

Variants & diseases

Exploring ClinGen and ClinVar resources to find out relationships between genetic diseases and genes/ variants implicated.

BIO392

ClinVar

A database of genomic variants and the interpretation of their relevance to disease

Search in different ways:

- Specific gene
- Specific variant (HGVS)
- Specific disease or phenotype

The screenshot shows the ClinVar homepage. At the top, there's a navigation bar with links for NCBI Resources, How To, Sign in to NCBI, and Help. Below that is a search bar with "ClinVar" selected, a search input field, and a "Search" button. A "COVID-19 Information" section is highlighted in orange, containing links to Public health information (CDC), Research information (NIH), SARS-CoV-2 data (NCBI), Prevention and treatment information (HHS), and Español. The main content area features a dark blue header with the ClinVar logo and a sub-header stating "ClinVar aggregates information about genomic variation and its relationship to human health". On the left, there's a "Using ClinVar" sidebar with links to About ClinVar, Data Dictionary, Downloads/FTP site, FAQ, Contact Us, and Factsheet. In the center, there's a "Tools" sidebar with links to ACMG Recommendations for Reporting of Incidental Findings, ClinVar Submission Portal, Submissions, Variation Viewer, Clinical Remapping - Between assemblies and RefSeqGenes, and RefSeqGene/LRG. On the right, there's a "Related Sites" sidebar with links to ClinGen, GeneReviews, GTR, MedGen, OMIM, and Variation.

ClinVar Resources How To Sign In to NCBI

ClinVar Search hemochromatosis

Create alert Advanced

Home About Access Help Submit Statistics FTP

COVID-19 Information X

[Public health information \(CDC\)](#) | [Research information \(NIH\)](#) | [SARS-CoV-2 data \(NCBI\)](#) | [Prevention and treatment information \(HHS\)](#) | [Español](#)

Clinical significance clear Tabular 100 per page Sort by Location Download:

Conflicting interpretations (0)
Benign (0)
Likely benign (0)
Uncertain significance (0)
Likely pathogenic (2)
Pathogenic (6)
Risk factor (0)

Molecular consequence
Frameshift (0)
Missense (5)
Nonsense (1)
Splice site (0)
ncRNA (0)
Near gene (0)
UTR (0)

Variation type
Deletion (0)
Duplication (0)
Indel (0)
Insertion (0)
Single nucleotide (6)

Variant length
Less than 51 bp (6)
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 clear
Practice guideline (0)
Expert panel (0)
Multiple submitters (6)

Search results
Items: 6

i Filters activated: Pathogenic, Multiple submitters. [Clear all](#) to show 930 items.

Variation Location	Gene(s)	Protein change	Condition(s)	Clinical significance (Last reviewed)	Review status	Accession
<input type="checkbox"/> NM_213653.3(HJV);c.959G>T (p.Gly320Val) 1. GRCh37: Chr1:145416614 GRCh38: Chr1:146018399	HJV	G320V, G207V, G94V	Hemochromatosis type 2A, Hemochromatosis type 1, not provided	Pathogenic (Oct 23, 2020)	criteria provided, multiple submitters, no conflicts	VCV000002365
<input type="checkbox"/> NM_145277.5(HJV);c.503T>C (p.Ile168Thr) 2. GRCh37: Chr1:145416497 GRCh38: Chr1:146018516	HJV	I281T, I168T, I55T	Hemochromatosis type 2A, not provided	Pathogenic (Sep 10, 2020)	criteria provided, multiple submitters, no conflicts	VCV000002368
<input type="checkbox"/> NM_014585.5(SLC40A1);c.1469G>A (p.Gly490Asp) 3. GRCh37: Chr2:190426851 GRCh38: Chr2:189562125	SLC40A1	G490D	Hemochromatosis type 4	Pathogenic (Jul 1, 2020)	criteria provided, multiple submitters, no conflicts	VCV000406376
<input type="checkbox"/> NM_014585.6(SLC40A1);c.533G>A (p.Arg178Gln) 4. GRCh37: Chr2:190430307 GRCh38: Chr2:189565581	SLC40A1	R178Q	Hemochromatosis type 4	Pathogenic/Likely pathogenic (Jul 1, 2020)	criteria provided, multiple submitters, no conflicts	VCV000839124
<input type="checkbox"/> NM_014585.6(SLC40A1);c.238G>A (p.Gly80Ser) 5. GRCh37: Chr2:190439920 GRCh38: Chr2:189575194	SLC40A1	G80S	Hemochromatosis type 4	Pathogenic/Likely pathogenic (Oct 6, 2020)	criteria provided, multiple submitters, no conflicts	VCV000986324
<input type="checkbox"/> NM_003227.4(TFR2);c.2101C>T (p.Arg701Ter) 6. GRCh37: Chr7:100224421	TFR2, LOC113687175	R530*, R701*	Hemochromatosis type 1, Hereditary hemochromatosis	Pathogenic (Oct 9, 2020)	criteria provided, multiple submitters, no conflicts	VCV000802342

