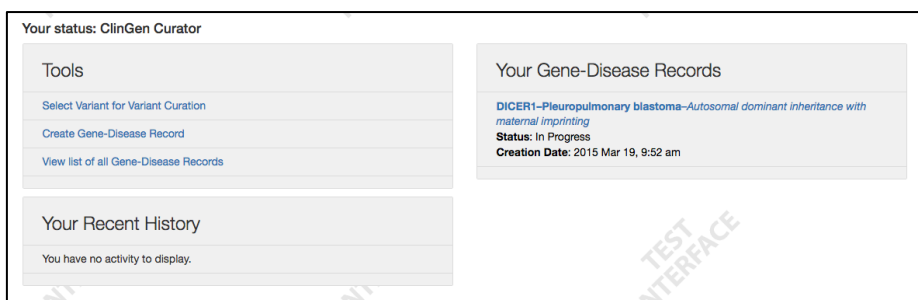


Variant Curation Interface – Quick Start Guide (July 2016)

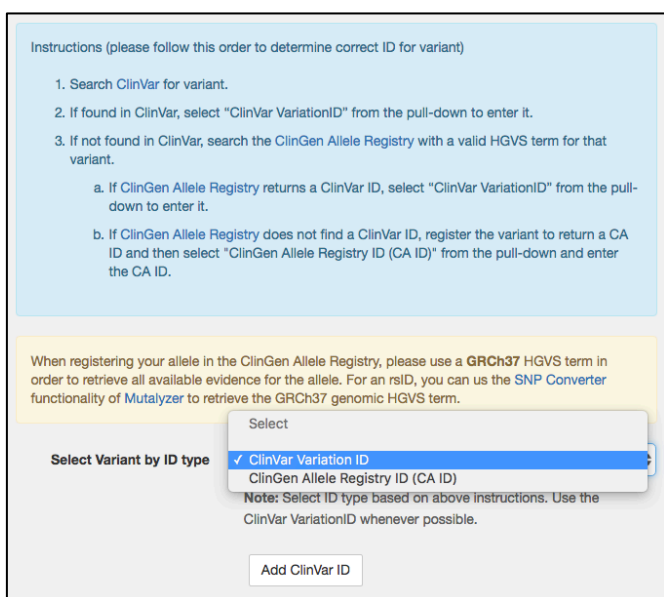
1. Go to <https://variant-curation-alpha1.demo.clinicalgenome.org/> and click the “Login” button. If you are registered but have not yet created a Persona account, you will be prompted to do so.



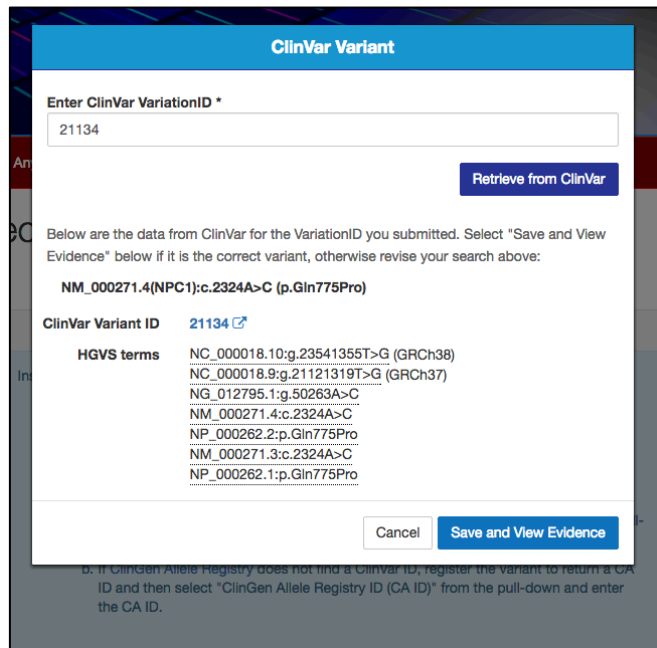
2. Select “Select Variant for Variant Curation” under the “Tools” Section



3. Read instructions carefully on how to select a variant, then choose whether you want to enter a ClinVar variant or a novel variant that you have registered with Baylor’s [ClinGen Allele Registry](#). Select “Add ClinVar ID.”



4. Type in the variant ID (ClinVar VariationID or CA ID, depending on selection), click “Retrieve from ClinVar” (or “Retrieve from ClinGen Allele Registry, if you have entered a CA ID). Once you are convinced the ID you have entered represents the correct variant, select “Save and View Evidence.”



