ClinVar

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H3Africa-RDWG/ClinGen Workshop February 4, 2021

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National Center for Biotechnology Information

What is ClinVar?

Using ClinVar

Submitting to ClinVar

ClinVar

- Archive of interpretations of variants relative to conditions
- Variant-level interpretations
  - Assertion/Clinical significance/Interpretation/Classification/
- Fully public and freely available
- Submission-driven database
- Curation support from NCBI staff

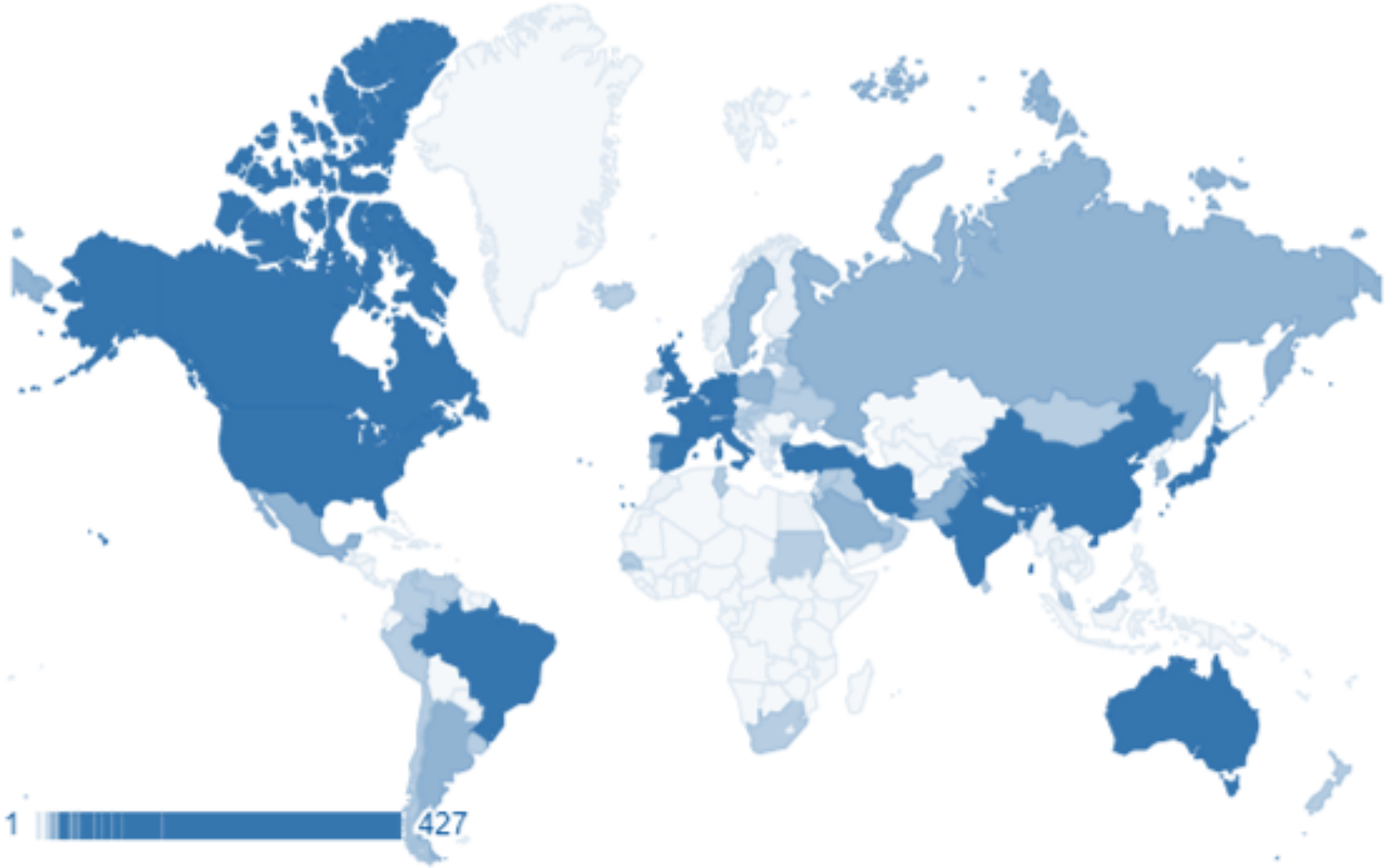
www.ncbi.nlm.nih.gov/clinvar

ClinVar is a global database

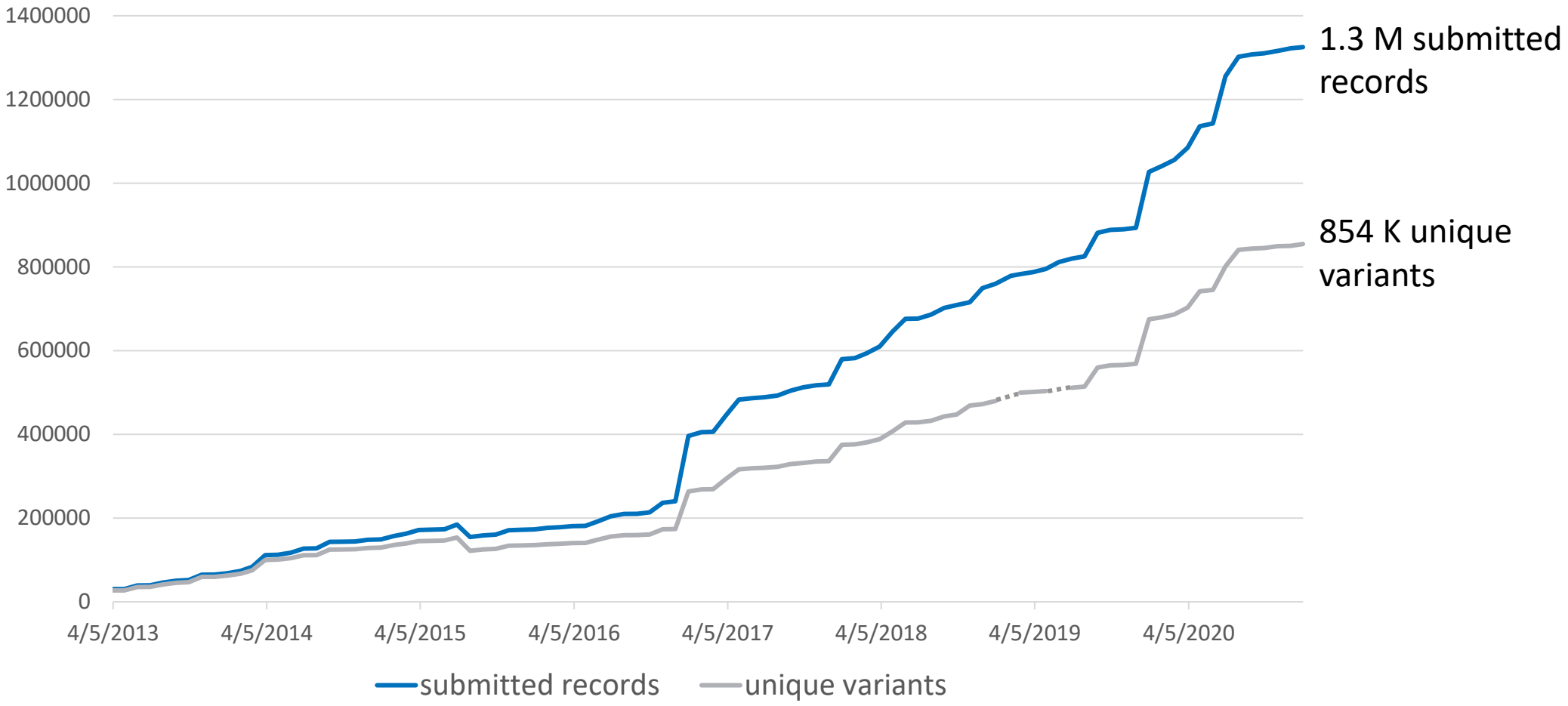
1.3 million
submitted records

Submitted by
>1800 organizations

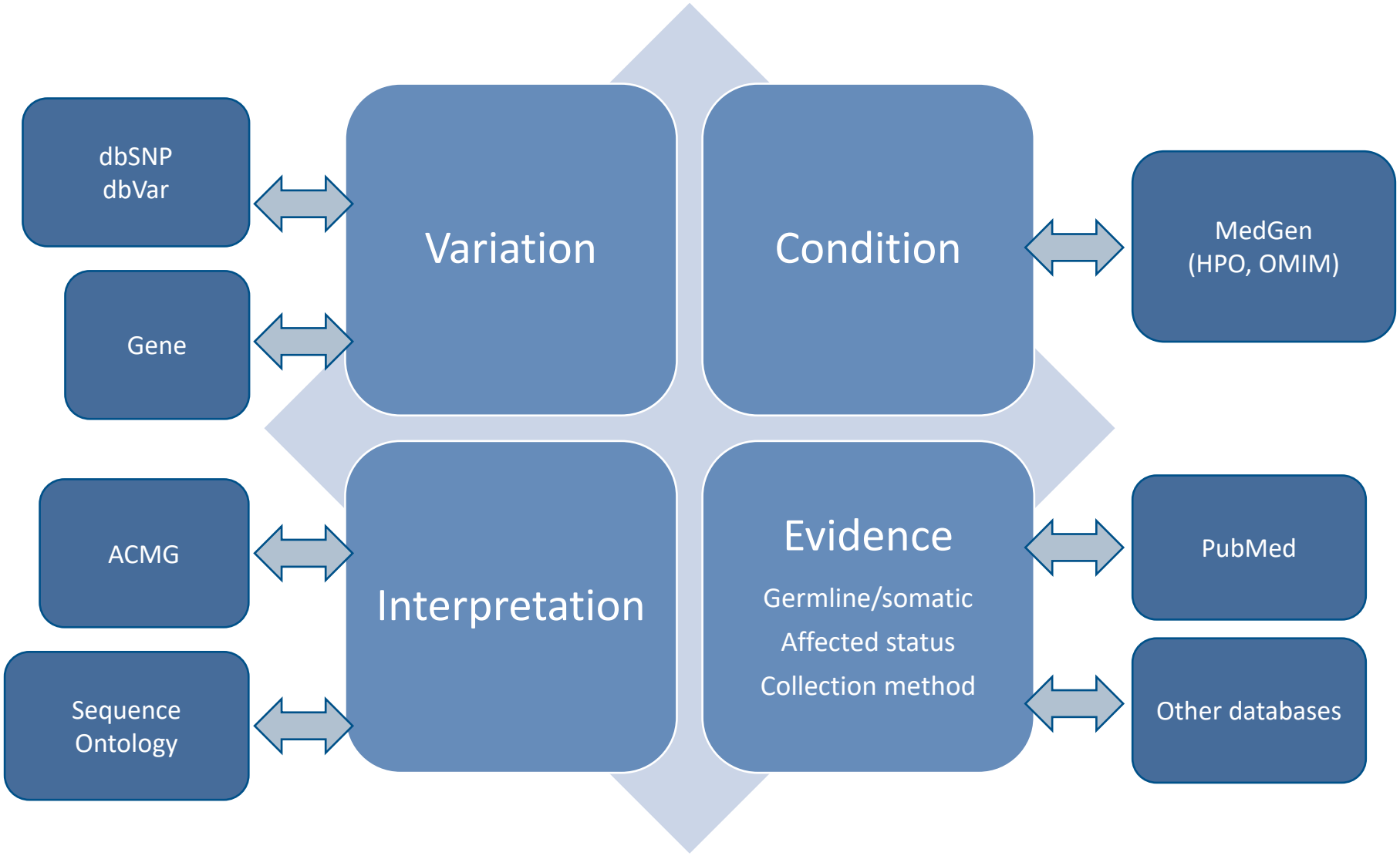
From
80 countries



Growth of data in ClinVar



ClinVar integrates four domains of information



ClinVar – Scope of data

Variant

- Anywhere in the genome
- Any type/size of variation
