

ClinGen Website Updates – January 2021

Several new features were released to the ClinGen website in January 2021, including:

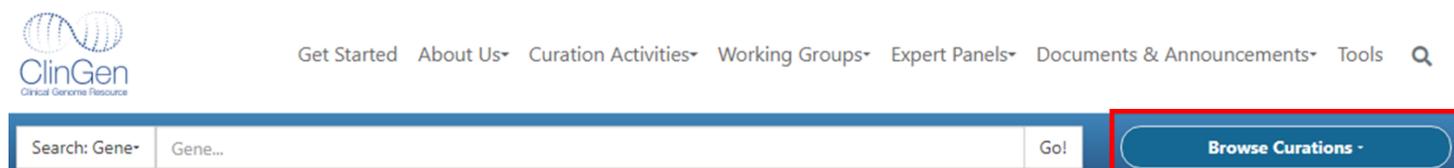
- [Improved navigation for browsing results by curation activity](#)
- [Tallies highlighting the total number of results returned for a particular query](#)
- [Column customization/querying](#)
- [Export options](#)
- [Ability to access gene-disease validity curations by Gene Curation Expert Panel \(GCEP\)](#)
- [Curations grouped by activity](#)
- [Basic information about a gene added to the top of each gene page \(“Gene Facts”\)](#)
- [Richer display of dosage sensitivity curation data](#)
- [Ability to search by genomic coordinates](#)
- [Actionability curation results differentiated by adult and pediatric indications](#)
- [Integration of pharmacogenomic curation information from CPIC and PharmGKB](#)

Click on each link or scroll down for additional information on each feature. An explanatory video is also available (LINK HERE).

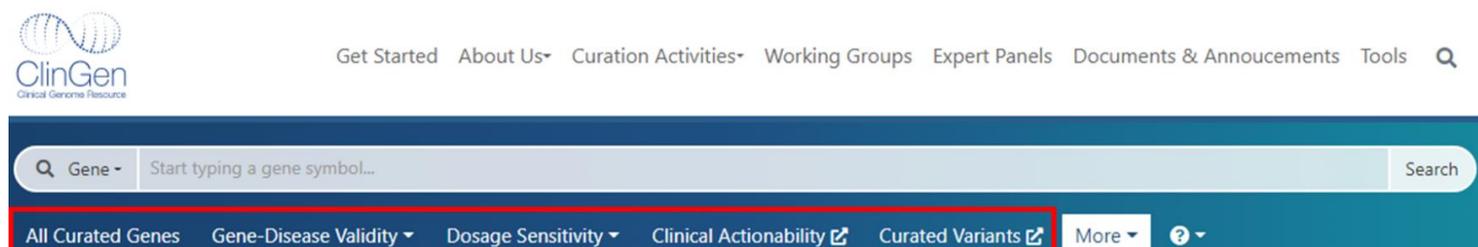
Improved Navigation for Browsing Results by Curation Activity

Previously, in order to browse curation results by activity (as opposed to searching for a specific gene or disease), you would need to click on the “Browse Curations” button, then select your activity of interest. Now, browsing menus are available across the bottom of the search bar for easier access.

Previous:



Current:



Tallies

Tallies are now included at the top right of search and curation browsing pages to indicate the number of applicable results returned for particular queries. For example, the tallies at the top of the “Curated Genes” page highlight the number of unique genes curated in total across ClinGen, as well as the individual gene totals for gene-disease validity, dosage sensitivity, and actionability:

The screenshot shows the ClinGen website header with navigation links: Get Started, About Us, Curation Activities, Working Groups, Expert Panels, Documents & Announcements, Tools, and a search icon. Below the header is a search bar with the text "Gene - Start typing a gene symbol..." and a "Search" button. A navigation bar contains links for Curated Genes, Gene-Disease Validity, Dosage Sensitivity, Clinical Actionability, Curated Variants, Statistics, and More. The main content area features the ClinGen logo and the text "Curated Genes". To the right, a table displays tallies for four categories: Unique Curated Genes (1857), Gene-Disease Validity Genes (902), Dosage Sensitivity Genes (1381), and Actionability Genes (156). The table is highlighted with a red border.

