Plateforme d'annotation de variants

Journées du GFCO 2022 – 10/12/2022

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Pas de liens d'intérêt

https://mobidetails.iurc.montp.inserm.fr/MD/

Question 1

- Etes vous un utilisateur régulier de MobiDetails?

(si > 70% de oui, on passe rapidement la présentation générale du logiciel)

Annotation platform

Annotation of genic variants only – for now?

Online DNA Variant Interpretation

davidbaux , welcome to MobiDetails: You can annotate and investigate variants in

19067 genes and 110804 isoforms

Canonical isoforms ~MANE but also some others

TP53

Run a new variant!

Gene info table:

Chr	Strand	Gene name	Genomic Accession #	Synonymous obs/exp* (CI)	Missense obs/exp* (CI)	Loss of function obs/exp* (CI)
17	-	tumor protein p53	NG_017013.2	1.07 (0.91-1.27)	0.82 (0.73-0.92)	0.20 (0.10-0.47)

Transcript info table:

RefSeq transcript**	Ensembl transcript	Number of exons	RefSeq protein	Uniprot ID
NM_001276696.3	ENST00000622645	12	NP_001263625.1	P04637
NM_001276695.2	ENST00000610538	12	NP_001263624.1	P04637
NM_001276695.3	ENST00000610538	12	NP_001263624.1	P04637
NM_001126114.2	ENST00000617185	12	NP_001119586.1	P04637
NM_001126113.2	ENST00000455263	12	NP_001119585.1	P04637
NM_001276696.2	ENST00000622645	12	NP_001263625.1	P04637
NM_001276696.1	ENST00000622645	12	NP_001263625.1	P04637
NM_001276695.1	ENST00000455263	12	NP_001263624.1	P04637
NM_001276760.1	ENST00000269305	11	NP_001263689.1	P04637
NM_000546.6 MD canonical RefSeqSelect MANESelect	ENST00000269305	11	NP_000537.3	P04637
NM_000546.5 RefSeqSelect	ENST00000269305	11	NP_000537.3	P04637
NM_001276760.2	ENST00000620739	11	NP_001263689.1	P04637
NM_001276760.3	ENST00000620739	11	NP_001263689.1	P04637
NM_001276761.2	ENST00000619485	11	NP_001263690.1	P04637
NM_001126112.2	ENST00000269305	11	NP_001119584.1	P04637
NM_001276761.3	ENST00000619485	11	NP_001263690.1	P04637
NM_001276761.1	ENST00000269305	11	NP_001263690.1	P04637
NM_001126118.1	ENST00000610292	10	NP_001119590.1	P04637
NM_001276698.3	ENST00000618944	8	NP_001263627.1	P04637

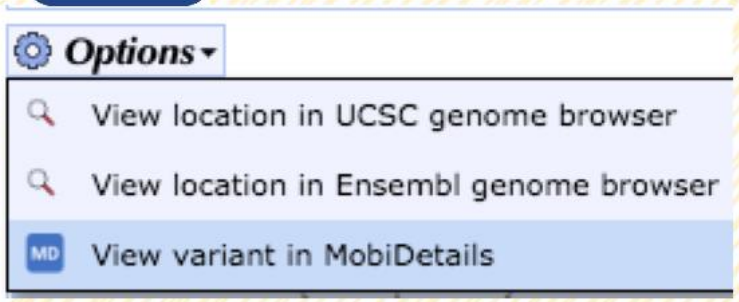
Annotations

References and versions of all resources used in MD:

Resource	Version	Reference
CADD	v1.6	Rentzsch et al., 2019
ClinGenSpecificationRegistry	v20220607	None et al., None
ClinPred	2018_hg19	Alirezaie et al., 2018
ClinVar	v20220606	Landrum et al., 2016
dbMTS	v1.0	Chang et al., 2020
dbNSFP	v4.1a	Liu et al., 2016
dbscSNV	v1.1	Jian et al., 2014
dbSNP	v154	Sherry et al., 2001
EpiSignature	v20210901	Foroutan et al., 2021
Eigen	v1.1	Ionita-Laza et al., 2016
FatHMM	from dbNSFP	Shihab et al., 2013
gnomAD	v2.0.1;v3	Karczewski et al., 2020
HexoSplice	Live web site	Tubeuf et al., 2020
InterVar	API	Li et al., 2017
LitVar	API	Allot et al., 2018
LOVD	API	Fokkema et al., 2011
MaxEntScan	2004	Yeo et al., 2004
MetaDome	v1.0.1	Wiel et al., 2019
MetaSVM-LR	from dbNSFP	Dong et al., 2015
Mistic	v1	Chennen, Weber et al., 2020
MPA	1.1	Yauy et al., 2018
MuPIT	API	Niknafs et al., 2013
Mutalyzer	API	Wildeman et al., 2008
mygene.info	API	Xin et al., 2016
panelApp	API	Stark et al., 2021
Polyphen-2	from dbNSFP	Adzhubei et al., 2010
regulomeDB	Live web site	Boyle et al., 2012
REVEL	from dbNSFP	Ioannidis et al., 2016
SIFT	from dbNSFP	Ng et al., 2003
SPiP	v2.1	Preprint: Leman et al., 2020
spliceAI	v1.3	Jaganathan et al., 2019
spliceAIlookup	API	None et al., None
SpliceAI-visual	internal implementation	De Sainte Agathe et al., 2022
togows	API	Katayama et al., 2010
VariantValidator	API	Freeman et al., 2018

https://mobidetails.iurc.montp.inserm.fr/MD/about

LOVD website



MD website

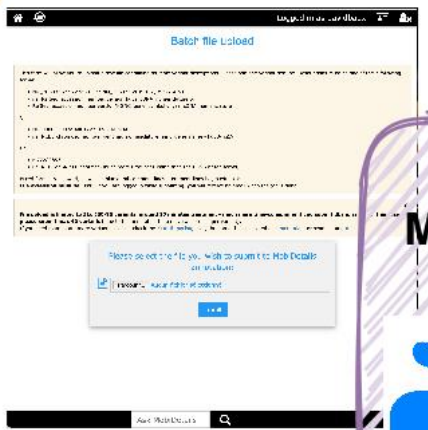
- HGVS cDNA
- HGVS genomic;HGNC gene symbol
- dbSNP rsid

Ask MobiDetails:

Obtain annotations

Single variant annotation

Batch variants annotations



MD website: Batch file upload

MD Live API: get JSON objects

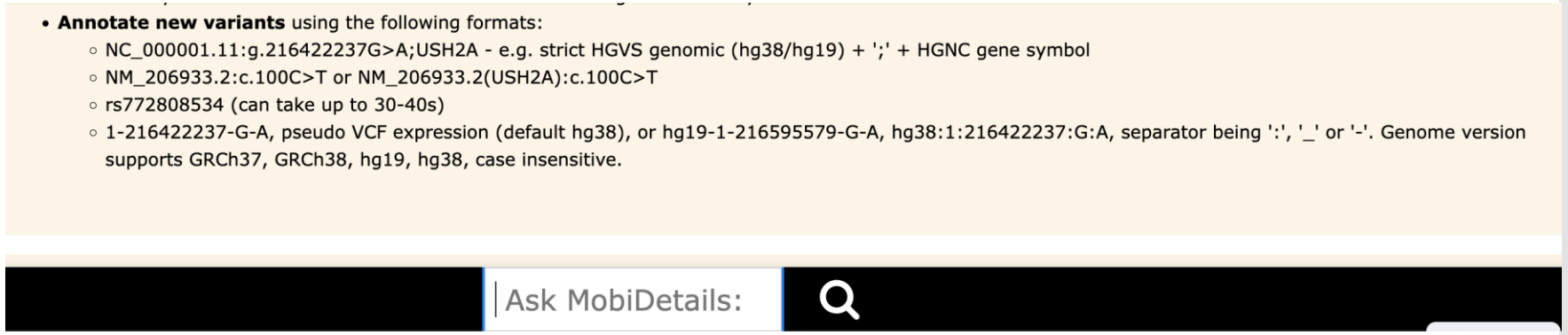
MobiDetails API (MDAPI) 0.5.2 OAS3

MDAPI.yaml

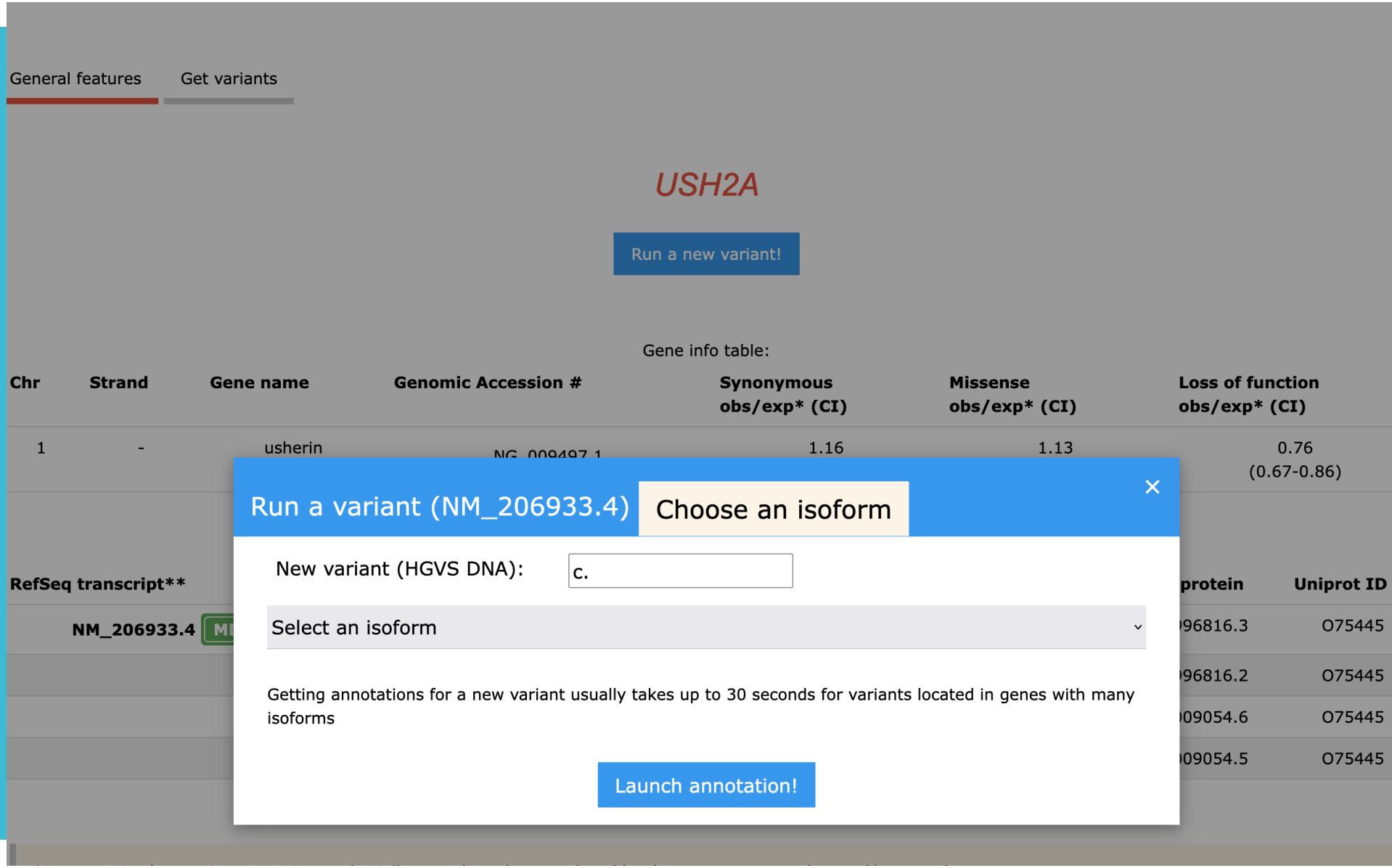
Get genes and variants descriptions in MobiDetails, in order to improve your interpretation of genetic variations.