- Single variant or combinations – haplotypes, genotypes

Condition

- Disease, phenotype, or drug response
- Single condition or combination

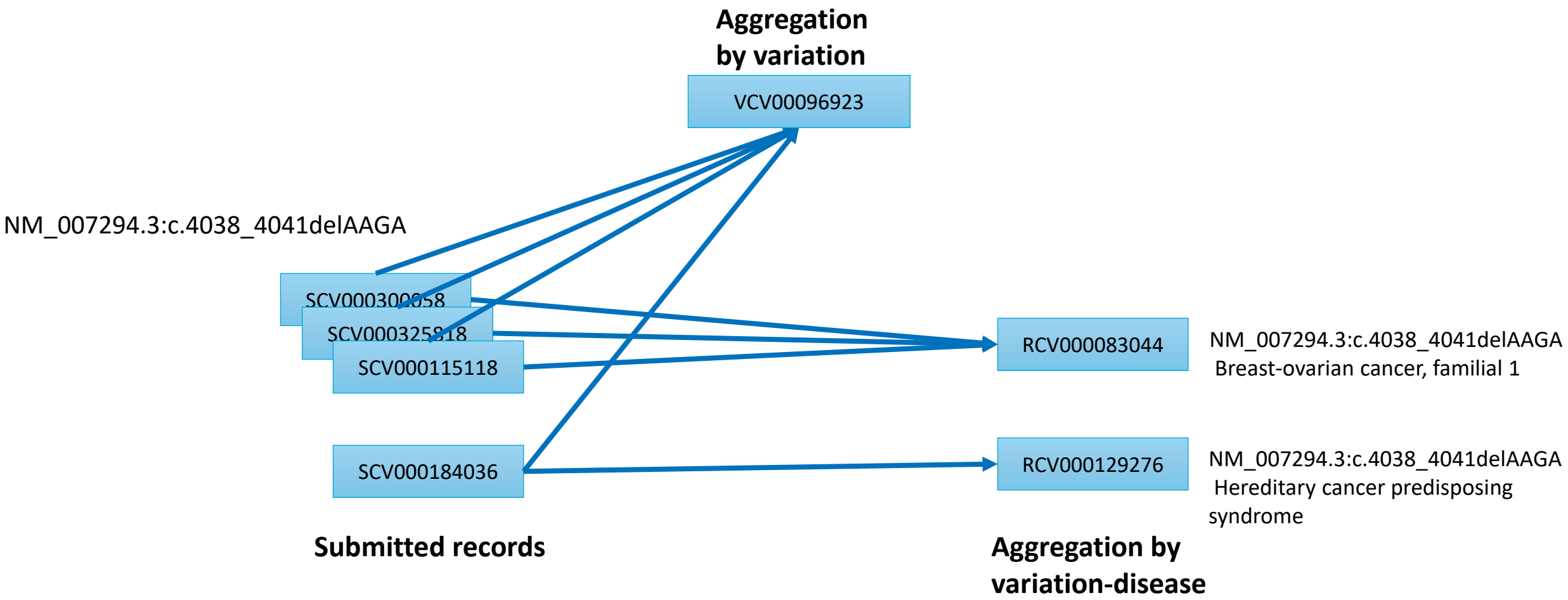
Interpretation

- Pathogenicity for Mendelian diseases
- Relationship to cancer
- Pharmacogenomics

ClinVar adds value to submitted data

- Archive submitted data
  - Each submitted record is assigned an accession (SCV) and version number
  - ClinVar maintains a history of changes to submitted records
- Standardize and validate submitted data
  - Submission requires standardized data, where possible (www.ncbi.nlm.nih.gov/clinvar/docs/authorities/)
  - Data validation (https://www.ncbi.nlm.nih.gov/clinvar/docs/validation/)
- Aggregate submitted data
  - By variant – records with VCV accession numbers
  - By variant-disease – records with RCV accession numbers

Aggregating submitted data in ClinVar

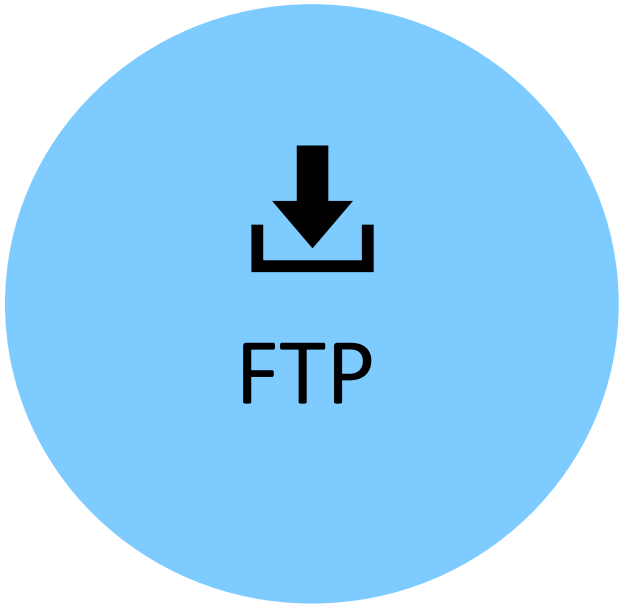


What is ClinVar?