1857	902	1381	156
Unique Curated Genes	Gene-Disease Validity Genes	Dosage Sensitivity Genes	Actionability Genes

The tallies at the top of an individual gene page will tell you how many curations from each activity are available for that gene:

The screenshot shows the ClinGen website header with navigation links: Get Started, About Us, Curation Activities, Working Groups, Expert Panels, Documents & Announcements, Tools, and a search icon. Below the header is a search bar with the text "Gene - Start typing a gene symbol..." and a "Search" button. A navigation bar contains links for All Curated Genes, Gene-Disease Validity, Dosage Sensitivity, Clinical Actionability, Curated Variants, and More. The main content area features the ClinGen logo and the text "MYH7" with a "View Gene Facts" button. To the right, a table displays tallies for three categories: Gene-Disease Validity Classifications (3), Dosage Sensitivity Classifications (1), and Clinical Actionability Assertions (3). The table is highlighted with a red border.

3	1	3
Gene-Disease Validity Classifications	Dosage Sensitivity Classifications	Clinical Actionability Assertions

Column Customization/Querying

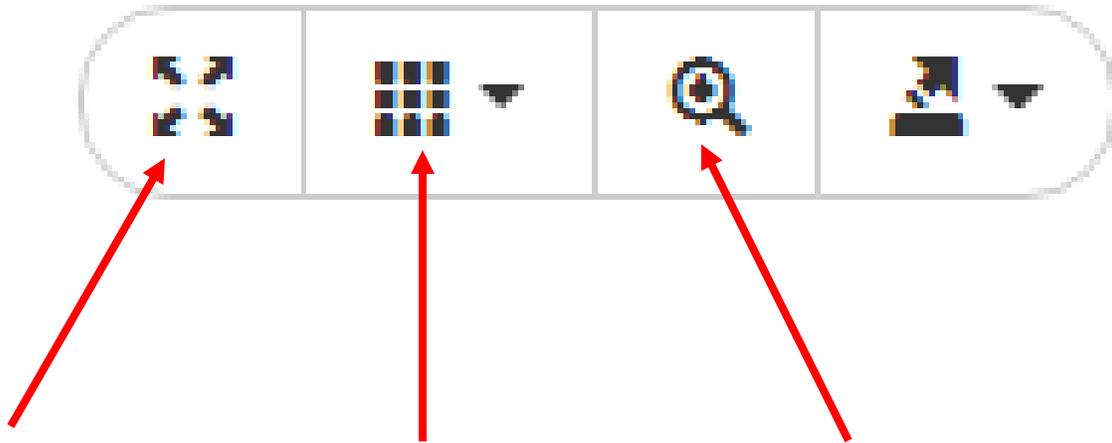
Within the pages allowing you to browse results by curation activity, information is organized into columns. The ClinGen website now gives you the ability to customize this display and run simple queries within the columns.

On the pages where this feature is available, the column customization options will be displayed at the top right, below the tallies:

The screenshot shows the ClinGen website header with navigation links: Get Started, About Us, Curation Activities, Working Groups, Expert Panels, Documents & Announcements, Tools, and a search icon. Below the header is a search bar with the text "Gene - Start typing a gene symbol..." and a "Search" button. A navigation bar contains links for Curated Genes, Gene-Disease Validity, Dosage Sensitivity, Clinical Actionability, Curated Variants, Statistics, and More. The main content area features the ClinGen logo and the text "Curated Genes". To the right, a table displays tallies for four categories: Unique Curated Genes (1857), Gene-Disease Validity Genes (902), Dosage Sensitivity Genes (1381), and Actionability Genes (156). Below the table, a search bar with the text "Search in table" and a trash icon is visible. At the top right, below the tallies, a set of icons for column customization is highlighted with a red border, including a refresh icon, a grid icon, a magnifying glass icon, and a dropdown arrow icon.

1857	902	1381	156
Unique Curated Genes	Gene-Disease Validity Genes	Dosage Sensitivity Genes	Actionability Genes

The options are as follows:



Full screen view Show/Hide Columns Search within Columns

- Full screen view: Maximizes the current view to fill the entire display screen
- Show/hide columns: Click on this pull-down menu to hide columns you aren't interested in or display additional columns that are currently hidden from view. Note: additional columns may differ across pages based on the content available.
- Search within columns: Perform limited searches within a particular column based on the information included therein. Some columns, particular those with extensive information (e.g., gene or disease name) allow text searches, and will return results based on text string matches within that column. Other columns that include more limited information (e.g., mode of inheritance) provide choices for specific values that can be searched within that column.

