar (24234437) corresponding to the query protein (see About section for more information) are shown. For each SNV, the relative amino acid position inside the protein sequence is presented and the predicted difference in LLPS and LSPT of the mutant protein compared to the WT is calculated and shown in different plots.

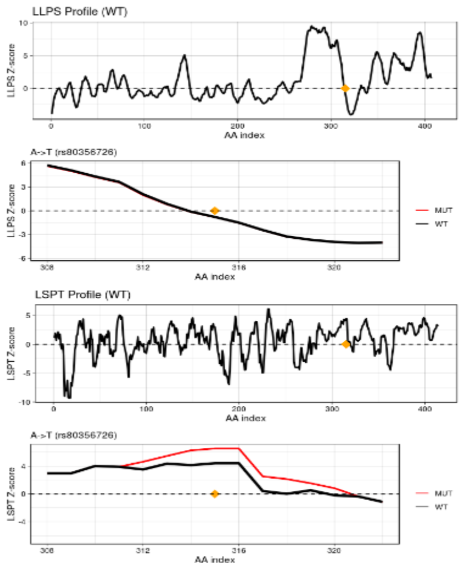


Q13148

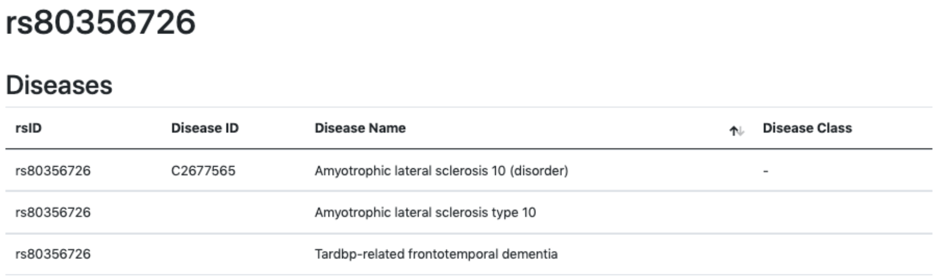
Show 10 entries

Variant	rsID Info	Δ(LLPS)	Δ(LSPT)	Profiles (LLPS and LSPT)
A->T (315aa)	rs80356726	-0.06	1.65	png
A->T (382aa)	rs367543041	-0.02	1.11	png
A->T (382aa)	rs367543041	-0.02	1.11	png
A->V (321aa)	VAR_083737	0.08	0.88	png
A->V (90aa)	rs80356715	0.09	0.88	png
A->V (90aa)	rs80356715	0.09	0.88	png
D->G (169aa)	rs80356717	1.19	-0.08	png
G->A (290aa)	rs121908395	-1.66	-0.38	png
G->A (290aa)	rs121908395	-1.66	-0.38	png
G->A (294aa)	rs80356721	-1.66	-0.38	png

Showing 1 to 10 of 43 entries



By clicking on a SNV name, the user can find additional information on the diseases related to the variant.



rs80356726

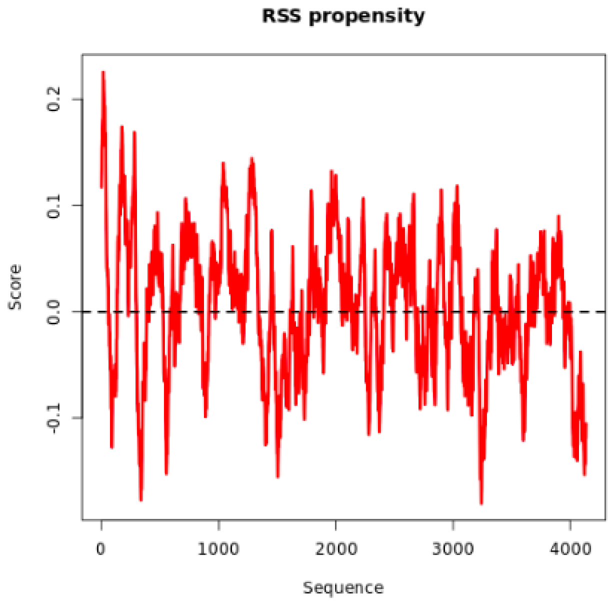
Diseases

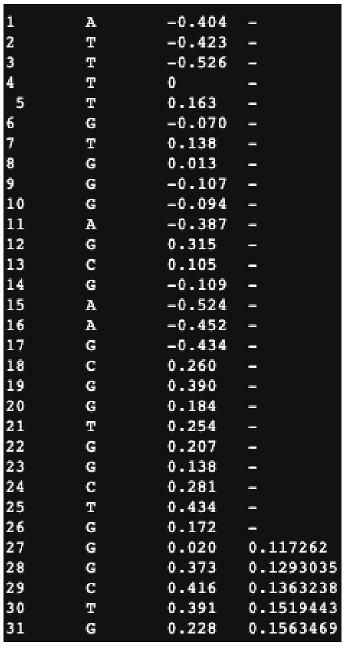
rsID	Disease ID	Disease Name	Disease Class
rs80356726	C2677565	Amyotrophic lateral sclerosis 10 (disorder)	-
rs80356726		Amyotrophic lateral sclerosis type 10	
rs80356726		Tardbp-related frontotemporal dementia	

RNA search

Searching for an RNA, the user can retrieve information about its condensate state and related references, as well as predicted and experimental protein-RNA interactions.