Generate annotations: MD website

- Nomenclature HGVS génomique + HGNC gene symbol:
  NC_000001.11:g.216422237G>A;USH2A
- Nomenclature HGVS ou pseudo-HGVS transcrit:
  NM_206933.4:c.100C>T ou NM_206933.4(USH2A):c.100C>T
- dbSNP rsid
  rs772808534
- Pseudo-VCF
  1-216422237-G-A, hg19-1-216595579-G-A, GRCh38:1:216422237:G:A,…



Generate annotations: MD website



Question 2

- Si vous êtes utilisateur, de quelle manière préférez-vous annoter les variants:
    a. Page gène + HGVS c.
    b. Fichier batch
    c. Moteur de recherche (MC) + NM_ + HGVS c.
    d. MC dbsnp id
    e. MC HGVS g. + HGNC gene symbol
    f. MC pseudo-VCF
    g. API
    h. Lien externe: LOVD, archigene…

Interpretation!

- Jusqu'à 8 sections d'interprétation:
  - Nomenclatures: hg19, hg38, génomique, transcrit, protéique, pseudo-VCF
  - Positions: exon/intron, site d'epissage le plus proche, lien MetaDome, sequences WT et mutante, pubmed IDs
  - Frequencies & db: gnomAD 2&3, dbSNP, clinvar, clingen criteria, classification ACMG, LOVD
  - Predictions (générales): CADD, Eigen, MPA
  - Splicing: MaxEntScan, dbscSNV, SPiP, SpliceAI, SpliceAI-visual (radar chart)
  - Missense: 9 prédicteurs dont 5 « meta » (radar chart)
  - miRNA target sites (dbMTS)
  - Classification

X
hg19
hg19 UCSC
ESP6500
gnomAD v2
CADD
hg19 InterVar
Clinvar search
dbSNP
RegulomeDB
hg38
hg38 UCSC
gnomAD v3
deCAF
CADD
hg38 InterVar
HexoSplice
AlphaFold
MD BRCA1

This variant has been annotated on at least one other transcript. You can check the following links:

- NM_007294.3(*BRCA1*):c.5074G>T

Nomenclatures

Features	Values	Descriptions
HGNC gene symbol (ID):	*BRCA1* (1100)	*HGNC gene symbol and corresponding ID*
HGVS DNA on transcript:	NM_007294.4:c.5074G>T MD canonical	*HGVS full nomenclature at DNA level on transcript*
HGVS Protein:	NP_009225.1:p.(Asp1692Tyr)	*HGVS full nomenclature at protein level*
HGVS genomic (hg19):	chr17:g.41219625C>A	*HGVS full nomenclature at genomic level (hg19)*
HGVS strict genomic (hg19):	NC_000017.10:g.41219625C>A	*HGVS full strict nomenclature at genomic level (hg19)*
pseudo VCF (hg19):	17-41219625-C-A	*chr-pos-ref-alt (hg19)*
HGVS genomic (hg38):	chr17:g.43067608C>A	*HGVS full nomenclature at genomic level (hg38)*
HGVS strict genomic (hg38):	NC_000017.11:g.43067608C>A	*HGVS full strict nomenclature at genomic level (hg38)*
pseudo VCF (hg38):	17-43067608-C-A	*chr-pos-ref-alt (hg38)*

Positions

Features	Values	Descriptions
Position in transcript:	Exon 16	*Exon/intron position in NM_007294.4*
Position / splice site	1 bp from donor	*Position relative to the nearest splice site*
Position / protein	1692 / 1862	*Position relative to the protein*
Position / domain	BRCT 1 (1642 - 1736)	*Position in a protein domain (UNIPROT: P38398)*
Position tolerance	0.30 : intolerant - Transcript view	*MetaDome score, the closer to 0, the more intolerant to variation*
Wild type sequence	GACTACTCATGTTGTTATGAAAACA G GTATACCAAGAACCTTTACAGAATA	*Wild type DNA sequence +/- 25 bp*
Mutant sequence	GACTACTCATGTTGTTATGAAAACA T GTATACCAAGAACCTTTACAGAATA	*Mutant type DNA sequence +/- 25 bp*

show Pubmed links | Export to DEFGEN (hg19) | Export to DEFGEN (hg38)

BRCA1 Get transcripts

Please first retrieve the transcripts Analyse Protein

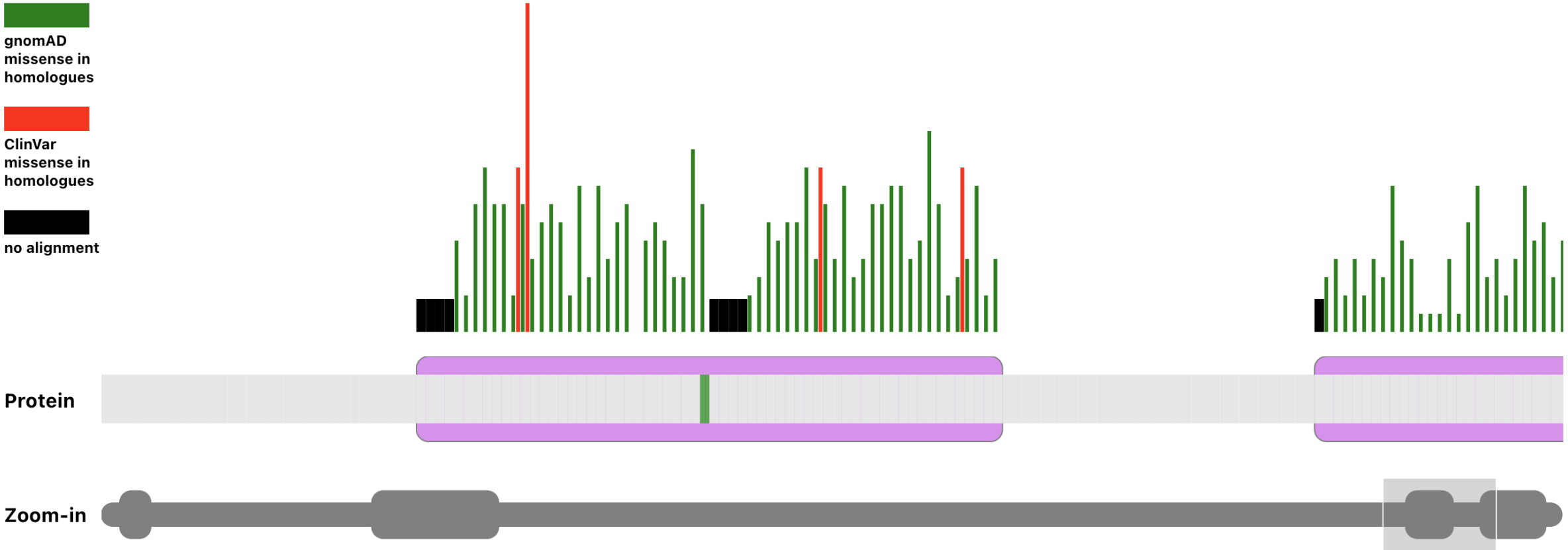
Graph control

Protein of BRCA1 (GENCODE: ENST00000357654.3, RefSeq: NM_007294.3, UniProt: P38398)

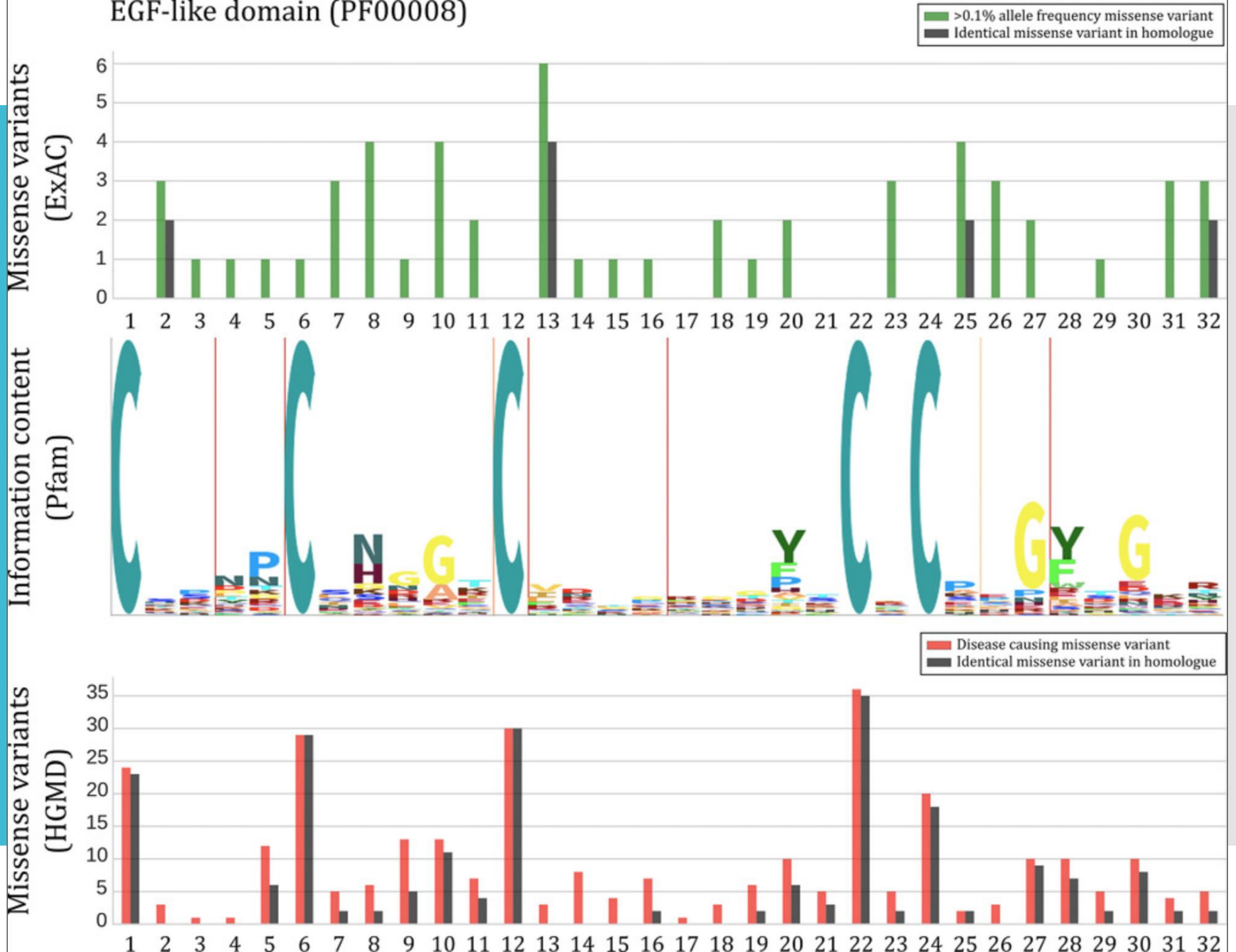
Show Meta-domain landscape Show Protein's Tolerance Landscape