NM_213653.3(HJV):c.959G>T (p.Gly320Val)

Cite this page

Interpretation:

Pathogenic

★★☆☆☆ criteria provided, multiple submitters, no conflicts

Review status:

6 (Most recent: Jul 4, 2021)

Submissions:

Oct 23, 2020

Last evaluated:

VCV000002365.10

Accession:

2365

Variation ID:

single nucleotide variant

Description:

Variant details

NM_213653.3(HJV):c.959G>T (p.Gly320Val)

Allele ID: 17404

Variant type: single nucleotide variant

Conditions

Variant length: 1 bp

Cytogenetic location: 1q21.1

Genomic location: 1: 146018399 (GRCh38) GRCh38 UCSC

1: 145416614 (GRCh37) GRCh37 UCSC

HGVS:

Nucleotide	Protein	Molecular consequence
NC_000001.10:g.145416614G>T		
NC_000001.11:g.146018399C>A		
NC_000001.11:g.146018398C>A	NP_001303696.1:p.Gly94Val	missense

... more HGVS

G320V, G207V, G94V

Protein change:

Other names:

Canonical SPDI: ②

Functional consequence:

Global minor allele frequency (GMAF):

Allele frequency:

Trans-Omics for Precision Medicine (TOPMed) 0.00035

Submitted interpretations and evidence

Interpretation (Last evaluated)	Review status (Assertion criteria)	Condition (Inheritance)	Submitter	Supporting information (See all)
Pathogenic (Dec 19, 2018)	criteria provided, single submitter (ICSL Variant Classification Criteria 09 May 2019) Method: clinical testing	Hemochromatosis type 2A Allele origin: germline	Illumina Clinical Services Laboratory,Illumina Accession: SCV000915351.1 Submitted: (Feb 01, 2019)	Evidence details Publications PubMed (6) Comment: Across a selection of the available literature, the HEF2 c.959G>T (p.Gly320Val) missense variant, described as the most common variant associated with juvenile hereditary hemochromatosis, has ... (more)
Pathogenic (May 01, 2017)	criteria provided, single submitter (Praxis fuer Humangenetik Tuebingen - Variant Classification Criteria) Method: clinical testing	not provided Allele origin: germline	CeGaT Praxis fuer Humangenetik Tuebingen Accession: SCV001249628.5 Submitted: (Jul 04, 2021)	Evidence details
Pathogenic (Apr 18, 2014)	criteria provided, single submitter (LMM Criteria) Method: clinical testing	Juvenile hemochromatosis (Autosomal recessive inheritance) Allele origin: germline	Laboratory for Molecular Medicine, Partners HealthCare Personalized Medicine Study: CSER-MedSeq Accession: SCV000221191.2 Submitted: (Mar 06, 2015)	Evidence details Publications PubMed (5) Comment: The Gly320Val variant in HFE2 is the most frequent pathogenic variant in HFE2 (also known as HJV) and has been reported in many patients with ... (more)
Pathogenic (Oct 23, 2020)	criteria provided, single submitter (Invitae Variant Classification Sherloc (09022015)) Method: clinical testing	not provided Allele origin: germline	Invitae Accession: SCV000546647.5 Submitted: (Jan 07, 2021)	Evidence details Publications PubMed (6) Comment: This sequence change replaces glycine with valine at codon 320 of the HJV protein (p.Gly320Val). The glycine residue is highly conserved and there is a ... (more)