Using ClinVar

Submitting to ClinVar

Accessing ClinVar Data



ClinVar Data by FTP

- XML
  - Comprehensive
  - ClinVarFullRelease: RCV records
  - ClinVarVariationRelease: VCV records
- VCF
  - Summary data
  - Limited to variants with precise location on the genome
- Tab-delimited summary files
  - variant_summary.txt
  - submission_summary.txt
  - gene_summary.txt

ftp.ncbi.nlm.nih.gov/pub/clinvar/

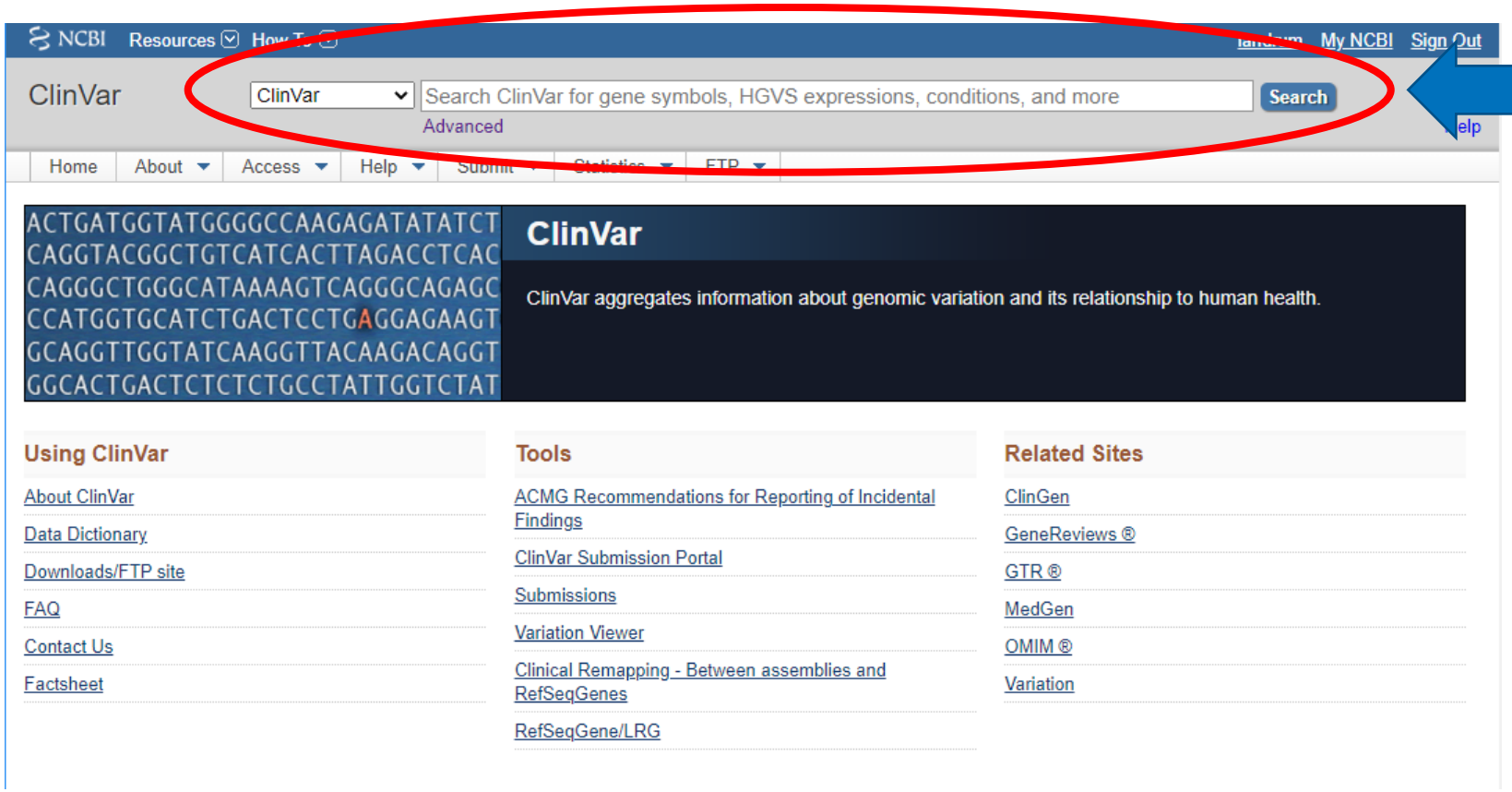
ClinVar Data by E-utilities

- via web services and a UNIX command line as Entrez Direct
- Esearch
- Esummary
- Efetch
- Elink

www.ncbi.nlm.nih.gov/clinvar/docs/maintenance_use/#api

Using ClinVar Data on the Website

Links to information about ClinVar



Search ClinVar

Searching ClinVar

- Some queries are more specific than others
- YouTube
- Options more for more advanced searches available

- HGVS expressions
  - NM_000016.5:c.296G>T
  - c.296G>T
  - p.Gly99Val
- rs numbers
- Protein changes
  - V600E
- Gene symbols
  - Official gene symbols from HGNC
- Diseases and phenotypes

www.ncbi.nlm.nih.gov/clinvar/docs/help/

Search results

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Clinical significance
Conflicting interpretations (371)
Benign (95)
Likely benign (340)
Uncertain significance (467)
Likely pathogenic (840)
Pathogenic (1,264)
Risk factor (0)

Molecular consequence
Frameshift (465)
Missense (1,258)
Nonsense (204)
Splice site (155)
ncRNA (96)
Near gene (0)
UTR (158)

Variation type
Deletion (667)
Duplication (223)
Indel (60)
Insertion (316)
Single nucleotide (2,097)

Variant length
Less than 51 bp (2,757)
Between 51 and 1000 bp (32)
Between 1 and 50 kb (71)
Between 50 and 500 kb (0)
Between 500 kb and 1 Mb (0)
Between 1 and 5 Mb (4)
Greater than 5 Mb (0)

Review status
Practice guideline (0)
Expert panel (0)
Multiple submitters (871)
Single submitter (1,608)
At least one star (2,850)
Conflicting interpretations (371)

Allele origin
Germline (2,983)

Tabular | 100 per page | Sort by Location | Download:

Showing for results for variants in the **ldlr** gene. *Search instead for all ClinVar records that mention **ldlr***