Example screen shot of "Show/hide columns":

Gene	Disease	MOI	Expert Panel	SOP	Classification	Last Eval.
A2ML1	Noonan syndrome with multiple lentiginos	AD	RASopathy	SOP5	No Re	06/07/2018
A2ML1	Noonan syndrome-like disorder with loose anagen hair	AD	RASopathy	SOP5	No Re	06/07/2018
A2ML1	Noonan syndrome	AD	RASopathy	SOP5	Disput	06/07/2018
A2ML1	Costello syndrome	AD	RASopathy	SOP5	No Re	06/07/2018

Example screen shot of “Search within columns”:

The screenshot shows the 'Gene-Disease Validity' interface. At the top, there are navigation tabs: 'Curated Genes', 'Gene-Disease Validity', 'Dosage Sensitivity', 'Clinical Actionability', 'Curated Variants', and 'More'. On the right, statistics are displayed: 1155 Total Curations, 903 Unique Genes, and 33 Expert Panels. A search bar is labeled 'Search in table'. Below it, a red arrow points to a search icon in a toolbar. The main table has columns: Gene, Disease, MOI, Expert Panel, SOP, Classification, and Last Eval. The first row of the table is highlighted with a red box and contains the following data: Gene (empty), Disease (empty), MOI (XL), Expert Panel (empty), SOP (empty), Classification (Moderate), and Last Eval (2018). Below this are four rows of data for genes FTSJ1, GDI1, NLGN3, and SYN1, each with associated disease, MOI, Expert Panel, SOP, Classification, and Last Eval date.

Gene	Disease	MOI	Expert Panel	SOP	Classification	Last Eval.
		XL			Moderate	2018
FTSJ1	non-syndromic X-linked intellectual disability	XL	Intellectual Disability and Autism	SOP5	Moderate	01/17/2018
GDI1	non-syndromic X-linked intellectual disability	XL	Intellectual Disability and Autism	SOP5	Moderate	05/24/2018
NLGN3	complex neurodevelopmental disorder	XL	Intellectual Disability and Autism	SOP5	Moderate	09/19/2018
SYN1	complex neurodevelopmental disorder	XL	Intellectual Disability and Autism	SOP6	Moderate	12/05/2018

Export Options

The same menu that includes the column customization options also includes an option to export the results of your current query.

A close-up of the toolbar shows four icons: a refresh icon, a grid icon with a dropdown arrow, a search icon, and a document icon with a dropdown arrow. A red arrow points from the document icon to a dropdown menu. The menu lists the following export options: JSON, XML, CSV, TXT, SQL, and MS-Excel. The text 'Export current screen' is positioned to the right of the menu.

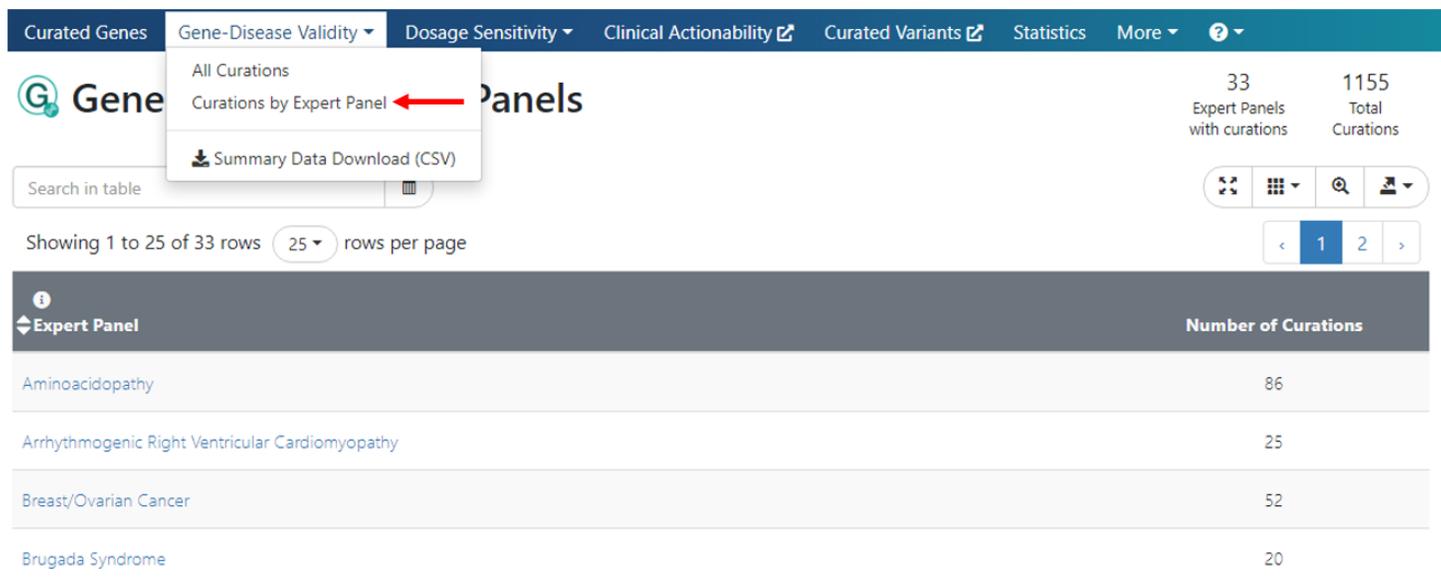
- JSON
- XML
- CSV
- TXT
- SQL
- MS-Excel