FEEDBACK

Tutorial: <https://www.youtube.com/watch?v=A8G3ej83ZgU>

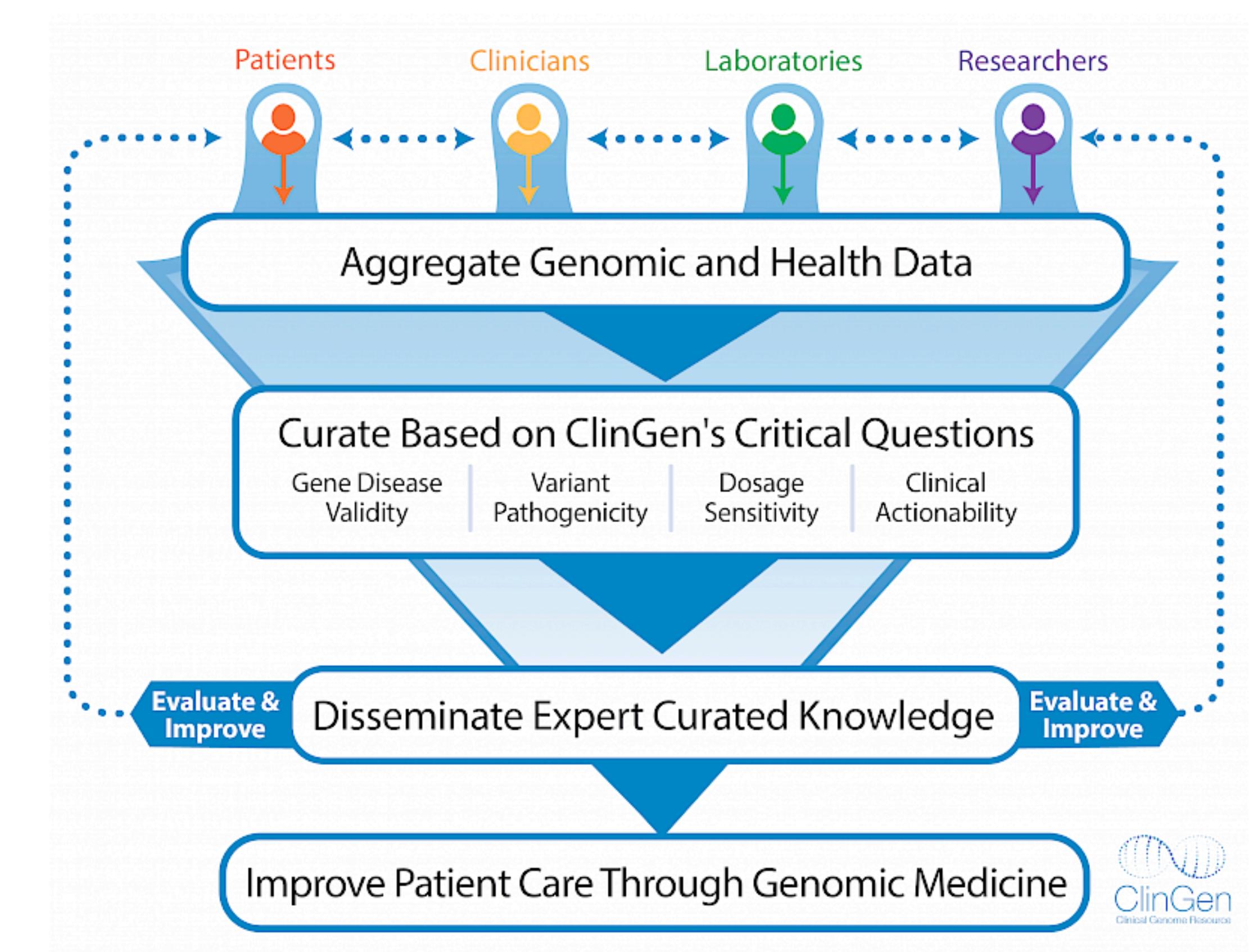
Explore ClinVar

Task: Create a relational list

Disease	Gene	Variants (HGVS https://varnomen.hgvs.org/bg-material/simple/)
Hemochromatosis	HJV	NM_213653.3:c.959G>T
Thalassemia		
Haemophilia		
Cystic Fibrosis		
Tay Sachs disease		
Fragile X syndrome		
Huntington's disease		

ClinGen

an authoritative central resource that defines the clinical relevance of genes and variants for use in precision medicine and research.