Search results

Items: 1 to 100 of 3062

<< First < Prev Page 1 of 31 Next > Last >>

	Variation *Location*	Gene(s)	Protein change	Condition(s)	Clinical significance (Last reviewed)	Review status	Accession
1.	GRCh38/hg38 19p13.2-13.13(chr19:8831147-13331227)x3 *GRCh37:* Chr19:8941823-13442041 *GRCh38:* Chr19:8831147-13331227	ACP5, GET3, CACNA1A, CALR, CDKN2D, CNN1, DHPS, DNASE2, DNM2, DNMT1, ELAVL3, EPOR, FARSA, GCDH, ICAM1, ICAM3, ICAM4, ILF3, JUNB, **LDLR**, LYL1, MAN2B1, NFIX, P2RY11, ...more		See cases	Likely pathogenic (May 6, 2011)	no assertion criteria provided	VCV000059110
2.	GRCh38/hg38 19p13.2(chr19:9735443-11228001)x1 *GRCh37:* Chr19:9846119-11338677 *GRCh38:* Chr19:9735443-11228001	CDKN2D, DNM2, DNMT1, ICAM1, ICAM3, ICAM4, ILF3, **LDLR**, P2RY11, PDE4A, PIN1, SMARCA4, ICAM5, TYK2, EIF3G, S1PR2, KEAP1, AP1M2, CARM1, TMED1, CDC37, KANK2, COL5A3, RDH8, ...more		See cases	Pathogenic (Jul 30, 2009)	no assertion criteria provided	VCV000146077
3.	GRCh38/hg38 19p13.2-13.12(chr19:10315258-14048994)x3 *GRCh37:* Chr19:10425934-14159806 *GRCh38:* Chr19:10315258-14048994	ACP5, GET3, CACNA1A, CALR, CDKN2D, CNN1, DHPS, DNASE2, DNM2, ELAVL3, EPOR, FARSA, GCDH, ICAM3, ILF3, JUNB, **LDLR**, LYL1, MAN2B1, NFIX, PDE4A, PRKCSH, RAD23A, RFX1, ...more		See cases	Pathogenic (Aug 12, 2011)	criteria provided, single submitter	VCV000059111
4.	GRCh38/hg38 19p13.2-13.13(chr19:10319474-13777860)x1 *GRCh37:* Chr19:10430150-13888674 *GRCh38:* Chr19:10319474-13777860	ACP5, GET3, CACNA1A, CALR, CDKN2D, CNN1, DHPS, DNASE2, DNM2, ELAVL3, EPOR, FARSA, GCDH, ICAM3, ILF3, JUNB, **LDLR**, LYL1, MAN2B1, NFIX, PDE4A, PRKCSH, RAD23A, SMARCA4, ...more		See cases	Pathogenic (Oct 1, 2010)	no assertion criteria provided	VCV000153069
5.	NC_000019.10:g.(11077742_11077775)_(11093595_11093630)del *GRCh38:* Chr19:11077742-11093630	**LDLR**, **LDLR**-AS1		Familial hypercholesterolemia 1	Pathogenic (Mar 1, 2004)	no assertion criteria provided	VCV000003709
6.	Single allele *GRCh37:* Chr19:11188452-11204306 *GRCh38:* Chr19:11077743-11093597	**LDLR**, **LDLR**-AS1		Familial hypercholesterolemia 1	Likely pathogenic	criteria provided, single submitter	VCV000369874

Filtered Search Results

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Clinical significance clear
- Conflicting interpretations (0)
- Benign (0)
- Likely benign (0)
- Uncertain significance (0)
- Likely pathogenic (302)
- ✓ Pathogenic (1,035)
- Risk factor (0)

Molecular consequence
- Frameshift (434)
- Missense (265)
- Nonsense (195)
- Splice site (106)
- ncRNA (13)
- Near gene (0)
- UTR (6)

Variation type
- Deletion (339)
- Duplication (122)
- Indel (40)
- Insertion (198)
- Single nucleotide (519)

Variant length clear
- ✓ Less than 51 bp (1,035)
- Between 51 and 1000 bp (0)
- Between 1 and 50 kb (0)
- Between 50 and 500 kb (0)
- Between 500 kb and 1 Mb (0)
- Between 1 and 5 Mb (0)
- Greater than 5 Mb (0)

Review status
- Practice guideline (0)
- Expert panel (0)
- Multiple submitters (548)
- Single submitter (371)
- At least one star (919)
- Conflicting interpretations (0)

Tabular 100 per page Sort by Location Download:

Showing for results for variants in the **ldlr** gene. *Search instead for all ClinVar records that mention **ldlr***

Search results

Items: 1 to 100 of 1035

<< First < Prev Page 1 of 11 Next > Last >>

Filters activated: Pathogenic, Less than 51 bp. Clear all to show 3062 items.

	Variation *Location*	Gene(s)	Protein change	Condition(s)	Clinical significance (Last reviewed)	Review status	Accession
1.	NM_000527.4(LDLR):c.-193_-187delinsTG *GRCh37:* Chr19:11200032-11200038 *GRCh38:* Chr19:11089356-11089362	LDLR, LDLR-AS1		Familial hypercholesterolemia 1	Pathogenic	no assertion criteria provided	VCV000440531
2.	NM_000527.4(LDLR):c.-172G>A *GRCh37:* Chr19:11200053 *GRCh38:* Chr19:11089377	LDLR, LDLR-AS1		Familial hypercholesterolemia 1	Pathogenic	no assertion criteria provided	VCV000440532
3.	NM_000527.4(LDLR):c.-151C>G *GRCh37:* Chr19:11200074 *GRCh38:* Chr19:11089398	LDLR, LDLR-AS1		Familial hypercholesterolemia 1	Pathogenic	no assertion criteria provided	VCV000440533
4.	NM_000527.4(LDLR):c.-150A>G *GRCh37:* Chr19:11200075 *GRCh38:* Chr19:11089399	LDLR, LDLR-AS1		Familial hypercholesterolemia 1	Pathogenic	no assertion criteria provided	VCV000440534
5.	NM_000527.4(LDLR):c.-135C>G *GRCh37:* Chr19:11200090 *GRCh38:* Chr19:11089414	LDLR, LDLR-AS1		Familial hypercholesterolemia, Familial hypercholesterolemia 1	Pathogenic/Likely pathogenic (Dec 20, 2019)	criteria provided, multiple submitters, no conflicts	VCV000250956
6.	NM_000527.4(LDLR):c.-98C>T *GRCh37:* Chr19:11200127 *GRCh38:* Chr19:11089451	LDLR, LDLR-AS1		Familial hypercholesterolemia 1	Pathogenic	no assertion criteria provided	VCV000440535
7.	NM_000527.5(LDLR):c.1A>T (p.Met1Leu) *GRCh37:* Chr19:11200225	LDLR, LDLR-AS1	M1L	Familial hypercholesterolemia, Familial	Pathogenic/Likely pathogenic (Apr 26, 2019)	criteria provided, multiple submitters, no conflicts	VCV000250968

Aggregate data – aggregated/calculated by ClinVar

Submitted data

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NM_000527.5(LDLR):c.1A>T (p.Met1Leu)

Cite this record

Interpretation:	Pathogenic/Likely pathogenic
Review status:	criteria provided, multiple submitters, no conflicts
Submissions:	5 (Most recent: Feb 8, 2022)
Last evaluated:	Apr 26, 2019
Accession:	VCV000230965.2
Variation ID:	230965
Description:	single nucleotide variant

Variant details | Conditions | Gene(s)

NM_000527.5(LDLR):c.1A>T (p.Met1Leu)

Allele ID:	248554
Variant type:	single nucleotide variant
Variant length:	1 bp
Cytogenetic location:	19p13.2
Genomic location:	19: 11089549 (GRCh38) GRCh38 UCSC 19: 11200223 (GRCh37) GRCh37 UCSC

HGVS:

Nucleotide	Protein	Molecular consequence
NC_000019.10:g.11089549A>T		
NC_000019.9:g.11200223A>T		
NM_000527.5:c.1A>T MANE SELECT	NP_000518.1:p.Met1Leu	missense

... more HGVS

Protein change:	M1L
Other names:	-
Canonical SPDI:	NC_000019.10:11089548:A:T
Functional consequence:	-
Global minor allele frequency (GMAF):	-
Allele frequency:	-
Links:	ClinGen: CA10594700 LDLR-LOVD, British Heart Foundation: LDLR_000445 dbSNP: rs879254580