ClinVar Variant

Enter ClinVar VariationID *

21134

Retrieve from ClinVar

Below are the data from ClinVar for the VariationID you submitted. Select “Save and View Evidence” below if it is the correct variant, otherwise revise your search above:

NM_000271.4(NPC1):c.2324A>C (p.Gln775Pro)

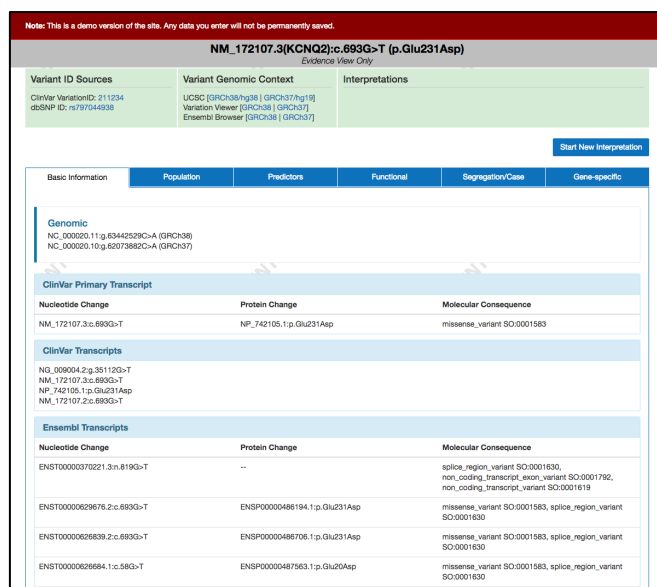
ClinVar Variant ID **21134**

HGVS terms

- NC_000018.10:g.23541355T>G (GRCh38)
- NC_000018.9:g.21121319T>G (GRCh37)
- NG_012795.1:g.50263A>C
- NM_000271.4:c.2324A>C
- NP_000262.2:p.Gln775Pro
- NM_000271.3:c.2324A>C
- NP_000262.1:p.Gln775Pro

Cancel Save and View Evidence

5. You will now be in the “Evidence View” for your selected variant. You can see all evidence associated with the variant, clicking between the tabs. In this version, the Basic Information, Population, and Predictors tabs all contain associated evidence for the variant. After viewing the evidence, if you would like to begin an Interpretation, click on the “Start New Interpretation” button in the upper right hand corner.



Note: This is a demo version of the site. Any data you enter will not be permanently saved.

NM_172107.3(KCNQ2):c.693G>T (p.Glu231Asp)

Evidence View Only

Variant ID Sources	Variant Genomic Context	Interpretations
ClinVar VariationID: 211234 dbSNP ID: rs797044938	UCSC [GRCh38/hg38] GRCh37/hg19 Variation Viewer [GRCh38] GRCh37 Ensembl Browser [GRCh38] GRCh37	

Start New Interpretation

Basic Information	Population	Predictors	Functional	Segregation/Case	Gene-specific																					
<p>Genomic</p> <p>NC_000020.11:g.63442529C>A (GRCh38) NC_000020.10:g.62073892C>A (GRCh37)</p> <p>ClinVar Primary Transcript</p> <table border="1"> <thead> <tr> <th>Nucleotide Change</th> <th>Protein Change</th> <th>Molecular Consequence</th> </tr> </thead> <tbody> <tr> <td>NM_172107.3:c.693G>T</td> <td>NP_742105.1:p.Glu231Asp</td> <td>missense_variant SO:0001583</td> </tr> </tbody> </table> <p>ClinVar Transcripts</p> <p>NG_009004.2:g.35112G>T NM_172107.3:c.693G>T NP_742105.1:p.Glu231Asp NM_172107.2:c.693G>T</p> <p>Ensembl Transcripts</p> <table border="1"> <thead> <tr> <th>Nucleotide Change</th> <th>Protein Change</th> <th>Molecular Consequence</th> </tr> </thead> <tbody> <tr> <td>ENST0000027221.3:n.819G>T</td> <td>--</td> <td>splice_region_variant SO:0001630, non_coding_transcript_exon_variant SO:0001782, non_coding_transcript_variant SO:0001619</td> </tr> <tr> <td>ENST0000029676.2:c.693G>T</td> <td>ENSP00000486194.1:p.Glu231Asp</td> <td>missense_variant SO:0001583, splice_region_variant SO:0001630</td> </tr> <tr> <td>ENST0000026639.2:c.693G>T</td> <td>ENSP00000486706.1:p.Glu231Asp</td> <td>missense_variant SO:0001583, splice_region_variant SO:0001630</td> </tr> <tr> <td>ENST0000026684.1:c.58G>T</td> <td>ENSP00000487563.1:p.Glu23Asp</td> <td>missense_variant SO:0001583, splice_region_variant SO:0001630</td> </tr> </tbody> </table>						Nucleotide Change	Protein Change	Molecular Consequence	NM_172107.3:c.693G>T	NP_742105.1:p.Glu231Asp	missense_variant SO:0001583	Nucleotide Change	Protein Change	Molecular Consequence	ENST0000027221.3:n.819G>T	--	splice_region_variant SO:0001630, non_coding_transcript_exon_variant SO:0001782, non_coding_transcript_variant SO:0001619	ENST0000029676.2:c.693G>T	ENSP00000486194.1:p.Glu231Asp	missense_variant SO:0001583, splice_region_variant SO:0001630	ENST0000026639.2:c.693G>T	ENSP00000486706.1:p.Glu231Asp	missense_variant SO:0001583, splice_region_variant SO:0001630	ENST0000026684.1:c.58G>T	ENSP00000487563.1:p.Glu23Asp	missense_variant SO:0001583, splice_region_variant SO:0001630
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6. Once you are in Interpretation mode, you will see the option to evaluate relevant criteria appear on the tab. You can evaluate criteria, enter text that describes the reason for your selection, and save both by clicking the “Save” button. Note that some criteria are disease-dependent, and you will not be able to evaluate these criteria until you have associated your interpretation with a disease (see step 7, below).