Display ClinVar variants: in this protein in homologue protein domains

Download current visualization Reset Zoom Reset Page



MetaDome



Wiel et al., 2017

BRCA1 Get transcripts

Please first retrieve the transcripts Analyse Protein

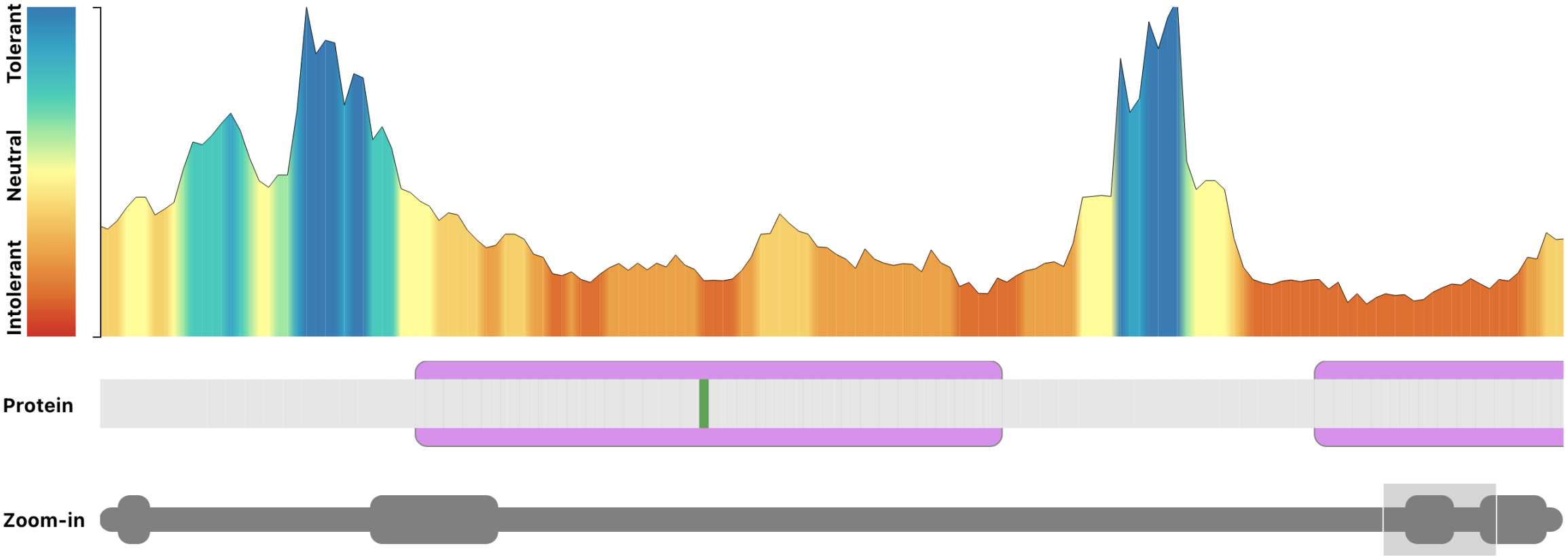
Graph control

Protein of BRCA1 (GENCODE: ENST00000357654.3, RefSeq: NM_007294.3, UniProt: P38398)

Show Meta-domain landscape Show Protein's Tolerance Landscape

Display ClinVar variants: in this protein in homologue protein domains

Download current visualization Reset Zoom Reset Page



PubMed links of articles citing this variant (49 citations) :

X

Full results available at LitVar2.

- Vallon-Christersson, J. et al., 2001 (Hum Mol Genet):
  Functional analysis of BRCA1 C-terminal missense mutations identified in breast and ovarian cancer families.
- Gudmundsdottir, K. et al., 2003 (Br J Cancer):
  CYP17 promoter polymorphism and breast cancer risk in males and females in relation to BRCA2 status.
- Karchin, R. et al., 2007 (PLoS Comput Biol):
  Functional impact of missense variants in BRCA1 predicted by supervised learning.
- Rowling, P. J. et al., 2010 (J Biol Chem):
  Toward classification of BRCA1 missense variants using a biophysical approach.
- Lee, M. S. et al., 2010 (Cancer Res):
  Comprehensive analysis of missense variations in the BRCT domain of BRCA1 by structural and functional assays.
- Iversen, E. S. Jr et al., 2011 (Cancer Epidemiol Biomarkers Prev):
  A computational method to classify variants of uncertain significance using functional assay data with application to BRCA1.
- Karinen, S. et al., 2011 (PLoS One):
  Data integration workflow for search of disease driving genes and genetic variants.
- Thomassen, M. et al., 2012 (Breast Cancer Res Treat):
  Characterization of BRCA1 and BRCA2 splicing variants: a collaborative report by ENIGMA consortium members.
- Janavicius, R. et al., 2010 (EPMA J):
  Founder BRCA1/2 mutations in the Europe: implications for hereditary breast-ovarian cancer prevention and control.

LitVar2

PMID23239986 • PMC3519833 Jan 1, 2012

Analysis of 30 Putative BRCA1 Splicing Mutations in Hereditary Breast and Ovarian Cancer Families Identifies Exonic Splice Site Mutations That Escape In Silico Prediction

Wappenschmidt B, Becker AA ... Schmutzler RK • PLoS One

RESULTS

Only 3/6 variants, 4304G>A,Q1395Q, 4794G>A,E1559K and 5193G>C, **D1692H** are predicted to be deleterious according to HSF and MaxEntScan algorithms (table S1).

Cite

PMID21769658 Apr 1, 2012

Characterization of BRCA1 and BRCA2 splicing variants: a collaborative report by ENIGMA consortium members.

Thomassen M, Blanco A ... Vega A • Breast Cancer Res Treat

ABSTRACT

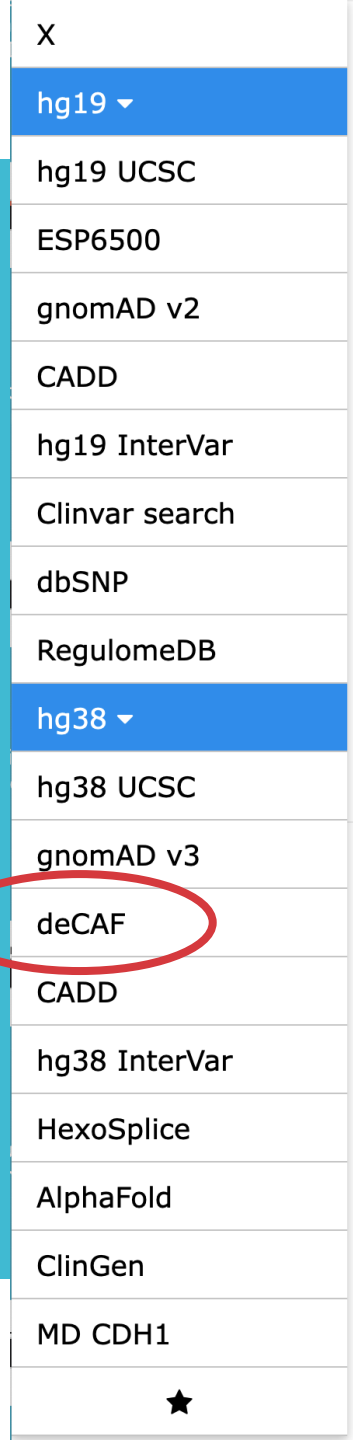
Abnormal splicing patterns expected to lead to a non-functional protein were observed for 7 variants (BRCA1 c.441+2T>A, c.4184_4185+2del, c.4357+1G>A, c.4987-2A>G, **c.5074G>C**, BRCA2 c.316+5G>A, and c.8754+3G>C).

Cite

Population Frequencies and Databases

Features	Values	Descriptions
gnomAD exome:	No match in gnomAD exome	*v2.0.1 Exomes global MAF*
gnomAD genome:	No match in gnomAD genome	*v2.0.1 Genomes global MAF*
gnomAD v3:	No match in gnomADv3	*v3 Genomes global MAF*
dbSNP rsid:	rs80187739	*Identifier for NCBI dbSNP*
Clinvar:	Pathogenic	*Clinvar interpretation*
hg38 InterVar:	Likely pathogenic with the following criteria: PM1 PM2 PP3 PP5 BP1 PM2: Absent from controls (or at extremely low frequency if recessive) in Exome Sequencing Project, 1000 Genomes Project, or Exome Aggregation Consortium	*Semi-automated ACMG classification - click on the intervar link to adjust* *- passing the mouse over a criterion will display the definition*
LOVD Matches:	Global Variome shared LOVD	*LOVD match in public instances*
LOVD Effect Reported:	unknown: 11 function affected: 16 function not affected: 2 function probably affected: 3	*Effects reported by LOVD submitters*
LOVD Effect Concluded:	not classified: 31 function affected: 1	*Effects concluded by LOVD curators*

deCAF



deCAF

deCODE Allele Frequency Browser

Search for a gene, variant or region…

Examples:

PCSK9
chr13-32398489-A-T
chr1:55039479-55039500

deCAF is a resource of variant allele frequencies made available to the public.

The dataset encompasses SNP and indel variant calls in 150,119 individuals from whole genome sequencing of the UK biobank.

deCAF

Variant

chr1-216247118-C-A

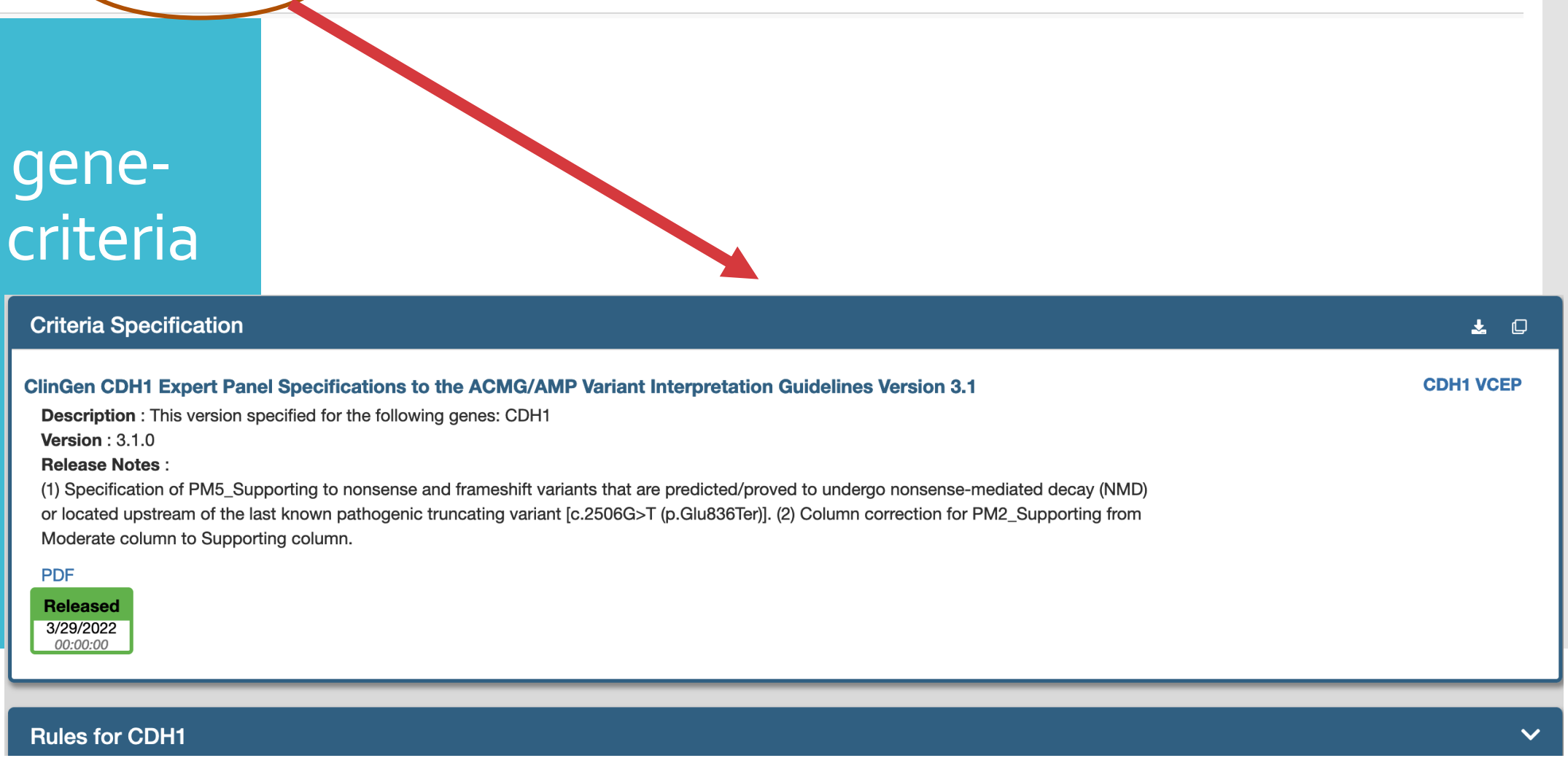
Max Impact	MODERATE
Max Consequence	missense_variant
HGVS Consequence	NP_009054.5:p.Cys759Phe,NP_996816.2:p.Cys759Phe
Gene	USH2A

Allele Count	508
Allele Number	276334
Allele Frequency	1.84e-3
Num Homozygotes	1

Ancestry	Allele Count	Allele Num	N Homozygotes	Allele Frequency
African	0	5926	0	0
British/Irish	508	264316	1	1.92e-3
South-Asian	0	6092	0	0

Clingen gene-specific criteria

gnomAD v3:	No match in gnomADv3	*v3 Genomes global MAF*
dbSNP rsid:	rs115408226	*Identifier for NCBI dbSNP*
Clinvar:	Uncertain_significance	*Clinvar interpretation*
ClinGen criteria:	GN007	*ClinGen ACMG specific rules for CDH1*



Clingen gene-specific criteria

PS2

Original ACMG Summary

De novo (both maternity and paternity confirmed) in a patient with the disease and no family history.
Note: Confirmation of paternity only is insufficient. Egg donation, surrogate motherhood, errors in embryo transfer, etc. can contribute to non-maternity.