Submitted interpretations and evidence

Interpretation (Last evaluated)	Review status (Assertion criteria)	Condition (Inheritance)	Submitter	Supporting information (Based)
Likely pathogenic (Mar 22, 2018)	criteria provided, single submitter (ACMG Guidelines, 2015) Method: literature only	Familial hypercholesterolemia (Autosomal dominant inheritance) Allele origin: germline	LDLR-LOVD, British Heart Foundation Assertion: SCV000844072 Submitted: (Apr 20, 2018)	Evidence details Publications Pubmed (4)
Pathogenic (Apr 26, 2018)	criteria provided, single submitter (Invitae Variant Classification Review (SOP000002)) Method: clinical testing	Familial hypercholesterolemia Allele origin: germline	Invitae Assertion: SCV000267264 Submitted: (Feb 06, 2020)	Evidence details Publications Pubmed (1) Comment: This sequence change affects the initiator methionine of the LDLR mRNA. The next in-frame methionine is located at codon 184. This variant is not present ... (more)
Pathogenic (-)	no assertion criteria provided Method: research	Familial hypercholesterolemia Allele origin: germline	Laboratorium voor Moleculaire Diagnostiek Experimentele Vasculaire Geneeskunde, Academisch Medisch Centrum Assertion: SCV000209614 Submitted: (Apr 20, 2017)	Evidence details

Functional evidence

There is no functional evidence in ClinVar for this variation. If you have generated functional data for this variation, please consider submitting that data to ClinVar.

Citations for this variant

Title	Author	Journal	Year	Link
The use of next-generation sequencing in clinical diagnosis of familial hypercholesterolemia.	Vandrovcova J et al.	Genetics in medicine : official journal of the American College of Medical Genetics	2015	PMID: 25650787
Molecular basis of autosomal dominant hypercholesterolemia: assessment in a large cohort of hypercholesterolemic children.	van der Graaf A et al.	Circulation	2011	PMID: 21282590

- The aggregate interpretation of the variant is **calculated** by ClinVar based on submitted interpretations.
- The review status (stars) indicates the level of review supporting the submitted interpretations.
- A VCV accession number is assigned to the record; the version number is incremented when supporting submissions are updated.

ClinVar Genomic variation as it relates to human health

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NM_000527.5(LDLR):c.1A>T (p.Met1Leu)

Cite this record

FEEDBACK

Interpretation: Pathogenic/Likely pathogenic

Review status: ★★☆☆ criteria provided, multiple submitters, no conflicts
Submissions: 3 (Most recent: Feb 6, 2020)
Last evaluated: Apr 26, 2019
Accession: VCV000250968.2
Variation ID: 250968
Description: single nucleotide variant

Variant details | Conditions | Gene(s)

NM_000527.5(LDLR):c.1A>T (p.Met1Leu)

Allele ID: 245334
Variant type: single nucleotide variant
Variant length: 1 bp
Cytogenetic location: 19p13.2
Genomic location: 19: 11089549 (GRCh38) GRCh38 UCSC
19: 11200225 (GRCh37) GRCh37 UCSC

HGVS:

Nucleotide	Protein	Molecular consequence
NC_000019.10:g.11089549A>T		
NC_000019.9:g.11200225A>T		
NM_000527.5:c.1A>T MANE SELECT	NP_000518.1:p.Met1Leu	missense

... more HGVS

Protein change: M1L
Other names: -
Canonical SPDI: NC_000019.10:11089548:A:T
Functional consequence: -
Global minor allele frequency (GMAF): -
Allele frequency: -
Links: ClinGen: CA10584720
LDLR-LOVD, British Heart Foundation: LDLR_000445
dbSNP: rs879254382

ClinVar Review Status

Review status is **calculated** by ClinVar based on:

- Expert review
- Consensus in the interpretation
- Transparency into the rules used for interpretation (assertion criteria)

★★★★	Practice guideline
★★★☆	Reviewed by expert panel
★★☆☆	✓ Transparency ✓ Consensus
★☆☆☆	✓ Transparency ✗ Consensus
☆☆☆☆	✗ Transparency

www.ncbi.nlm.nih.gov/clinvar/docs/review_status/

Calculating aggregate interpretation

- A submitted interpretation is on each submitted record (SCV)
- An aggregate interpretation is **calculated** for each VCV record

Select SCVs to include in the calculation based on review status

Do those SCVs agree or disagree on pathogenicity? (ACMG terms)

Are there non-ACMG interpretations?

Precedence:
1. Practice guidelines
2. Expert panel
3. criteria provided, single submitter
4. no assertion criteria provided

Examples:
1. Pathogenic
2. Pathogenic/Likely pathogenic
3. Conflicting interpretations of pathogenicity

Examples:
1. Pathogenic, drug response
2. Pathogenic/Likely pathogenic, risk factor

www.ncbi.nlm.nih.gov/clinvar/docs/clinsig/

Three tabs of summary data

Variant tab: general facts about the variant

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NM_000527.5(LDLR):c.1A>T (p.Met1Leu)

Cite this record

FEEDBACK

Interpretation: Pathogenic/Likely pathogenic

Review status: ★★☆☆ criteria provided, multiple submitters, no conflicts
Submissions: 3 (Most recent: Feb 6, 2020)
Last evaluated: Apr 26, 2019
Accession: VCV000250968.2
Variation ID: 250968
Description: single nucleotide variant

Variant details | Conditions | Gene(s)

NM_000527.5(LDLR):c.1A>T (p.Met1Leu)

Allele ID: 245334
Variant type: single nucleotide variant
Variant length: 1 bp
Cytogenetic location: 19p13.2
Genomic location: 19: 11089549 (GRCh38) GRCh38 UCSC
19: 11200225 (GRCh37) GRCh37 UCSC

HGVS:

Nucleotide	Protein	Molecular consequence
NC_000019.10:g.11089549A>T		
NC_000019.9:g.11200225A>T		
NM_000527.5:c.1A>T MANE SELECT	NP_000518.1:p.Met1Leu	missense

... more HGVS

Protein change: M1L
Other names: -
Canonical SPDI: NC_000019.10:11089548:A:T
Functional consequence: -
Global minor allele frequency (GMAF): -
Allele frequency: -
Links: ClinGen: CA10584720
LDLR-LOVD, British Heart Foundation: LDLR_000445
dbSNP: rs879254382

Conditions tab: a summary of the conditions for which the variant was interpreted

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NM_000527.5(LDLR):c.1A>T (p.Met1Leu)