Export current screen

Export options include JSON, XML, CSV, TXT, SQL, and MS-Excel.

Gene-Disease Validity Curations Sorted by GCEP

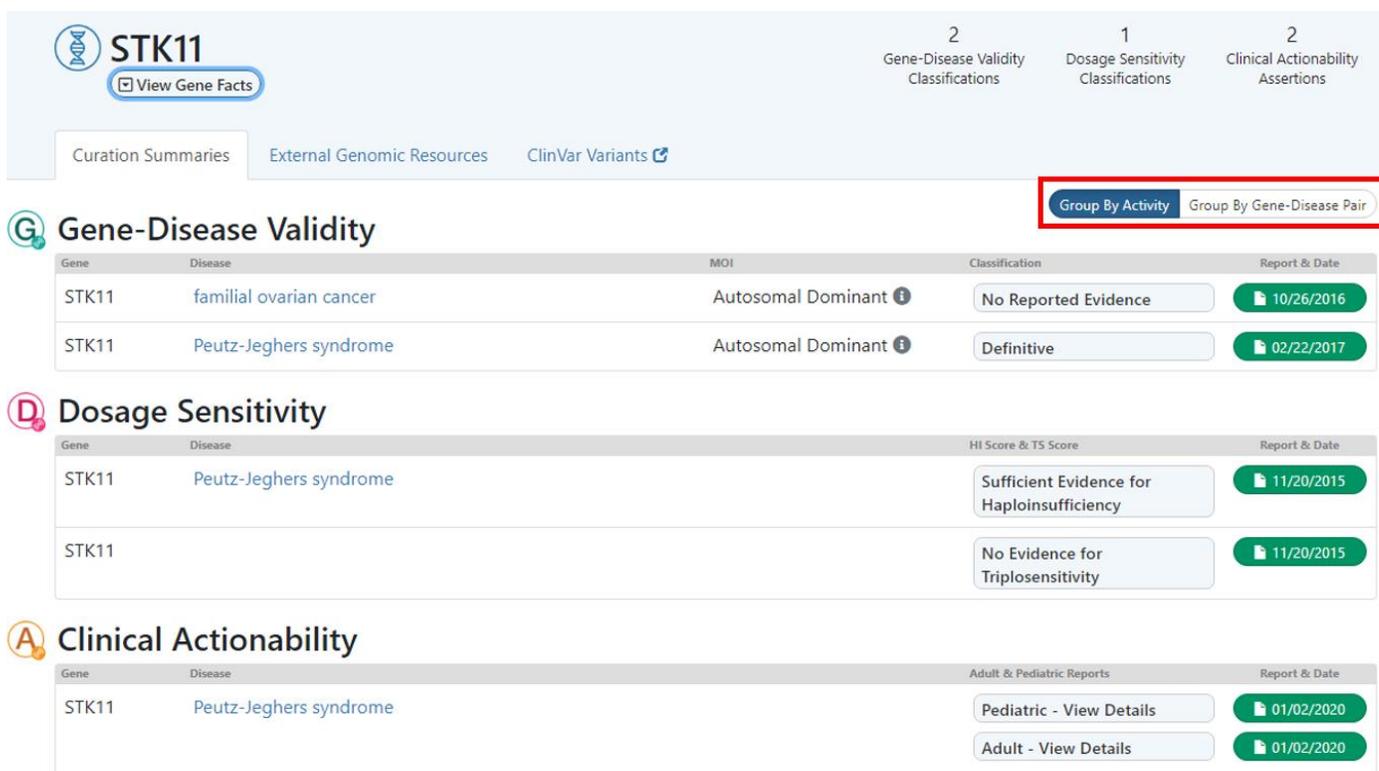
You now have the ability to browse available gene-disease validity curations sorted by the gene curation expert panel (GCEP) that completed them. ClinGen currently has over 30 different GCEPs focused on different clinical domains, so this may be a helpful way to browse if you are interested in a specific disease area. You can access this feature from the “Gene Disease Validity” tab in the “Browse” navigation bar:



Expert Panel	Number of Curations
Aminoacidopathy	86
Arrhythmogenic Right Ventricular Cardiomyopathy	25
Breast/Ovarian Cancer	52
Brugada Syndrome	20

Curations Grouped by Activity

Previously, when searching for a specific gene on clinicalgenome.org, curation results were grouped by disease. This display could sometimes become difficult to read if the gene had been evaluated for more than one disease across more than one curation activity. Now, this information will be grouped by curation activity (gene-disease validity, dosage sensitivity, clinical actionability, or pharmacogenomic). Users have the ability to toggle back to the “Group by Gene-Disease Pair” display if they prefer.



STK11 [View Gene Facts](#)

2 Gene-Disease Validity Classifications | 1 Dosage Sensitivity Classifications | 2 Clinical Actionability Assertions

Curation Summaries | External Genomic Resources | ClinVar Variants

Gene-Disease Validity

Gene	Disease	MOI	Classification	Report & Date
STK11	familial ovarian cancer	Autosomal Dominant ⓘ	No Reported Evidence	10/26/2016
STK11	Peutz-Jeghers syndrome	Autosomal Dominant ⓘ	Definitive	02/22/2017

Dosage Sensitivity

Gene	Disease	HI Score & TS Score	Report & Date
STK11	Peutz-Jeghers syndrome	Sufficient Evidence for Haploinsufficiency	11/20/2015
STK11		No Evidence for Triplosensitivity	11/20/2015

Clinical Actionability

Gene	Disease	Adult & Pediatric Reports	Report & Date
STK11	Peutz-Jeghers syndrome	Pediatric - View Details	01/02/2020
		Adult - View Details	01/02/2020

Gene Facts

Basic information from various external sources will be available at the top of each gene page. Click on the “View Gene Facts” button to expand the display area and view information such as HGNC symbol, gnomAD pLI and LOEUF scores, DECIPHER HI Index score, and MANE Select/MANE Plus Clinical transcript information. Click the button again to collapse the display area.

The screenshot shows the ZEB2 gene page. At the top left is the ZEB2 logo and a "View Gene Facts" button. To the right, there are three statistics: 1 Gene-Disease Validity Classifications, 1 Dosage Sensitivity Classifications, and 0 Clinical Actionability Assertions. Below this is the "Gene Facts" section with a sub-header "External Data Attribution". It lists various attributes: HGNC Symbol (ZEB2), HGNC Name (zinc finger E-box binding homeobox 2), Gene type (protein-coding gene), Locus type (gene with protein product), Previous symbols (ZFH18), Alias symbols (KIAA0569, SIP-1, SIP1), %HI (0.37), pLI (1), LOEUF (0.11), Cytoband (2q22.3), Genomic Coordinates (GRCh37/hg19: chr2:145141942-145277958 and GRCh38/hg38: chr2:144384081-144520119), and MANE Select Transcript (NM_014795.4 and ENST00000627532.3). The Function is described as a transcriptional inhibitor that binds to DNA sequence 5'-CACCT-3' in different promoters.

Richer Display of Dosage Sensitivity Curation Data

For several years, ClinGen dosage sensitivity Curation information has been made publicly available via a separate site, <https://dosage.clinicalgenome.org>. Single-gene dosage curations were cataloged on clinicalgenome.org and were viewable if queried, but dosage curations for larger genomic regions were not supported. With the latest update to the clinicalgenome.org, users are able to access both single gene and genomic region dosage curations without going to a separate site.