Very Strong

≥Two patients meet the HDGC individual phenotype criteria w/ parental confirmation.

Strong

One patient meets the HDGC individual phenotype criteria w/ parental confirmation.

Instructions: Use ClinGen's de novo point system for a highly specific phenotype (see Table S2).

PS3

Original ACMG Summary

Well-established in vitro or in vivo functional studies supportive of a damaging effect on the gene or gene product.
Note: Functional studies that have been validated and shown to be reproducible and robust in a clinical diagnostic laboratory setting are considered the most well-established.

Strong

RNA assay demonstrating abnormal out-of-frame transcripts.

Moderate

RNA assay demonstrating abnormal in-frame transcript.

Instructions: This rule can only be applied to demonstrate splicing defects.

PS4

Original ACMG Summary

The prevalence of the variant in affected individuals is significantly increased compared to the prevalence in controls.
Note 1: Relative risk (RR) or odds ratio (OR), as obtained from case-control studies, is >5.0 and the confidence interval around the estimate of RR or OR does not include 1.0. See manuscript for detailed guidance.
Note 2: In instances of very rare variants where case-control studies may not reach statistical significance, the prior observation of the variant in multiple unrelated patients with the same phenotype, and its absence in controls, may be used as moderate level of evidence.

Very Strong

≥Sixteen families meet HDGC criteria.

Strong

Four - Fifteen families meet HDGC criteria.

Moderate

Two or three families meet HDGC criteria.

Supporting

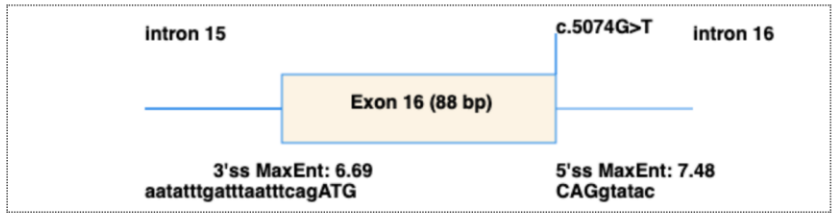
One family meets HDGC criteria.

Question 3

- Quel est votre outil favori pour analyser l'epissage:
  a. MaxEntScan
  b. SSF-like algorithm (e.g. HSF)
  c. NNSplice
  d. SpliceAI
  e. SpliceAI-visual
  f. Squirls
  g. Pangolin
  h. SPiP

Splicing predictions

The exonic splicing context of the variant including natural splice sites scores is summarized in the graph below:



MaxEntScan scores are presented in the two following tables. Selected scores have:

- a |variation| > 15% and
- a raw score for mutant or wild-type of at least 3

The upper sequence shows the variation site in red, and the lower sequence the putative splice site considered by MaxEntScan (putative introns are shown as lower case and exons as upper case).

Position / splice site 1 bp from donor

MaxEntScan 5'ss scores

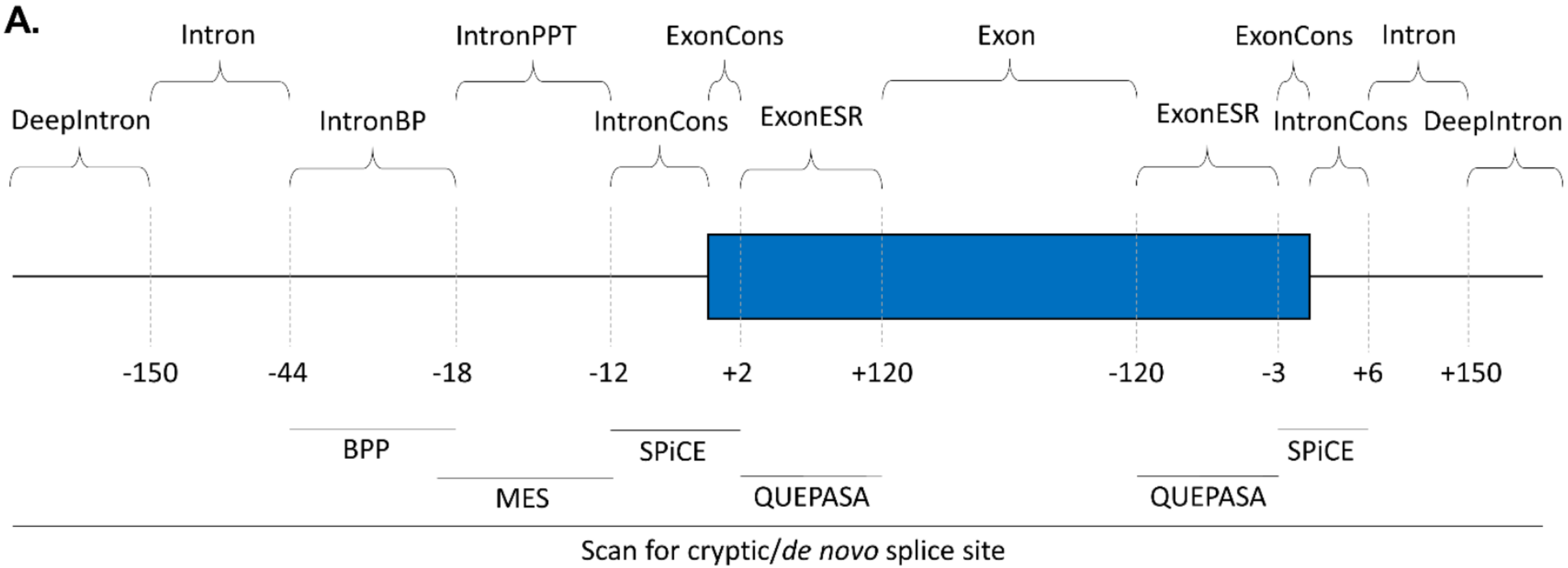
Wild-type sequence	Score	Mutant sequence	Score	Variation(%)
... CAGGTATAC ... ... **CAG**gtatac ...	7.48	... CATGTATAC ... ... **CAT**gtatac ...	-2.47	-133.02

MaxEntScan 3'ss scores

Wild-type sequence	Score	Mutant sequence	Score	Variation(%)
No MaxEnt 3'ss score performed (exonic variant far form 3'ss).				

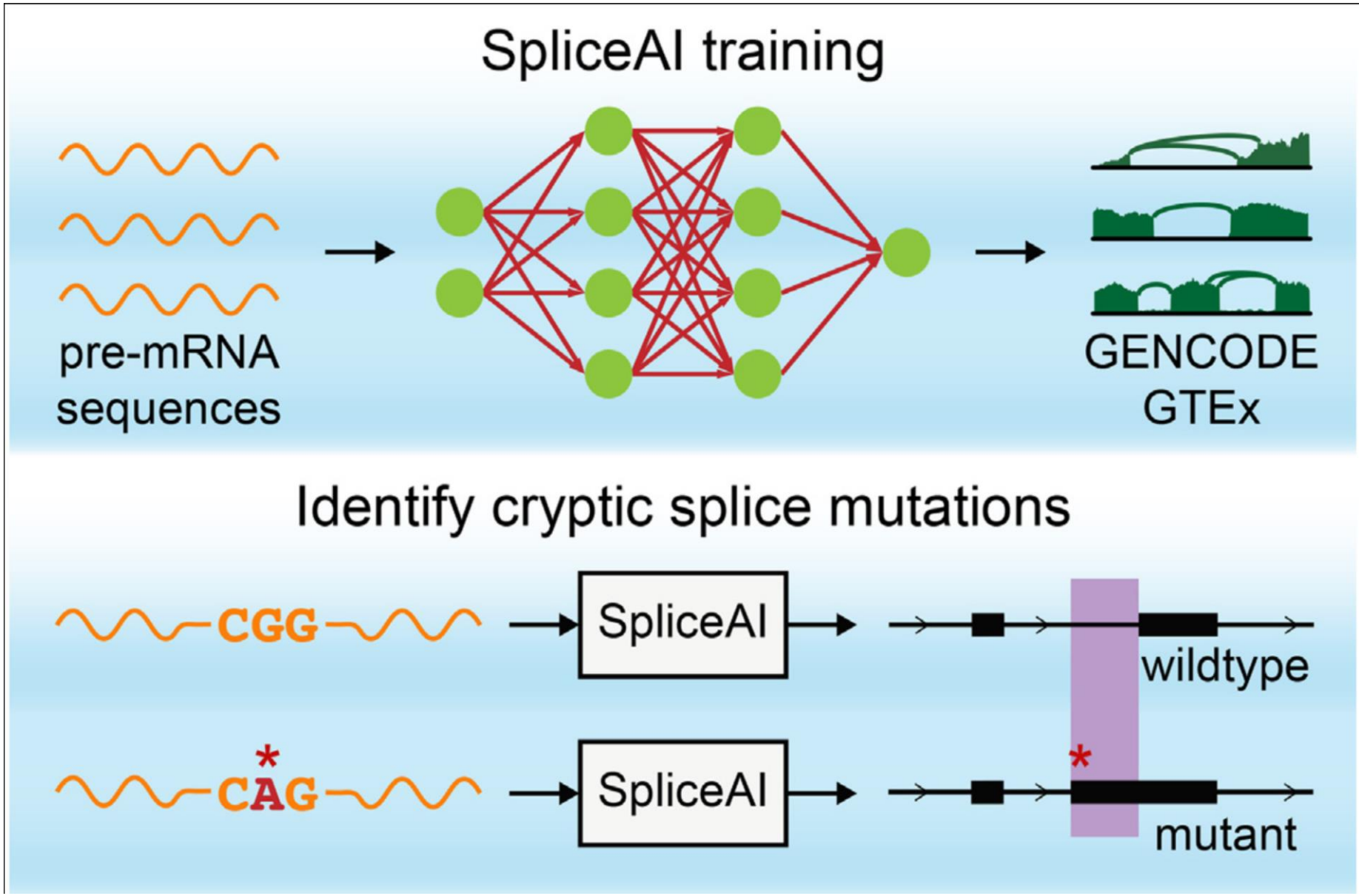
SPiP results and predictions:

Features	Values	Descriptions
Interpretation	Alteration of the consensus splice site	Overall interpretation of SPiP
Risk	98.41 % [91.47 % - 99.96 %]	The risk for the variant to alter splicing