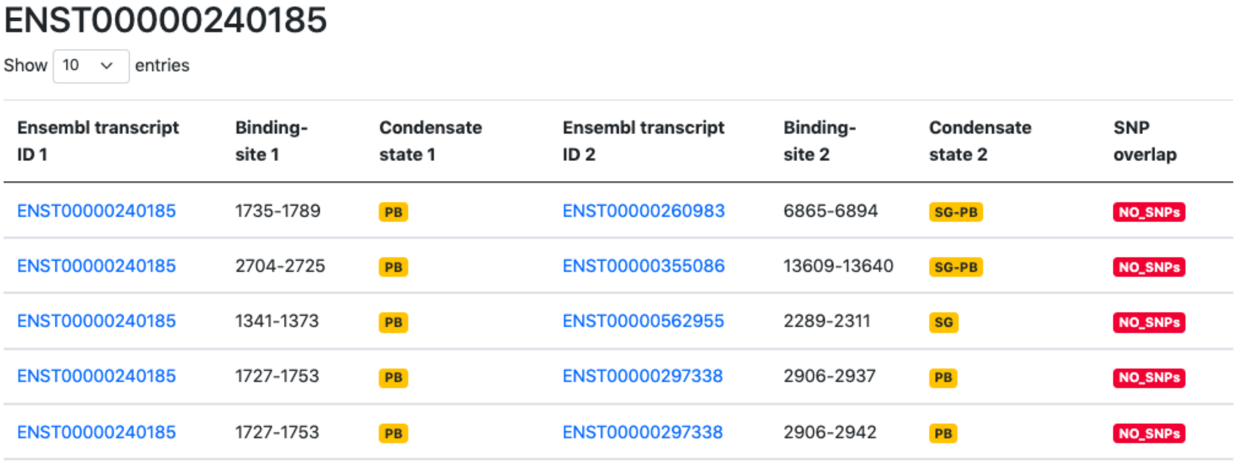
In addition, the predicted RNA secondary structure content obtained with CROSS algorithm is shown and a single-nucleotide propensity profile is available both as a graph and as a table. (see CROSS tutorial page for more information on the output files).





```
1          A          -0.404  -
2          T          -0.423  -
3          T          -0.526  -
4          T          0       -
 5         T          0.163   -
6          G          -0.070  -
7          T          0.138   -
8          G          0.013   -
9          G          -0.107  -
10         G          -0.094  -
11         A          -0.387  -
12         G          0.315   -
13         C          0.105   -
14         G          -0.109  -
15         A          -0.524  -
16         A          -0.452  -
17         G          -0.434  -
18         C          0.260   -
19         G          0.390   -
20         G          0.184   -
21         T          0.254   -
22         G          0.207   -
23         G          0.138   -
24         C          0.281   -
25         T          0.434   -
26         G          0.172   -
27         G          0.020   0.117262
28         G          0.373   0.1293035
29         C          0.416   0.1363238
30         T          0.391   0.1519443
31         G          0.228   0.1563469
```

High-throughput experimental RNA-RNA interactions retrieved from the RISE database are available. For each RNA the total number of interactors is shown together with the number of interactors belonging to condensates between parentheses. For each RNA pair, we show the condensate state information and the binding site location of both RNAs and the SNVs overlapping with at least one of the binding sites.

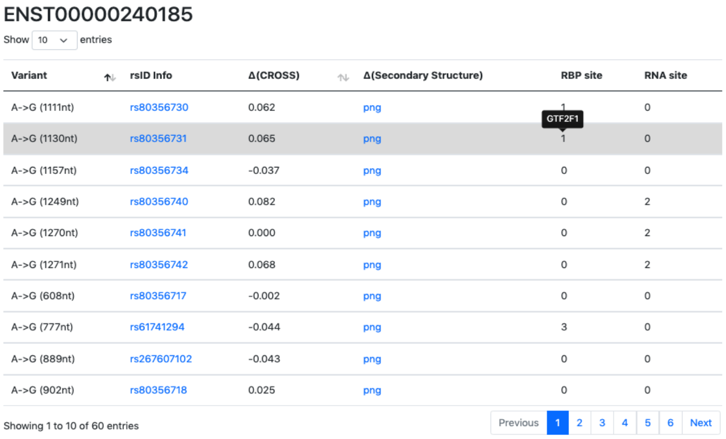


ENST00000240185

Ensembl transcript ID 1	Binding-site 1	Condensate state 1	Ensembl transcript ID 2	Binding-site 2	Condensate state 2	SNP overlap
ENST00000240185	1735-1789	PB	ENST00000260983	6865-6894	SG-PB	NO_SNPs
ENST00000240185	2704-2725	PB	ENST00000355086	13609-13640	SG-PB	NO_SNPs
ENST00000240185	1341-1373	PB	ENST00000562955	2289-2311	SG	NO_SNPs
ENST00000240185	1727-1753	PB	ENST00000297338	2906-2937	PB	NO_SNPs
ENST00000240185	1727-1753	PB	ENST00000297338	2906-2942	PB	NO_SNPs