Clicking on the “Dosage Sensitivity” button in the “Browse” navigation bar will display a list of genes and genomic regions with dosage curations. Region curations are listed first and are designated with an “R” icon on the left side of the list. Single gene dosage curations are designated with a “G” icon. Users can remove either regions or genes from the display using the button at the top center.

The screenshot shows the "Dosage Sensitivity" interface. At the top, there is a navigation bar with "All Curated Genes", "Gene-Disease Validity", "Dosage Sensitivity" (highlighted), "Clinical Actionability", "Curated Variants", and "More". Below the navigation bar, there are two buttons: "Genes: On" and "Regions: On". To the right, there are statistics: 1492 Total Curations, 1420 Total Genes, and 72 Total Regions. Below this is a search bar and a table. The table has columns: Gene/Region, GRCh37, HI Score, TS Score, OMIM, Morbid, %HI, pLI, LOEUF, and Last Eval. The first row shows a region curation: "1 copy: 14q telomere; 3 copies: 14q telomere" with GRCh37 coordinates 14:106050000-107289540, HI Score 40 (Dosage Sensitivity Unlikely), TS Score 40 (Dosage Sensitivity Unlikely), and Last Eval 07/31/2014. The second row shows a gene curation: "1 copy: 2q telomere|3 copies: 2q telomere" with GRCh37 coordinates 2:242930600-243102476, HI Score 40 (Dosage Sensitivity Unlikely), TS Score 40 (Dosage Sensitivity Unlikely), and Last Eval 04/24/2014.

Within this table of ClinGen dosage sensitivity curations, we have added columns (applicable to the single gene curations only) to describe whether or not the gene has an entry in OMIM, whether or not the gene is considered OMIM “Morbid” (i.e., associated with a disease per OMIM), its DECIPHER HI Index score, and its gnomAD pLI and LOEUF scores.

D Dosage Sensitivity Genes: On Regions: Off

1492 Total Curations 1420 Total Genes 72 Total Regions

Search in table GRCh37 Enter cytoband or genomic coordinates Go!

Showing 1 to 25 of 1420 rows 25 rows per page

Gene/Region	GRCh37	HI Score	TS Score	OMIM	Morbid	%HI	pLI	LOEUF	Last Eval.
A4GALT	22 43088121 43117307	30 (Autosomal Recessive)	0 (No Evidence)	✓	✓	73.08	0	1.65	12/11/2014
AAGAB	15 67493013 67547336	3 (Sufficient Evidence)	0 (No Evidence)	✓	✓	50.94	0	1.04	02/28/2013
AARS1	16 70286297 70323412	0 (No Evidence)	0 (No Evidence)	✓	✓	24.74	0	0.62	01/11/2018

Clicking on the green box with the date last evaluated will open the full dosage curation report. Regular users of ClinGen dosage sensitivity data will notice that these reports are very similar to the ones currently displayed on <https://dosage.clinicalgenome.org>. All of the data is the same, but there are minor differences in the style of the display. ClinGen dosage sensitivity data will remain available on both sites for the foreseeable future, though we encourage users to start utilizing clinicalgenome.org in order to take advantage of the other curation information (e.g., gene-disease validity, clinical actionability) available at that site in order to get a comprehensive view of their gene(s) of interest.

Ability to Search by Genomic Coordinates

Users now have the ability to search the clinicalgenome.org website by genomic coordinates, using either GRCh37 or GRCh38. There are two ways of doing this, resulting in two different types of results.

Searching by genomic coordinates within the Dosage Sensitivity page in the “Browse” navigation bar:

After clicking on the “Dosage Sensitivity” button within the “Browse” navigation bar, you are taken to a table containing all ClinGen dosage sensitivity curations, as described above. Searching by genomic coordinates from this page will return only applicable dosage sensitivity curations, including both single genes and regions. Genes within your search region that have not been curated by ClinGen dosage sensitivity will also be returned (and marked as “awaiting review” or “not reviewable,” in the case of pseudogenes), but you will not know if they have been evaluated by any other ClinGen activity.