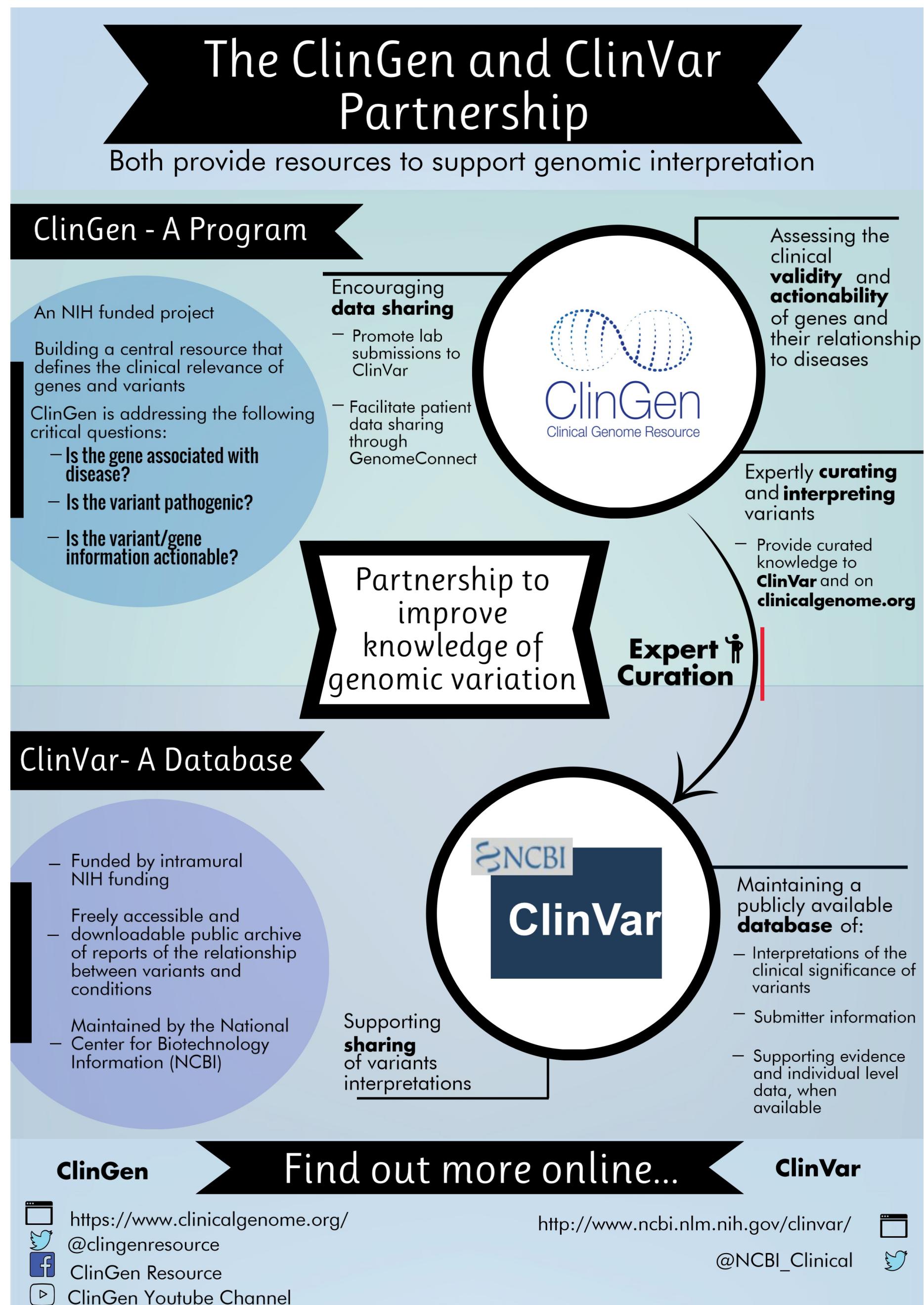


ClinGen curation activities

- Gene Disease **Validity**: Can variation in this gene cause disease?
- **Dosage** Sensitivity: Does loss or gain of a copy of this gene or genomic region result in disease?
- Variant Pathogenicity: Which changes in this gene cause disease?
- Clinical Actionability: Are there actions that could be taken to improve outcomes for patients with this genetic risk?

ClinGen & ClinVar Partnership

- Have established a **collaborative working relationship**. ClinVar has two members on ClinGen's Steering Committee and other NCBI staff participate in various ClinGen Working Groups.
- ClinGen and ClinVar **goals are aligned** and both projects play a critical role in the growing data sharing movement within the clinical genetics community.
- **ClinVar is a critical resource for ClinGen**. It serves as the primary site for deposition and retrieval of variant data and annotations from individual submitters.
- ClinGen relies on ClinVar as a source for existing data on variants, which are submitted to ClinVar from diverse sources. **ClinGen Expert Panels review data in ClinVar** to as part of the variant curation process and **submit their own classifications to ClinVar as expert-reviewed records**.
- **ClinGen is providing input to ClinVar on the structure and layout of the database** that is instrumental to its development.
- Other specific ways in which the two groups are working together:
 - ClinGen provides recommendations to ClinVar related to the underlying data structure and user interface.





Get Started About Us Curation Activities Working Groups Expert Panels Documents & Announcements Tools



Gene CFTR

Search

All Curated Genes Gene-Disease Validity Dosage Sensitivity Clinical Actionability Curated Variants Statistics More ?