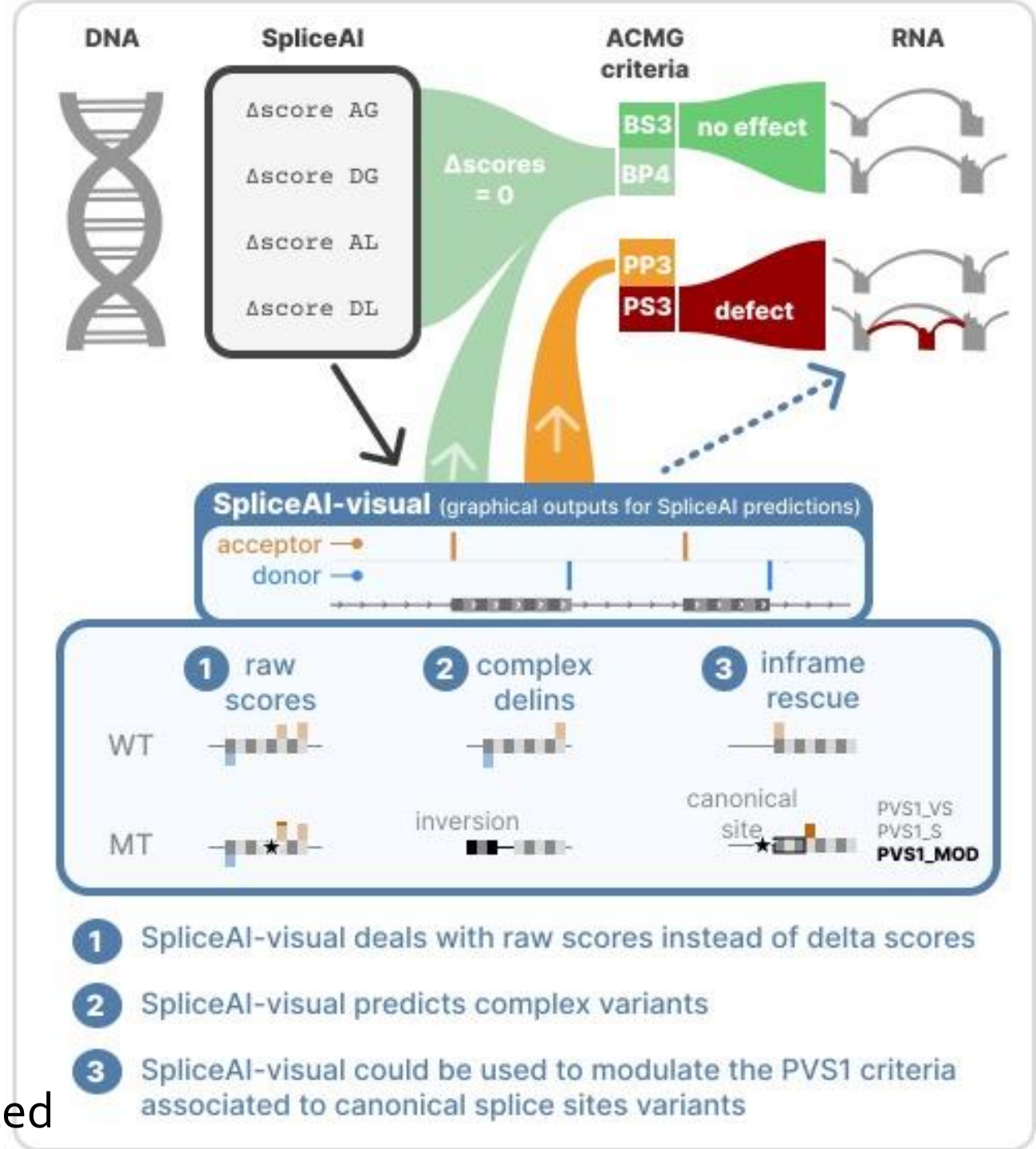
Leman et al., 2022

SpliceAI-visual



Jaganathan et al., 2019

SpliceAI-visual



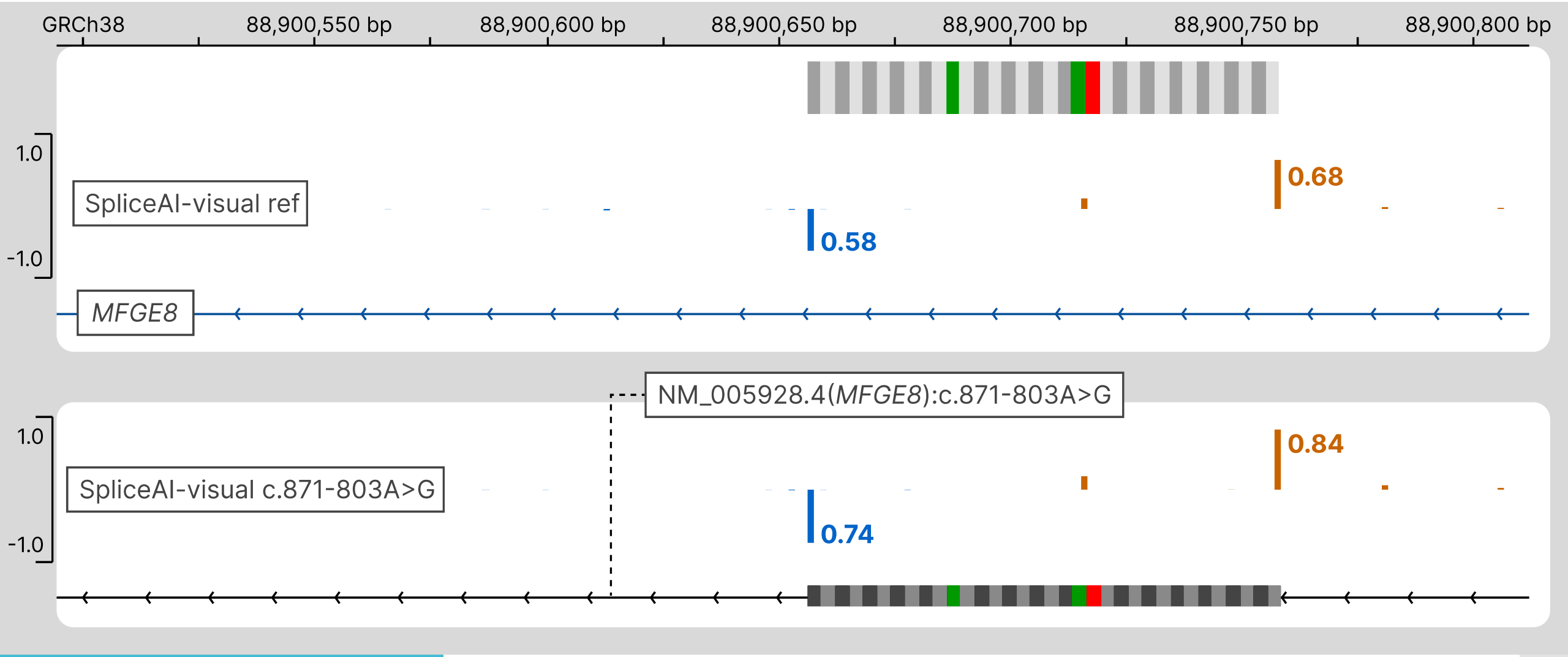
J.M. De Sainte Agathe et al., submitted

SpliceAI-visual

- SpliceAI
  - sortie numérique
  - Delta scores
- SpliceAI-visual
  - Sortie graphique
  - Scores bruts
  - Indels!

spliceAI AG:	0.00 (43)
spliceAI AL:	0.00 (-2)
spliceAI DG:	0.16 (43)
spliceAI DL:	0.02 (-1)
spliceAI lookup (500) AG:	0.15 (144)
spliceAI lookup (500) AL:	0.00 (-2)
spliceAI lookup (500) DG:	0.16 (43)
spliceAI lookup (500) DL:	0.00 (-1)

***MFGE8* c.871-803A>G**
Yamaguchi et al., 2010



***MFGE8* c.871-803A>G**

Yamaguchi et al., 2010

J.M. De Sainte Agathe et al., submitted

Missense predictions

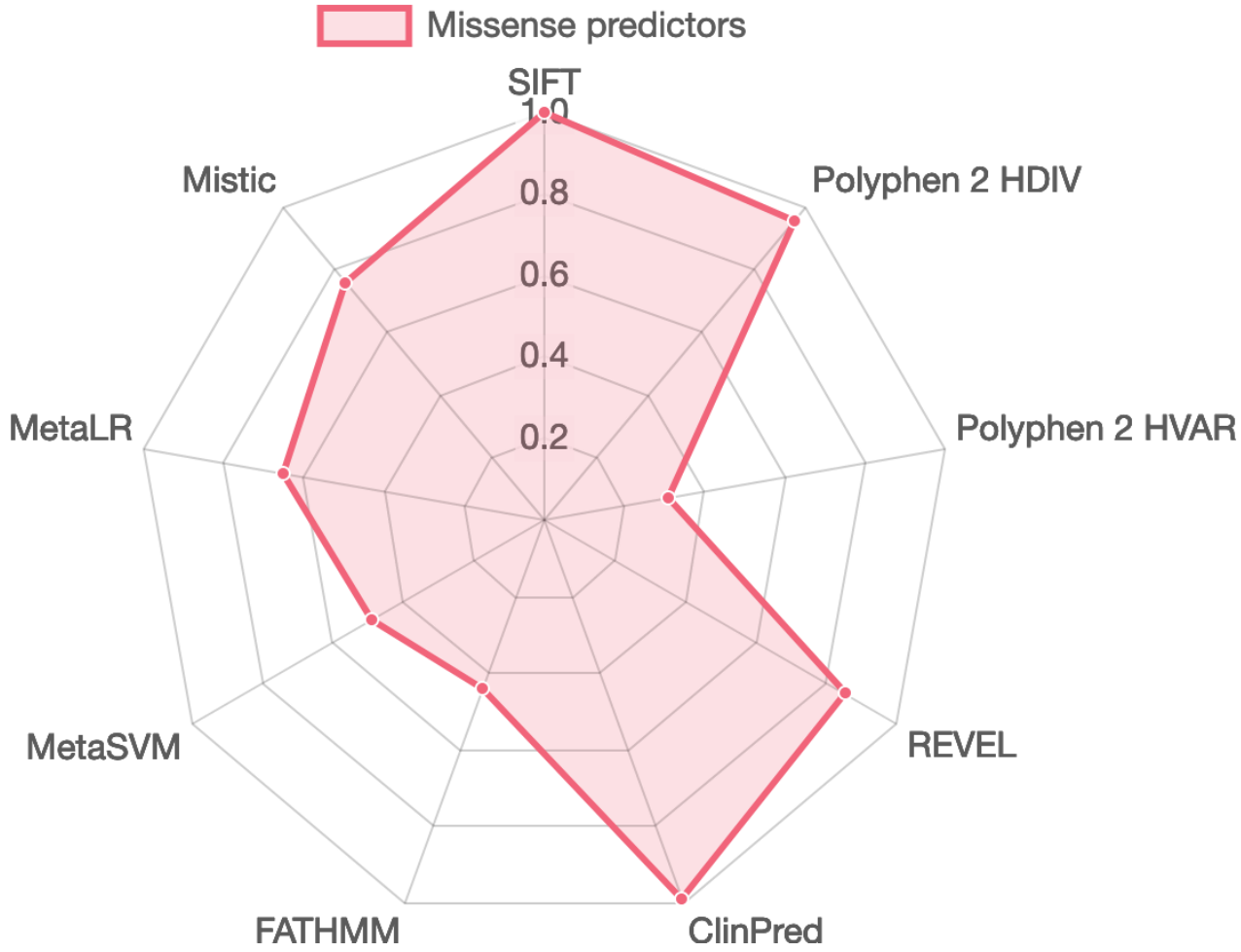
Missense predictions: p.(Asp1692Tyr)