As in the other sections, by hovering over the column's name, the labels are explained and relevant links to literature are provided.

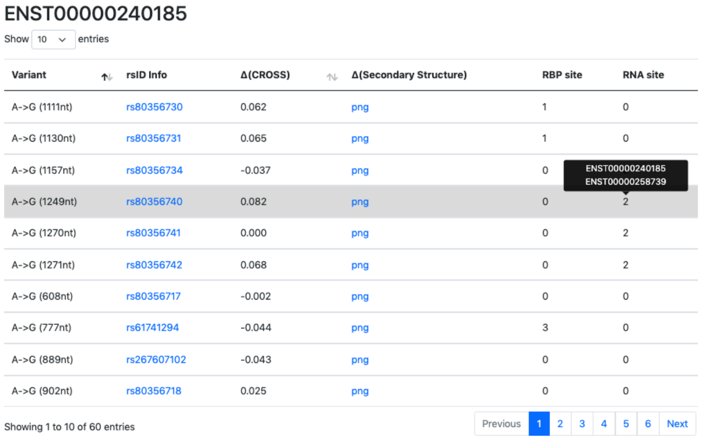
In the variant section, we report the relative position of the SNV in the RNA, as well as the difference in secondary structure propensity of the mutant compared to the WT. The change in the propensity profile is also plotted. For each SNV, we report the RBPs and RNAs that interact with the query RNA in a region containing the SNV. As for the protein counterpart, clicking on the SNV name leads to more information about the diseases related to it.



ENST00000240185

Variant	rsID Info	Δ(CROSS)	Δ(Secondary Structure)	RBP site	RNA site
A->G (1111nt)	rs80356730	0.062	png	1	0
A->G (1130nt)	rs80356731	0.065	png	1	0
A->G (1157nt)	rs80356734	-0.037	png	0	0
A->G (1249nt)	rs80356740	0.082	png	0	2
A->G (1270nt)	rs80356741	0.000	png	0	2
A->G (1271nt)	rs80356742	0.068	png	0	2
A->G (608nt)	rs80356717	-0.002	png	0	0
A->G (777nt)	rs61741294	-0.044	png	3	0
A->G (889nt)	rs267607102	-0.043	png	0	0
A->G (902nt)	rs80356718	0.025	png	0	0

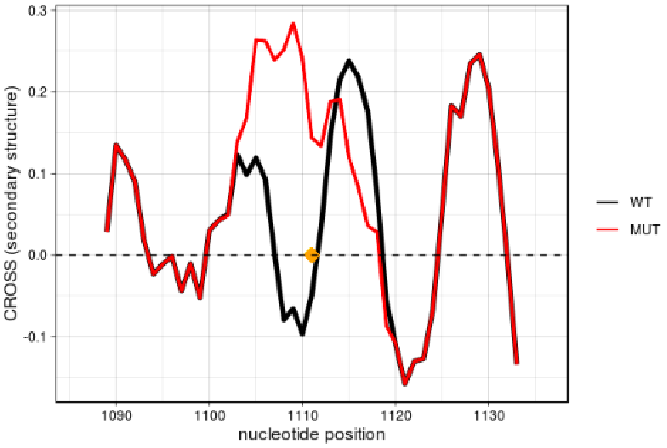
Showing 1 to 10 of 60 entries



ENST00000240185

Variant	rsID Info	Δ(CROSS)	Δ(Secondary Structure)	RBP site	RNA site
A->G (1111nt)	rs80356730	0.062	png	1	0
A->G (1130nt)	rs80356731	0.065	png	1	0
A->G (1157nt)	rs80356734	-0.037	png	0	0
A->G (1249nt)	rs80356740	0.082	png	0	2
A->G (1270nt)	rs80356741	0.000	png	0	2
A->G (1271nt)	rs80356742	0.068	png	0	2
A->G (608nt)	rs80356717	-0.002	png	0	0
A->G (777nt)	rs61741294	-0.044	png	3	0
A->G (889nt)	rs267607102	-0.043	png	0	0
A->G (902nt)	rs80356718	0.025	png	0	0

Showing 1 to 10 of 60 entries



Finally in the Download section, PRALINE raw data for proteins, RNAs, their interactions and variants are available to the public.