Genes

matching search term "CFTR"

43001
Total Genes
Matched by Search

2115
Curated Genes
Matched by Search

CFTR



Showing 1 to 5 of 5 rows 50 rows per page

Gene Symbol	HGNC ID	Gene Name	Gene Type	Curations	Last Eval.
CFTR	HGNC:1884	CF transmembrane conductance regulator	gene with protein product	G D A V P	08/22/2016
CFTR-AS1	HGNC:40144	CFTR antisense RNA 1	RNA, long non-coding	G D A V P	
CFTRP1	HGNC:16182	CFTR pseudogene 1	pseudogene	G D A V P	
CFTRP2	HGNC:51351	CFTR pseudogene 2	pseudogene	G D A V P	
CFTRP3	HGNC:51352	CFTR pseudogene 3	pseudogene	G D A V P	

Showing 1 to 5 of 5 rows 50 rows per page

All Curated Genes Gene-Disease Validity ▾ Dosage Sensitivity ▾ Clinical Actionability ▾ Curated Variants ▾ Statistics More ?

CFTR

View Gene Facts

0 Gene-Disease Validity Classifications 1 Dosage Sensitivity Classifications 0 Clinical Actionability Assertions 0 Variant Pathogenicity Assertions 2 / 3 CPIC / PharmGKB High Level Records

Curation Summaries External Genomic Resources ClinVar Variants

D Dosage Sensitivity

Gene Disease

CFTR	cystic fibrosis MONDO:0009061	30 (Gene Associated with Autosomal Recessive Phenotype)
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HI Score & TS Score Report & Date

08/22/2016

P Pharmacogenomics - CPIC

Gene Drug CPIC Level Date Accessed

CFTR	ivacaftor	Level A	09/20/2021
CFTR	ataluren	Level C	09/20/2021

CPIC Clinical Guidelines

P Pharmacogenomics - PharmGKB

Gene Drug Highest Level of Evidence Last Curated

CFTR	ivacaftor	Level 1A	03/24/2021
	ivacaftor / lumacaftor	Level 1A	03/24/2021
	ivacaftor / tezacaftor	Level 1A	03/24/2021

View Provisional

CFTR

View Gene Facts

0 Gene-Disease Validity Classifications 1 Dosage Sensitivity Classifications 0 Clinical Actionability Assertions 0 Variant Pathogenicity Assertions 2 / 3 CPIC / PharmGKB High Level Records

Gene Facts External Data Attribution

HGNC Symbol CFTR (HGNC:1884) [HGNC](#) [Entrez](#) [Ensembl](#) [OMIM](#) [UCSC](#) [Uniprot](#) [GeneReviews](#) [ClinVar](#)

HGNC Name CF transmembrane conductance regulator

Gene type protein-coding gene

Locus type gene with protein product

Previous symbols CF, ABCC7

Alias symbols MRP7, ABC35, TNR-CFTR, dJ760C5.1, CFTR/MRP

%HI 2.33 (Read more about the DECIPIER Haploinsufficiency Index)

pLI 0 (Read more about gnomAD pLI score)

LOEUF 1.31 (Read more about gnomAD LOEUF score)

Cytoband 7q31.2

Genomic Coordinates GRCh37/hg19: chr7:117120017-117308719 [NCBI](#) [Ensembl](#) [UCSC](#)
GRCh38/hg38: chr7:117480025-117668665 [NCBI](#) [Ensembl](#) [UCSC](#)

MANE Select Transcript NM_000492.4 (Read more about MANE Select)

Function Epithelial ion channel that plays an important role in the regulation of epithelial ion and water transport and fluid homeostasis (PubMed:10792060, PubMed:11524016, PubMed:11707463, PubMed:12588899, PubMed:1258899, PubMed:13036051, PubMed:19398555, PubMed:19621064, PubMed:22178883, PubMed:15010471, PubMed:1712898, PubMed:1712898, PubMed:8910473, PubMed:9804160, PubMed:12529365, PubMed:17182731, PubMed:26846474, ... (Source: PMID:10792060)

Gene-Disease Validity Classifications Tutorial:

<https://www.clinicalgenome.org/docs/gene-disease-validity-classifications-tutorial/>

Explore ClinGen

Task: Create a relational list

Gene	Gene name	Chromosomal location	Gene product	Disease
CFTR	CF transmembrane conductance regulator	7q31.2	epithelial ion channel, transport of chloride ions across the cell membrane	Cystic fibrosis
CYBB				
HJV				
CDKN2A				
KRAS				
TP53				
				Fragile X syndrome