Note: This is a demo version of the site. Any data you enter will not be permanently saved.

NM_172107.3(KCNQ2):c.693G>T (p.Glu231Asp)
This interpretation is not yet associated with a disease

Calculate Pathogenicity

Variant ID Sources ClinVar VariationID: 211234 dbSNP ID: rs797044938	Variant Genomic Context UCSC [GRCh38/hg38 GRCh37/hg19] Variation Viewer [GRCh38 GRCh37] Ensembl Browser [GRCh38 GRCh37]	Interpretations My Interpretations: In Progress, (last edited 2016 Jul 16, 2:40 pm) ✓
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Variant Interpretation Record Associate with Disease

BS1 BS2 BS3 BS4 BP1 BP2 BP3 BP4 BP5 BP6 BP7 PP1 PP2 PP3 PP4 PP5 PM1 PM2 PM3 PM4 PM5 PM6 PS1 PS2 PS3 PS4 PVS1

Basic Information Population Predictors Functional Segregation/Case Gene-specific

Highest Minor Allele Frequency
Population: N/A
Source: N/A
Allele Frequency: 0
Variant Alleles: N/A
Total # Alleles Tested: N/A
Desired CR: 95
CI - lower: N/A
CI - upper: N/A
ExAC Constraint Score
View pLI in ExAC

Population Criteria Evaluation

BA1: Allele frequency is > 5% in ExAC, 1000 Genomes, or ESP
PM2: Absent from controls (or at extremely low frequency if recessive) in ExAC, 1000 Genomes, or ESP

BA1 met: ☐
- or -
PM2 met: ☐
MAF cutoff (%): 5

Explain criteria selection:

Note that the “Calculate Pathogenicity” and criteria bar are not functional in this version (indicated by the yellow bar to their left).

7. To associate an Interpretation with a disease and be able to evaluate disease-dependent criteria, save any evaluations and click the “Associate with Disease” button (see above), found toward the upper right. Enter the desired Orphanet ID and click OK. Now all disease-independent criteria evaluation boxes will become active and you will see the disease term under the variant name in the gray title area. Your interpretation, along with the Orphanet ID will also display in the green bar under “My Interpretations.”

Note: This is a demo version of the site. Any data you enter will not be permanently saved.

NM_172107.3(KCNQ2):c.693G>T (p.Glu231Asp)
This interpretation is associated with the disease **Benign familial neonatal seizures**

Calculate Pathogenicity

Variant ID Sources ClinVar VariationID: 211234 dbSNP ID: rs797044938	Variant Genomic Context UCSC [GRCh38/hg38 GRCh37/hg19] Variation Viewer [GRCh38 GRCh37] Ensembl Browser [GRCh38 GRCh37]	Interpretations My Interpretations: ORPHA1949, In Progress, (last edited 2016 Jul 16, 2:53 pm) ✓
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Variant Interpretation Record Edit Disease

BS1 BS2 BS3 BS4 BP1 BP2 BP3 BP4 BP5 BP6 BP7 PP1 PP2 PP3 PP4 PP5 PM1 PM2 PM3 PM4 PM5 PM6 PS1 PS2 PS3 PS4 PVS1

Basic Information Population Predictors Functional Segregation/Case Gene-specific

Note: Click on the home icon at the top of any page to return to the “Dashboard” – if you select the same variant and return to its View Evidence page, you will now see a “Continue Interpretation” button and be able to continue evaluating the same variant. The next version will include improved navigation.