Cite this record

FEEDBACK

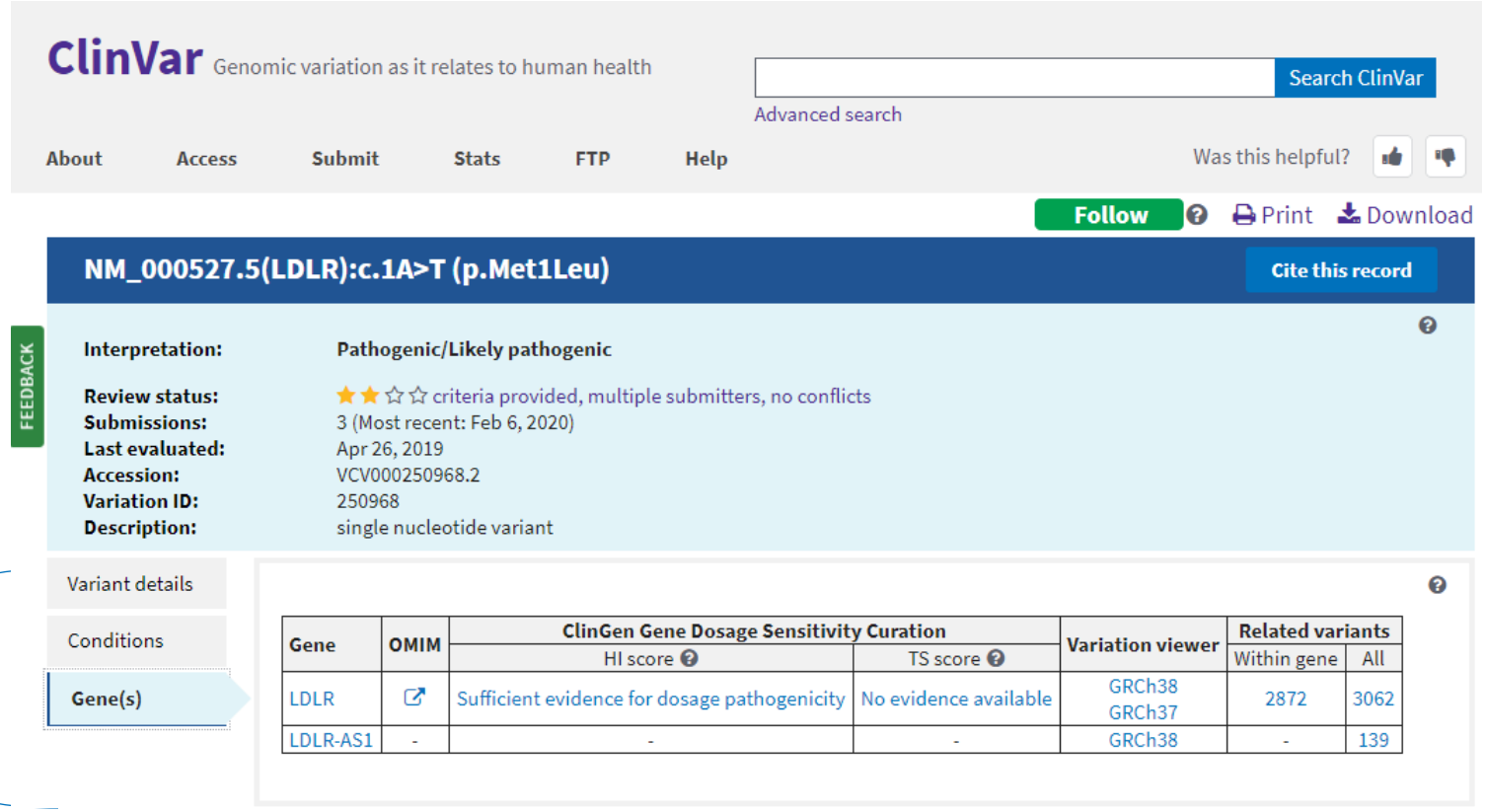
Interpretation:	**Pathogenic/Likely pathogenic**
Review status:	★★☆☆ criteria provided, multiple submitters, no conflicts
Submissions:	3 (Most recent: Feb 6, 2020)
Last evaluated:	Apr 26, 2019
Accession:	VCV000250968.2
Variation ID:	250968
Description:	single nucleotide variant

Variant details | **Conditions** | Gene(s)

Aggregate interpretations per condition

Interpreted condition	Interpretation	Number of submissions	Review status	Last evaluated	Variation/condition record
Familial hypercholesterolemia 1	Likely pathogenic	2	criteria provided, single submitter	Mar 25, 2016	RCV000238419.3
Familial hypercholesterolemia	Pathogenic	1	criteria provided, single submitter	Apr 26, 2019	RCV001220717.1

Gene(s) tab: a summary of the genes affected by the variant



Gene	OMIM	ClinGen Gene Dosage Sensitivity Curation		Variation viewer	Related variants	
		HI score	TS score		Within gene	All
LDLR		Sufficient evidence for dosage pathogenicity	No evidence available	GRCh38 GRCh37	2872	3062
LDLR-AS1	-	-	-	GRCh38	-	139

Aggregate data – aggregated/calculated by ClinVar

Submitted data

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Was this helpful?

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NM_000527.5(LDLR):c.1A>T (p.Met1Leu)

Cite this record

Interpretation:	Pathogenic/Likely pathogenic
Review status:	criteria provided, multiple submitters, no conflicts
Submissions:	5 (Most recent: Feb 8, 2022)
Last evaluated:	Apr 26, 2019
Accession:	VCV000230965.2
Variation ID:	230965
Description:	single nucleotide variant

Variant details | Conditions | Gene(s)

NM_000527.5(LDLR):c.1A>T (p.Met1Leu)

Allele ID:	248554
Variant type:	single nucleotide variant
Variant length:	1 bp
Cytogenetic location:	19p13.2
Genomic location:	19: 11089549 (GRCh38) GRCh38 UCSC 19: 11200223 (GRCh37) GRCh37 UCSC

HGVS:

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NC_000019.9:g.11200223A>T		
NM_000527.5:c.1A>T MANE SELECT	NP_000518.1:p.Met1Leu	missense

... more HGVS

Protein change:	M1L
Other names:	-
Canonical SPDI:	NC_000019.10:11089548:A:T
Functional consequence:	-
Global minor allele frequency (GMAF):	-
Allele frequency:	-
Links:	ClinGen: CA10594700 LDLR-LOVD, British Heart Foundation: LDLR_000445 dbSNP: rs879254580

Submitted interpretations and evidence

Interpretation (Last evaluated)	Review status (Assertion criteria)	Condition (Inheritance)	Submitter	Supporting information (Based)
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Pathogenic (-)	no assertion criteria provided Method: research	Familial hypercholesterolemia Allele origin: germline	Laboratorium voor Moleculaire Diagnostiek Experimentele Vasculaire Geneeskunde, Academisch Medisch Centrum Assertion: SCV000209614 Submitted: (Apr 20, 2017)	Evidence details

Functional evidence

There is no functional evidence in ClinVar for this variation. If you have generated functional data for this variation, please consider submitting that data to ClinVar.

Citations for this variant

Title	Author	Journal	Year	Link
The use of next-generation sequencing in clinical diagnosis of familial hypercholesterolemia.	Vandrovcova J et al.	Genetics in medicine : official journal of the American College of Medical Genetics	2015	PMID: 25650787
Molecular basis of autosomal dominant hypercholesterolemia: assessment in a large cohort of hypercholesterolemic children.	van der Graaf A et al.	Circulation	2011	PMID: 21282590

Submitted data

- Each row represents a submitted record
- An SCV accession number is assigned by ClinVar
- Review status is calculated by ClinVar based on that submitted record
- All other data is displayed as submitted

FEEDBACK

Submitted interpretations and evidence

Interpretation (Last evaluated)	Review status (Assertion criteria)	Condition (Inheritance)	Submitter	Supporting information (See all)
Likely pathogenic (Mar 25, 2016)	criteria provided, single submitter (ACGS Guidelines, 2013) Method: literature only	Familial hypercholesterolemia (Autosomal dominant inheritance) Allele origin: germline	LDLR-LOVD, British Heart Foundation Accession: SCV000294407.2 Submitted: (Apr 20, 2016)	Evidence details Publications PubMed (1)
Pathogenic (Apr 26, 2019)	criteria provided, single submitter (Invitae Variant Classification Sherloc (09022015)) Method: clinical testing	Familial hypercholesterolemia Allele origin: germline	Invitae Accession: SCV001392726.1 Submitted: (Feb 06, 2020)	Evidence details Publications PubMed (7) Comment: This sequence change affects the initiator methionine of the LDLR mRNA. The next in-frame methionine is located at codon 264. This variant is not present ... (more)
Pathogenic (-)	no assertion criteria provided Method: research	Familial hypercholesterolemia Allele origin: germline	Laboratorium voor Moleculaire Diagnostiek Experimentele Vasculaire Geneeskunde,Academisch Medisch Centrum Accession: SCV000605992.1 Submitted: (Apr 25, 2017)	Evidence details