Features	Values	Prediction	Descriptions
SIFT:	0.0	Damaging	*Threshold < 0.05 for Damaging - single score*
Polyphen 2 HumDiv:	0.958	Probably Damaging	*Thresholds > 0.454|0.957 for Possibly and Probably Damaging - single score*
Polyphen 2 HumVar:	0.311	Benign	*Thresholds > 0.447|0.909 for Possibly and Probably Damaging - single score*
Fathmm:	-1.25	Tolerated	*Threshold ≤ -1.5 for Damaging - single score*
REVEL:	0.852	Damaging	*Thresholds 0.2|0.5 for Benign, Uncertain, Damaging - meta score*
ClinPred:	0.990	Damaging	*Threshold ≥ 0.5 for Damaging - meta score*
Meta SVM:	0.4280 (10)	Damaging	*Threshold ≥ 0 for Damaging (reliabilty index: 0-10), 10:high - meta score*
Meta LR:	0.6531 (10)	Damaging	*Threshold ≥ 0.5 for Damaging (reliabilty index: 0-10), 10:high - meta score*
Mistic:	0.76	Damaging	*Threshold ≥ 0.5 for Damaging - meta score*

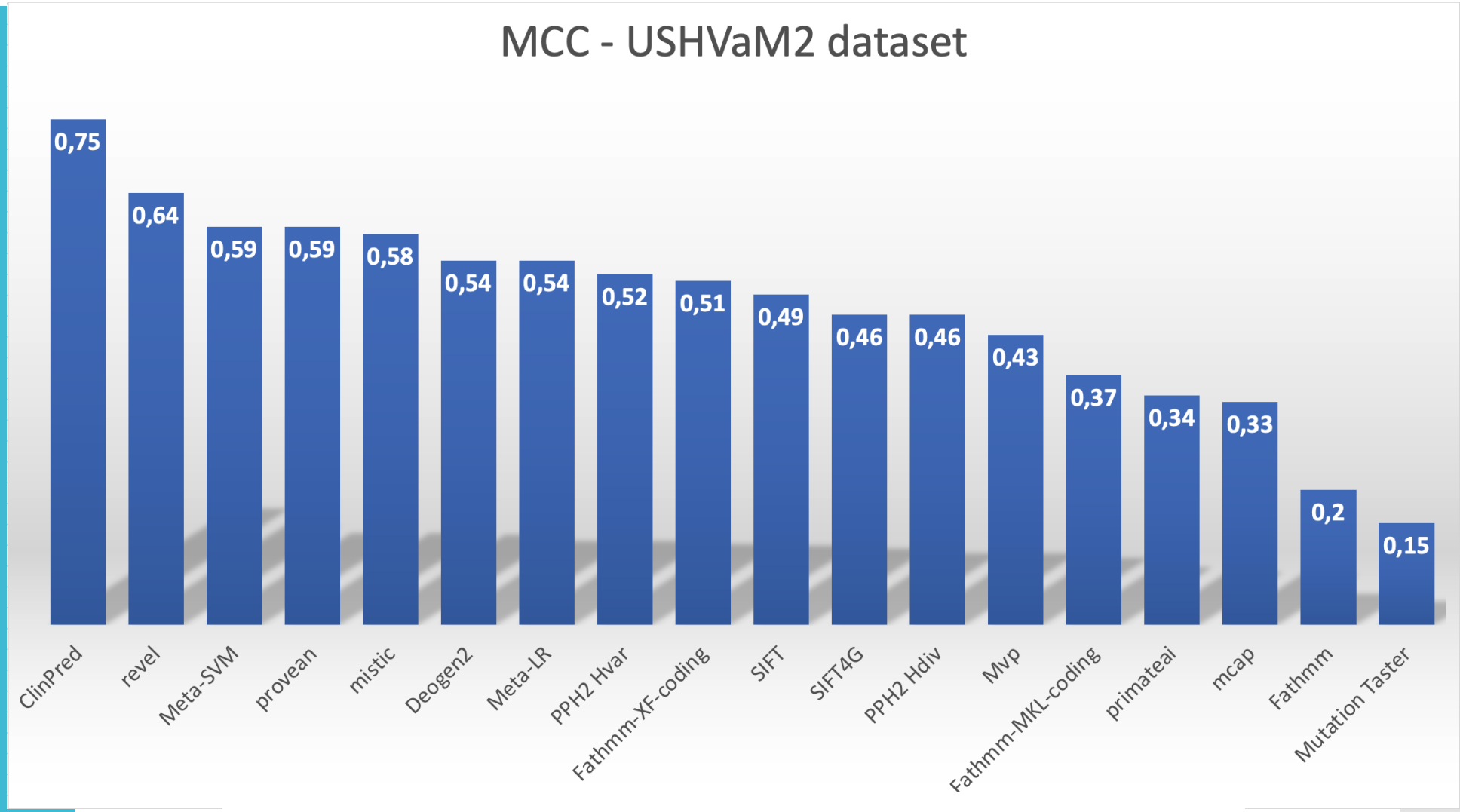
Missense predictions

Radar view of missense predictors

Values are normalised (0-1), 0 being the less damaging and 1 the most for each predictor.
Mean normalised score of all single predictors: 0.677 (2.709 / 4) - for meta predictors: 0.749 (3.745 / 5)



1633 manually curated variants in 100+ genes: 505 ~pathogenic / 1128 ~neutral

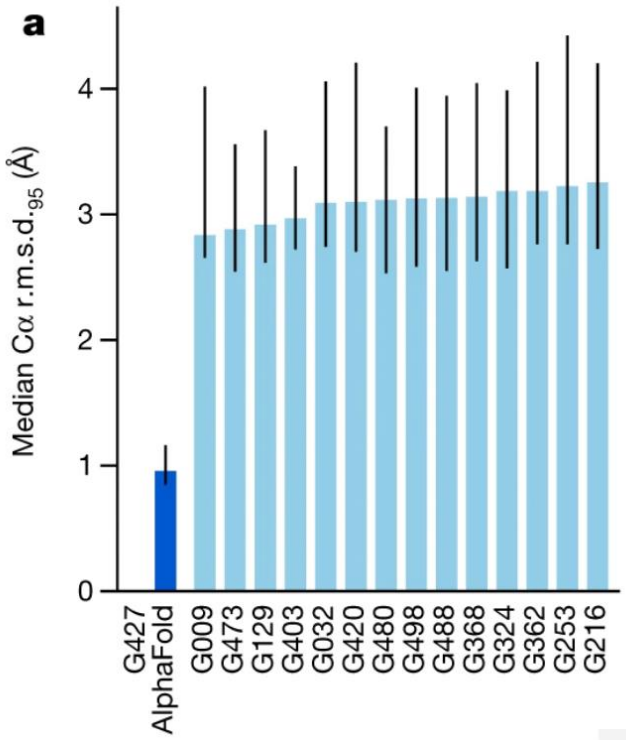


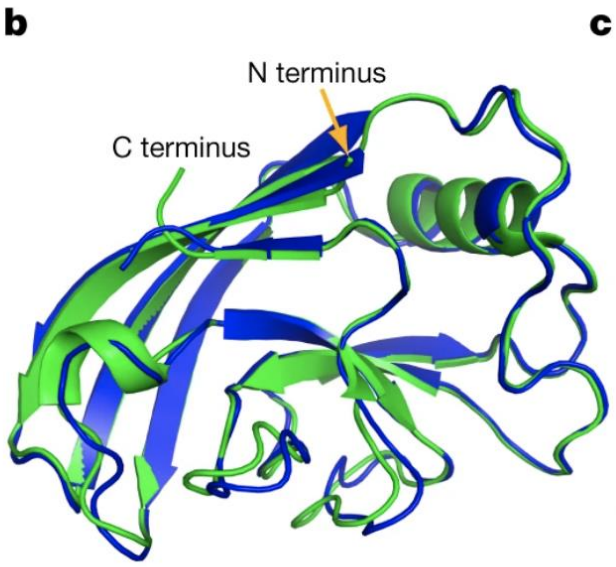
$$MCC = \frac{TP \times TN - FP \times FN}{\sqrt{(TP + FN)(TN + FP)(TP + FP)(TN + FN)}}.$$

proportion of analysed variants?

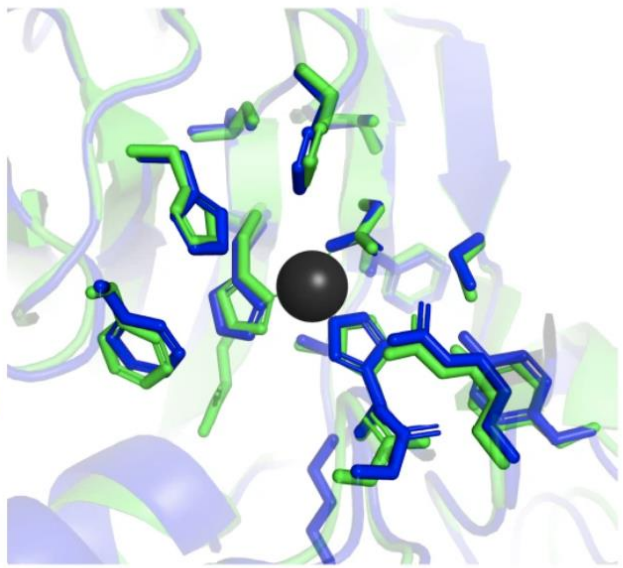
U2 dataset	% analysed pathogenic	% analysed neutral
ClinPred	99,21	99,56
revel	99,21	99,29
Meta-SVM	99,21	99,29
provean	41,58	48,23
mistic	95,05	95,74
Deogen2	97,03	93,71
Meta-LR	99,21	99,29
PPH2 Hvar	97,03	88,56
Fathmm-XF-coding	96,24	96,37
SIFT	94,26	90,51
SIFT4G	99,21	98,58
PPH2 Hdiv	97,03	88,56
Mvp	99,21	64,1
Fathmm-MKL-coding	100	99,38
primateai	98,81	96,37
mcap	97,43	42,64
Fathmm	51,09	67,91
Mutation Taster	98,81	98,49