Citations for this variant

- Citations from submissions
- A small number of citations curated by NCBI staff

Text-mined citations from LitVar

- www.ncbi.nlm.nih.gov/CBBresearch/Lu/Demo/LitVar/#

Citations for this variant

FEEDBACK

Title	Author	Journal	Year	Link
The use of next-generation sequencing in clinical diagnosis of familial hypercholesterolemia.	Vandrovcova J *et al.*	Genetics in medicine : official journal of the American College of Medical Genetics	2013	PMID: 23680767
Molecular basis of autosomal dominant hypercholesterolemia: assessment in a large cohort of hypercholesterolemic children.	van der Graaf A *et al.*	Circulation	2011	PMID: 21382890
Update and analysis of the University College London low density lipoprotein receptor familial hypercholesterolemia database.	Leigh SE *et al.*	Annals of human genetics	2008	PMID: 18325082
Two novel point mutations causing receptor-negative familial hypercholesterolemia in a South African Indian homozygote.	Langenhoven E *et al.*	Atherosclerosis	1996	PMID: 8831933
Three-dimensional structure of a cysteine-rich repeat from the low-density lipoprotein receptor.	Daly NL *et al.*	Proceedings of the National Academy of Sciences of the United States of America	1995	PMID: 7603991
Disulfide bridges of a cysteine-rich repeat of the LDL receptor ligand-binding domain.	Bieri S *et al.*	Biochemistry	1995	PMID: 7548065
Structures and functions of multiligand lipoprotein receptors: macrophage scavenger receptors and LDL receptor-related protein (LRP).	Krieger M *et al.*	Annual review of biochemistry	1994	PMID: 7979249

Text-mined citations for rs879254382 LitVar 30

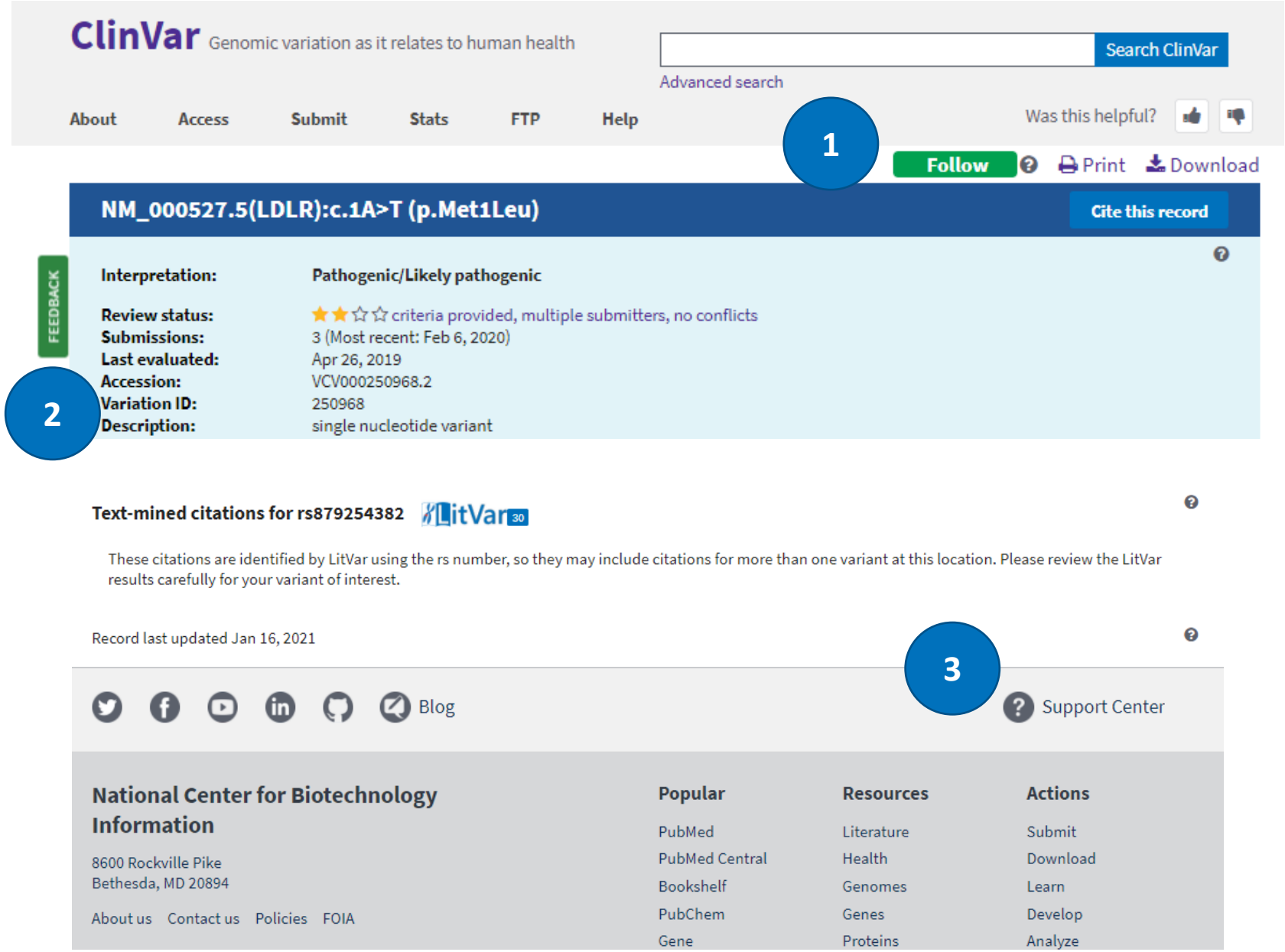
These citations are identified by LitVar using the rs number, so they may include citations for more than one variant at this location. Please review the LitVar results carefully for your variant of interest.

1. Follow variants of interest

- Be alerted when the aggregate interpretation of a variant changes
- www.ncbi.nlm.nih.gov/clinvar/docs/alerts/

2. Send us your feedback

3. Ask us for help



What is ClinVar?

Using ClinVar

Submitting to ClinVar

Who submits to ClinVar?

- Clinical genetics testing labs
- Research labs
- Locus specific databases
- Clinical providers
- Patient registries
- OMIM®, GeneReviews®
- Expert panels
- Practice guidelines

Submitters and their submissions

This page lists all submitters and the summary of their contributions, ordered inversely by the number of submissions. We acknowledge their support.

Note that the number of submissions for any submitter may be different from the number of variants found in a search based on the name of that submitter. A submission is for the interpretation of a variant and a condition; if the submitter has interpreted the variant with respect to more than one condition, then the count of submissions will be higher than the search result.

Submitter	Maximum review status	Total submissions	Submissions with interpretations	Total Genes	Last updated
Invitae	Assertion criteria	392984	392981	12740	Oct 09, 2020
Illumina Clinical Services Laboratory; Illumina	Assertion criteria	208455	208455	2818	Dec 18, 2020
GeneDx	Assertion criteria	121912	121778	26759	Nov 20, 2020
Ambry Genetics	Assertion criteria	72593	72593	1714	Nov 30, 2020
EGL Genetic Diagnostics; Eurofins Clinical Diagnostics	Assertion criteria	45028	45028	2408	Sep 19, 2018
Color	Assertion criteria	43495	43495	84	May 19, 2020
OMIM; Johns Hopkins University	-	32029	32029	5262	Jan 15, 2021
Laboratory for Molecular Medicine; Partners HealthCare Personalized Medicine	Assertion criteria	24235	24161	1751	Jun 03, 2020
Counsyl	Assertion criteria	20976	20976	346	Aug 05, 2019
CeGaT Praxis fuer Humangenetik Tuebingen	Assertion criteria	20219	20219	6296	Aug 26, 2020
Integrated Genetics/Laboratory Corporation of America; Laboratory Corporation of America	Assertion criteria	18507	18483	849	Dec 31, 2020
PreventionGenetics	Assertion criteria	18417	18417	1562	Nov 12, 2020
Cincinnati Children's Hospital Medical Center Laboratory of Genetics and Genomics; Cincinnati Children's Hospital Medical Center	Assertion criteria	17788	17788	19587	Apr 27, 2020
Natera, Inc.	-	15814	15814	358	Dec 28, 2020
Genetic Services Laboratory; University of Chicago	Assertion criteria	15337	15337	1256	Nov 01, 2020
Quest Diagnostics Nichols Institute San Juan Capistrano	Assertion criteria	13734	13734	16430	Jul 31, 2020
Athena Diagnostics Inc	Assertion criteria	13050	13050	797	Sep 25, 2019
ARUP Laboratories, Molecular Genetics and Genomics; ARUP Laboratories	Assertion criteria	10411	10411	940	Jul 20, 2020
Mendelics	Assertion criteria	9265	9265	1772	Nov 23, 2020
Evidence-based Network for the Interpretation of Germline Mutant Alleles (ENIGMA); c/o QIMR Berghofer Medical Research Institute	Expert panel	7456	7455	9	Aug 19, 2019