DeepMind EMBL-EBI

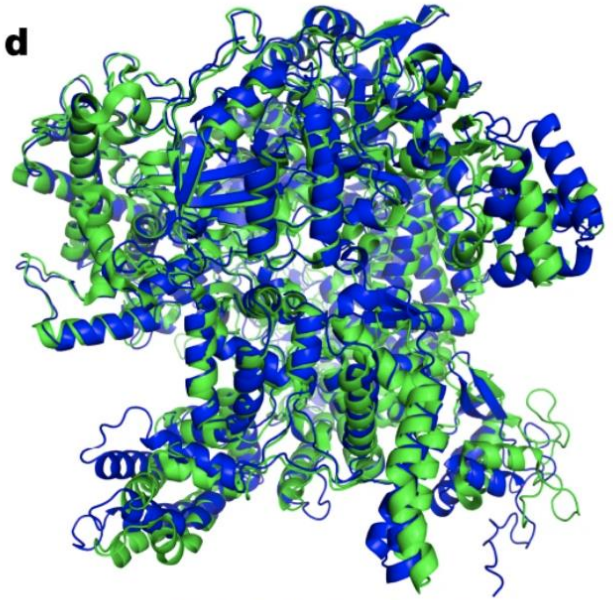




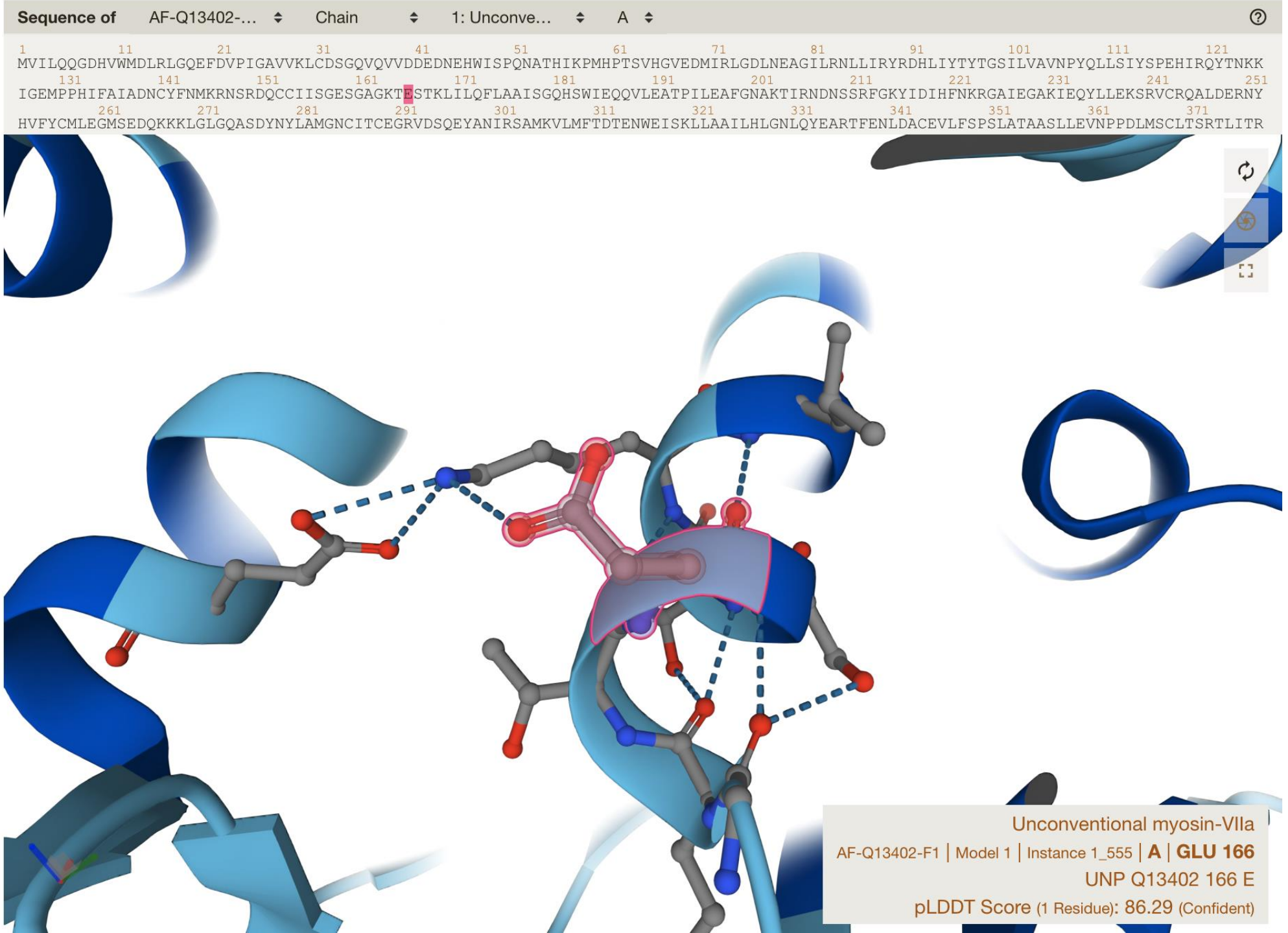
AlphaFold Experiment
r.m.s.d.$_{95}$ = 0.8 Å; TM-score = 0.93



AlphaFold Experiment
r.m.s.d. = 0.59 Å within 8 Å of Zn



AlphaFold Experiment
r.m.s.d.$_{95}$ = 2.2 Å; TM-score = 0.96


Sequence of AF-Q13402-... Chain 1: Unconve... A
1 11 21 31 41 51 61 71 81 91 101 111 121
MVILQQGDHVWMDLRLGQEFDVPIGAVVKLCDSGQVQVVDDEDNEHWISPQNATHIKPMHPTSVHGVEDMIRLGDLNEAGILRNLLIRYRDHLIYTYTGSILVAVNPYQLLSIYSPEHIRQYTNKK
131 141 151 161 171 181 191 201 211 221 231 241 251
IGEMPPHIFAIADNCYFNMKRNSRDQCCIISGESGAGKTESTKLILQFLAAISGQHSWIEQQVLEATPILEAFGNAKTIRNDNSSRFGKYIDIHFNKRGAIEGAKIEQYLLEKSRVCRQALDERNY
261 271 281 291 301 311 321 331 341 351 361 371
HVFYCMLEGMSEDQKKKLGLGQASDYNYLAMGNCITCEGRVDSQEYANIRSAMKVLMFTDTENWEISKLLAAILHLGNLQYEARTFENLDACEVLFSPSLATAASLLEVNPPDLMSCLTSRTLITR
Unconventional myosin-VIIa
AF-Q13402-F1 | Model 1 | Instance 1_555 | A | GLU 166
UNP Q13402 166 E
pLDDT Score (1 Residue): 86.29 (Confident)

Add your classification

Classification History

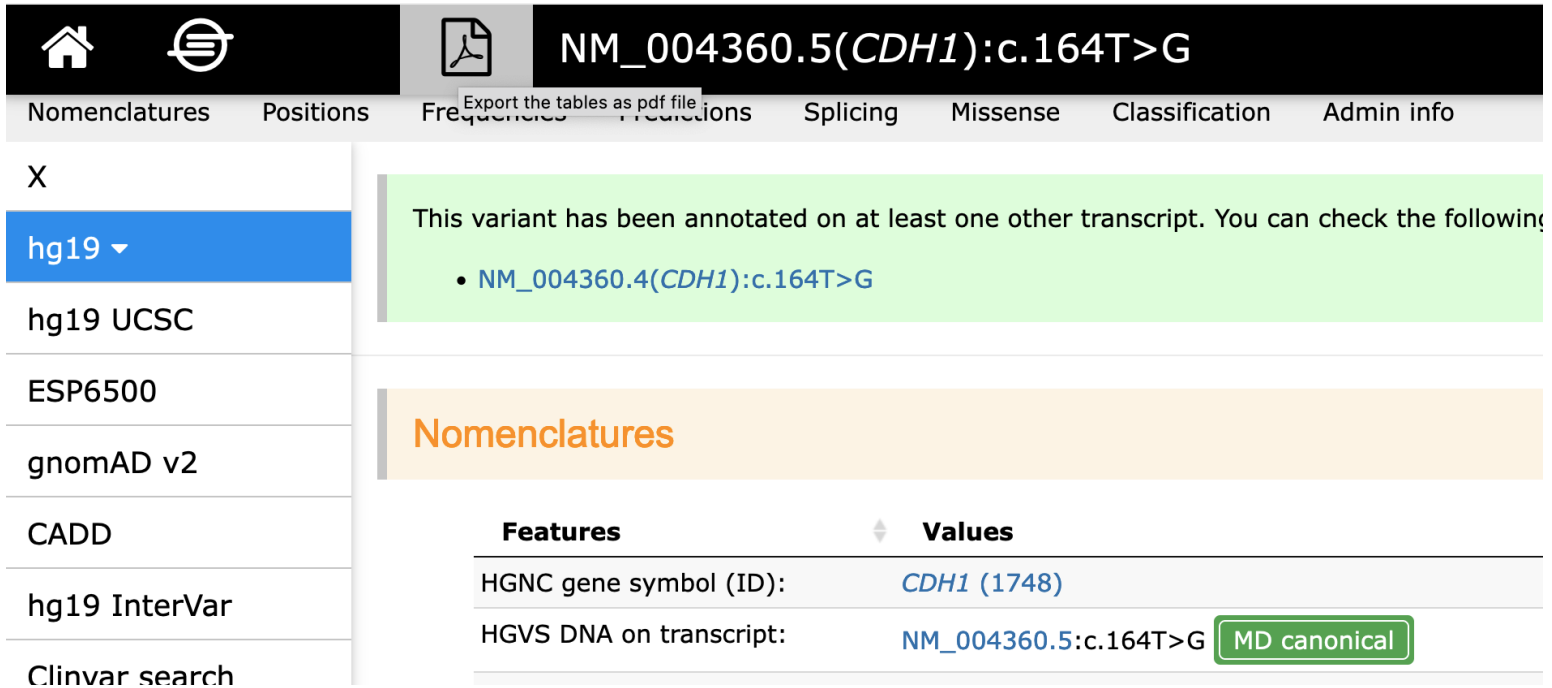
By assigning an ACMG class to this variant, you also contribute to the international knowledge on DNA variants, as we will submit the variant and the classification to the Global Variome Shared LOVD (Read more).

Your LOVD export status is currently On - This means the data will be exported.
You can modify it at your profile page.

Variant	User	Date	ACMG Classification	Comments
NM_000492.3(*CFTR*):c.220C>T Current	CFTR-France	2020-06-18	Class 4 (likely pathogenic)	None
NM_000492.3(*CFTR*):c.220C>T Current	CFTR-France	2022-10-06	Class 5 (pathogenic)	CFTR-RD-causing

- Multiple classes by multiple users
- Secured contact form
- Classification history
- Classification and variant automatically sent to GVLOVDShared

Export pdf


NM_004360.5(CDH1):c.164T>G
Export the tables as pdf file
Nomenclatures
Positions
Splicing
Missense
Classification
Admin info
X
hg19
hg19 UCSC
ESP6500
gnomAD v2
CADD
hg19 InterVar
Clinvar search
This variant has been annotated on at least one other transcript. You can check the following
NM_004360.4(CDH1):c.164T>G
Nomenclatures
Features
Values
HGNC gene symbol (ID):
CDH1 (1748)
HGVS DNA on transcript:
NM_004360.5:c.164T>G
MD canonical

Export pdf

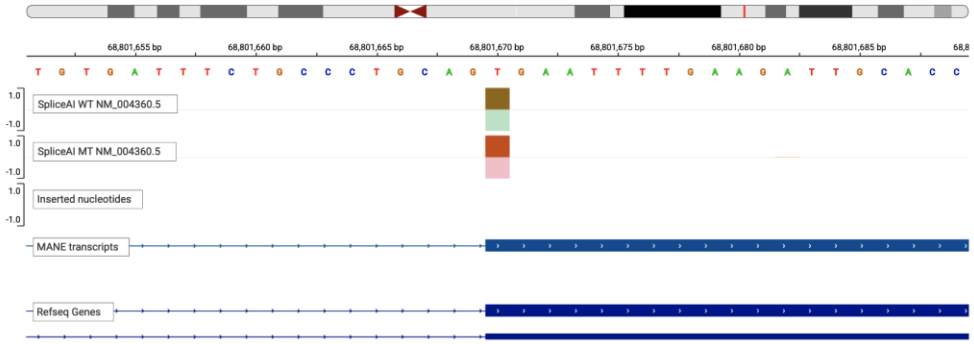
NM_004360.5(CDH1):c.164T>G

- MobiDetails

Table of Content

Click on a page number to get to the corresponding page (i.e. page numbers are clickable ;)).

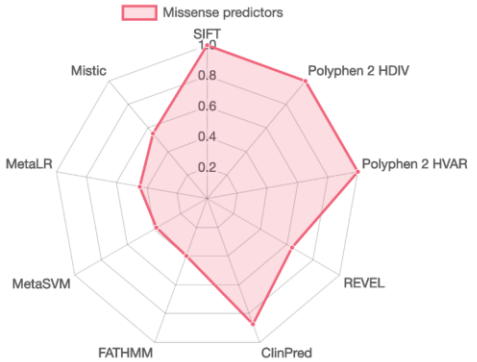
Export pdf



Missense predictions

Missense radar

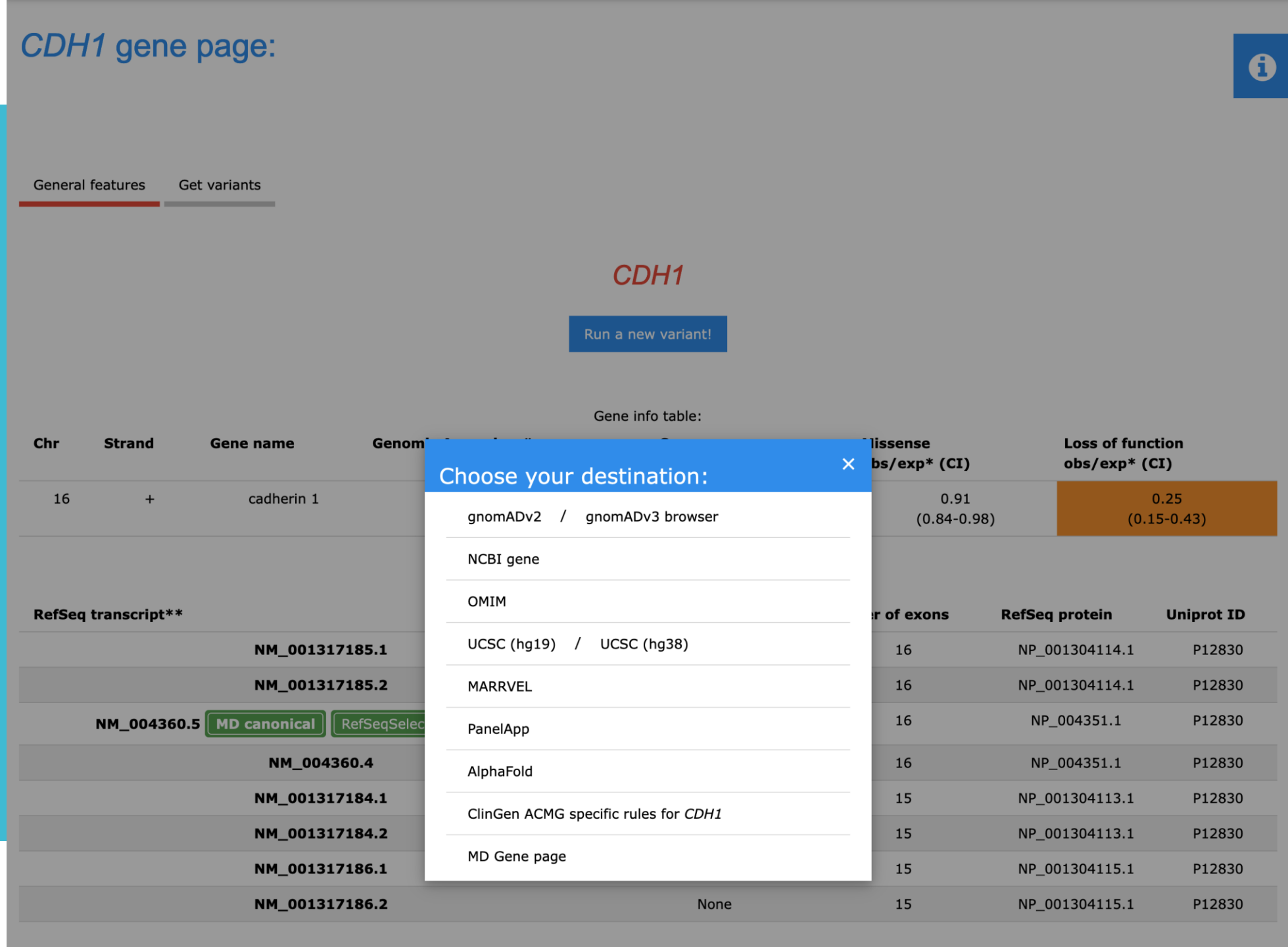
Values are normalised (0-1), 0 being the less damaging and 1 the most for each predictor.



Missense predictions

Features	Values	Prediction	Descriptions
SIFT:	0.0	Damaging	Threshold < 0.05 for Damaging - single score
Polyphen 2 HumDiv:	1.0	Probably Damaging	Thresholds > 0.454|0.957 for Possibly and Probably Damaging - single score
Polyphen 2 HumVar:	1.0	Probably Damaging	Thresholds > 0.447|0.909 for Possibly and Probably Damaging - single score
Fathmm:	-0.06	Tolerated	Threshold ≤ -1.5 for Damaging - single score
REVEL:	0.640	Damaging	Thresholds 0.2|0.5 for Benign, Uncertain, Damaging - meta score
ClinPred:	0.876	Damaging	Threshold ≥ 0.5 for Damaging - meta score
Meta SVM:	-0.0994 (9)	Tolerated	Threshold ≥ 0 for Damaging (reliabilty index: 0-10), 10:high - meta score
Meta LR:	0.4486 (9)	Tolerated	Threshold ≥ 0.5 for Damaging (reliabilty index: 0-10), 10:high - meta score
Mistic:	0.55	Damaging	Threshold ≥ 0.5 for Damaging - meta score

Retrieve gene information



Registered users have access to special features

- Classify variants, contact other users
- Manage your preferences, get an API token (key)

Username: davidbaux

Institute: Montpellier University Hospital

Country: France

E-mail: david.baux@inserm.fr

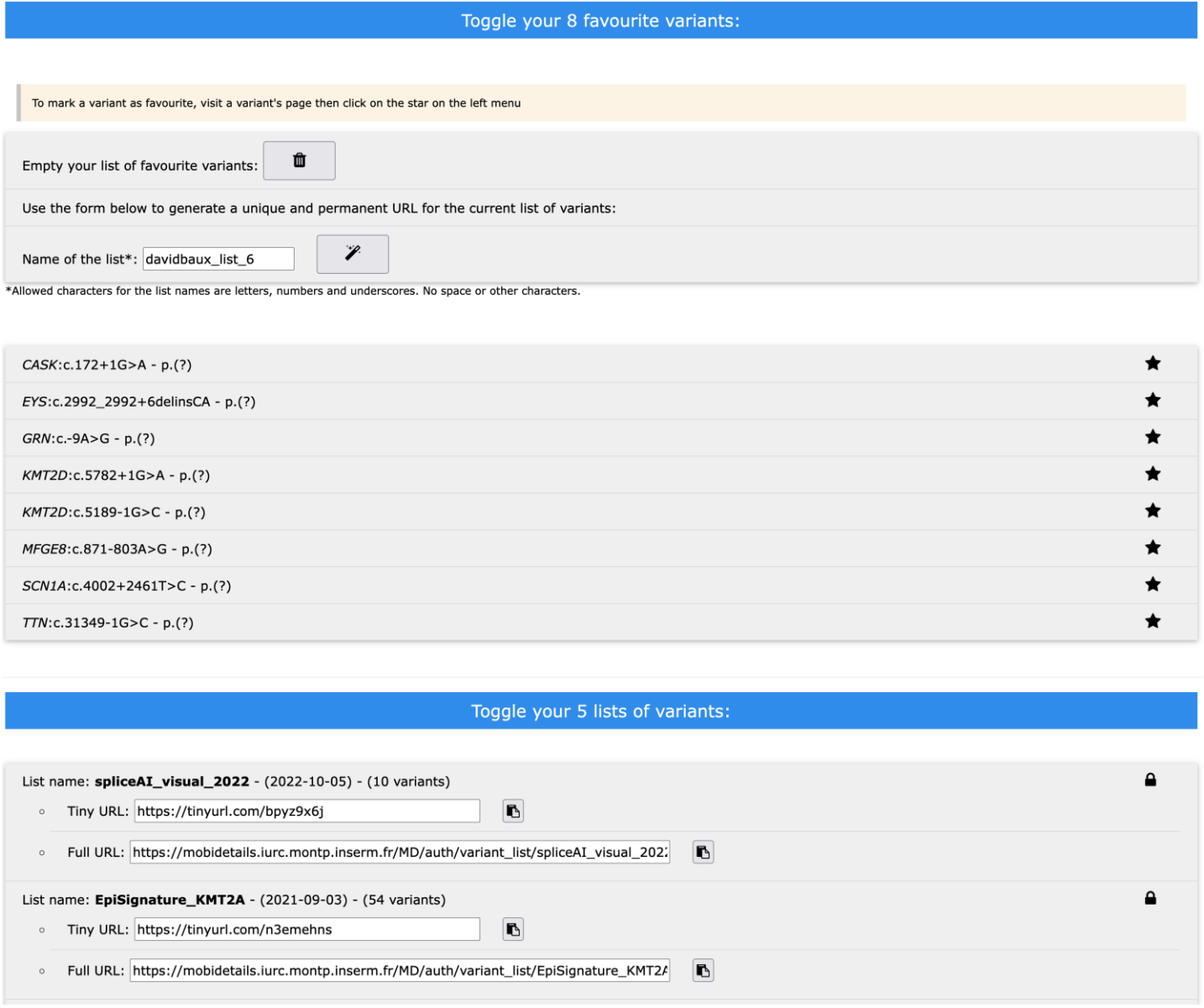
Contact service is **enabled** --

LOVD export is **enabled** --

You are currently identified as an academic user

API key: False_API_key_hhsfhetghtrilbhyelbyhliubelhb

Registered users have access to special features



- Shortcuts to favourite variants
- Manage lists of variants => unique URLs (publications?)

Question 4

- Avez-vous un compte et utilisez vous les fonctionnalités liées?
  a. Je ne suis pas utilisateur
  b. Je ne suis pas utilisateur mais je vais essayer
  c. Je n'ai pas de compte
  d. J'ai un compte mais je ne l'utilise pas
  e. J'ai un compte et je me connecte mais je n'utilise pas spécialement les fonctionnalités liées (classification et variants…)
  f. J'ai un compte et j'utilise les fonctionnalités

Merci aux utilisateurs fidèles et à ceux qui rapportent des bugs / idées d'améliorations:

- Laurence Lodé
- Flora Ponelle
- Alessandro Liquori
- Alexis Billes
- Camille Verebi
- Luke Mansard
- Vuthy Ea
- Juliette Nectoux
- Corinne Thèze
- Thomas Besnard
- …

Les organisations

- CFTR-France
- LOVD
- Archigene

People

Olivier Ardouin

Corinne Bareil

David Baux

Thomas Guignard

Simon Cabello

Souphatta Sasorith

Charles Van Goethem

Laboratoire de génétique moléculaire: groupe neurosensoriel

- Anne-Françoise Roux
- Christel Vaché
- Valérie faugère
- Julie Bianchi
- Corinne Baudoin

Batch file upload

Your batch file submission returned the following results:

NM_033632.3:c.1321C>T

NM_033360.4:c.64C>G

NM_006218.4:c.1606A>G

NM_002524.5:c.419C>T

NM_004448.4:c.929C>T

NM_005228.5:c.2590G>A

NM_004333.6:c.1399T>C

NM_000455.5:c.1283C>G

NM_004304.5:c.3604G>A

NM_001282386.1:c.394C>T

NM_000077.4:c.247C>T

NM_004333.6:c.1803A>T

NM_000546.5:c.376-2A>G

NM_002524.5:c.178G>A

NM_002755.4:c.607G>A

NM_007294.3:c.5153-27_5153-23del

NM_007294.3:c.5559C>G

NM_007294.3:c.130T>A

NM_007294.3:c.4676-1G>A

NM_007294.3:c.5216A>T

NM_000059.3:c.8524C>T

NM_000059.3:c.8893G>T

NM_000059.3:c.10207G>T

NM_000059.3:c.92G>C

NM_000059.3:c.8332_8487dup: returned an error: ' MobiDetails currently only accepts variants of length < 50 bp (SNVs ans small insertions/deletions) '