www.ncbi.nlm.nih.gov/clinvar/docs/submitter_list/

Register your organization to submit to ClinVar

1

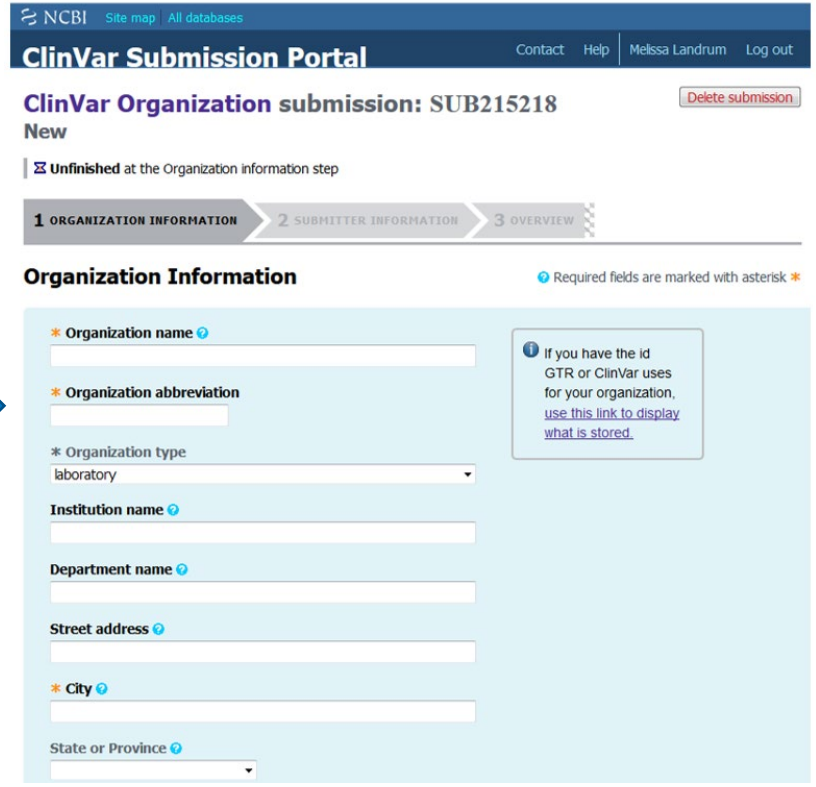
- Login to ClinVar's Submission Portal with your NCBI account

2

- Provide information about your organization in Submission Portal

3

- Once approved, you are ready to submit data



www.ncbi.nlm.nih.gov/clinvar/docs/submission_portal/

What data can be submitted?

Submit

- Variants that were interpreted for clinical significance for a disease or evaluated for functional significance

Do not submit

- Variants from GWAS studies
- Variants that were observed but not interpreted
- Variants only evaluated by computational methods

Minimal fields

- Variant
- Condition
- Clinical significance
- Allele origin
  - E.g. germline or somatic
- Affected status
  - E.g. yes, no, unknown
- Collection method
  - E.g. clinical testing or research

Optional fields

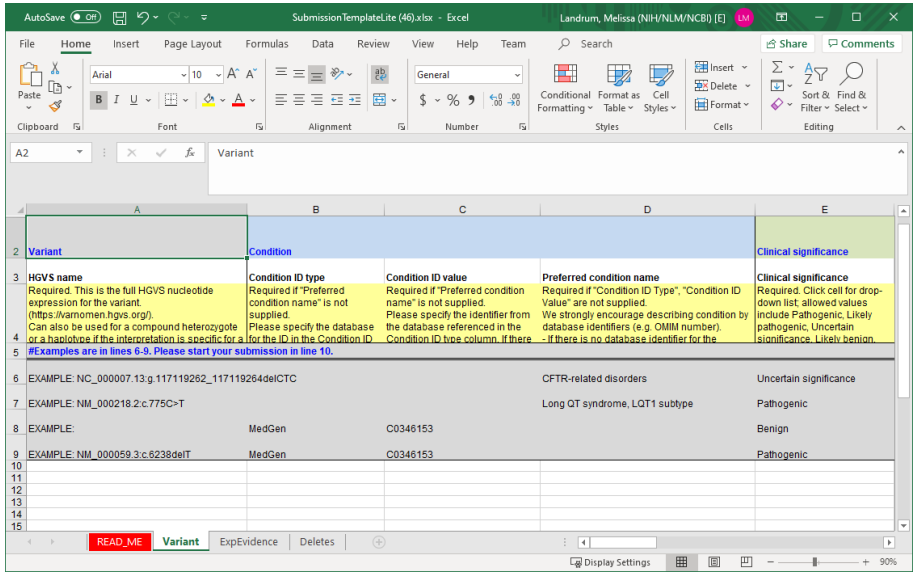
- Date last evaluated
- Comment on clinical significance
- Citations
- Mode of inheritance
- Gene
- Zygosity
- Number of individuals

Formats for submission

Batch (file)

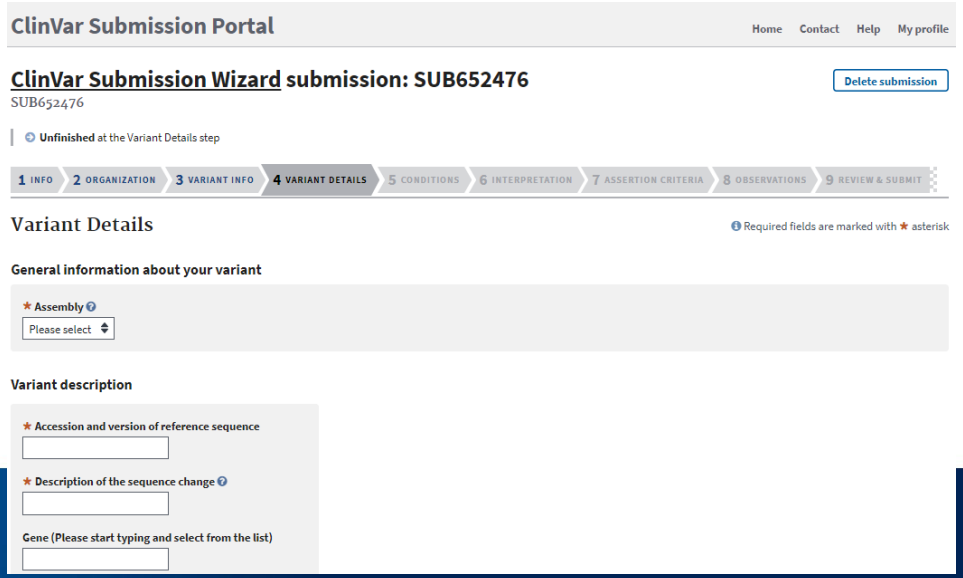
- Good for more than a handful of variants
- Good for repeat submitters

- Two Excel templates (ftp.ncbi.nlm.nih.gov/pub/clinvar/submission_templates/)
  - Full: all variant types, many data types for evidence
  - Lite: only variants described with HGVS, limited options for evidence



Single submission wizard

- Good for a small number of variants
- Good for infrequent submitters



What to expect after submission

- Some data is validated immediately in the Submission Portal
  - Choose to stop and fix errors
  - Or choose to submit any records that pass validation and fix the errors later
- A ClinVar curator reviews and processes your submitted data
  - If there are errors or questions, the curator will contact you
- Data is published on the web site, in ftp files, and by E-utilities
- You receive a summary of the successful submission

Updating your data in ClinVar

- Your organization owns your submitted data; updates can be made only by your organization
- You can update your submitted records at any time after they are published
- Records can be updated in file submissions
  - Include the SCV accession number
  - Indicate “Update”
- Or use the Single SCV Update form in ClinVar’s Submission Portal
- Monitoring your submissions
  - submission_summary.txt
  - summary of conflicting_interpretations.txt

Thank you.

This research was supported by the Intramural Research Program of the NIH, National Library of Medicine.

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Kuljeet Kaur

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