GRCh37 Search Results
Location: chr16:28822635-29046499

Genes: On Regions: On

13 Total Genes 1 Total Regions

Search in table Enter cytoband or genomic coordinates

Showing 1 to 14 of 14 rows 25 rows per page

Gene/Region	GRCh37	HI Score	TS Score	OMIM	Morbid	%HI	pLI	LOEUF	Report
16p11.2 recurrent region (distal, BP2-BP3) (includes SH2B1)	16 28822635 29046499	3 (Sufficient Evidence)	1 (Little Evidence)			-	-	-	<input type="button" value="Complete"/>
RPS15AP33	16 28825263 28825648	-1 (Pseudogene)	-1 (Pseudogene)			-	-	-	<input type="button" value="Not Reviewable"/>
ATXN2L	16 28834369 28848558	Not Yet Evaluated	Not Yet Evaluated	✓		25.43	1	0.14	<input type="button" value="Awaiting Review"/>
TUFM	16 28853732 28857729	30 (Autosomal Recessive)	0 (No Evidence)	✓	✓	20.48	0	0.74	<input type="button" value="Complete"/>

Searching by genomic coordinates within the top-level search bar:

Users may also choose to search by genomic coordinates (GRCh37 or GRCh38) using the main search bar at the top of each page. To do this, select “Region” and your preferred genome build from the pull-down menu at the right of the search bar (“Gene” is typically set as the default).

ClinGen
Clinical Genome Resource

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

- Gene Symbol
- Disease Name
- Drug Name
- Region (GRCh37)
- Region (GRCh38)
- Variant
- Website Content

Searching using the top-level search bar will return only single genes within the searched region. It will also indicate which curation activities evaluated this gene (not just limited to dosage sensitivity).

GRCh37 Location Search Results

Location: chr16:28822635-29046499

13
Total
Genes

0
Total
Regions

Search in table 

Showing 1 to 13 of 13 rows 25 rows per page

Gene	Cytoband	Chromosome	Start	Stop	Relationship	Activity	Last Eval.
ATP2A1	16p11.2	16	28889809	28915830	Contained	  	08/22/2016
ATP2A1-AS1	16p11.2	16	28890278	28891242	Contained	  	

Actionability Curation Results Differentiated by Adult and Pediatric Indications

The ClinGen Actionability working group evaluates the clinical actionability of gene-disease pairs separately for pediatric and adult indications. Users are now able to differentiate between the two reports when they are available for the same gene.

Clinical Actionability

Gene	Disease	Adult & Pediatric Reports	Report & Date
STK11	Peutz-Jeghers syndrome MONDO:0008280	Adult - View Details Pediatric - View Details	 01/02/2020  01/02/2020

Integration of Pharmacogenomic Information from CPIC and PharmGKB

In [collaboration with CPIC and PharmGKB](#), clinicalgenome.org will now display pharmacogenomic curation information for genes that have been evaluated by one or both of those groups.

F5 [View Gene Facts](#)

2 Gene-Disease Validity Classifications 1 Dosage Sensitivity Classifications 3 Clinical Actionability Assertions

[Curation Summaries](#) [External Genomic Resources](#) [ClinVar Variants](#)

[Group By Activity](#) [Group By Gene-Disease Pair](#)

G Gene-Disease Validity

Gene	Disease	MOI	Classification	Report & Date
F5	congenital factor V deficiency	Autosomal Recessive ⓘ	Definitive	03/25/2020
F5	thrombophilia due to activated protein C resistance	Autosomal Dominant ⓘ	Definitive	09/30/2019

D Dosage Sensitivity

Gene	Disease	HI Score & TS Score	Report & Date
F5	congenital factor V deficiency	Gene Associated with Autosomal Recessive Phenotype	01/11/2018
F5		No Evidence for Triplosensitivity	01/11/2018

A Clinical Actionability

Gene	Disease	Adult & Pediatric Reports	Report & Date
F5	congenital factor V deficiency	Adult - View Details	11/10/2017
F5	thrombophilia due to activated protein C resistance	Adult - View Details	04/04/2016
		Adult - View Details	11/02/2015

Pharmacogene - CPIC

Gene	Drug	CPIC Level	Date	CPIC Clinical Guidelines
F5	eltrombopag	Level C	10/14/2020	None
	hormonal contraceptives for systemic use	Level C		

Pharmacogene - PharmGKB

Gene	Drug	Highest Level of Evidence	Date	Information
F5	hormonal contraceptives for systemic use	Level 3	10/14/2020	View

If you have any questions, comments, or feedback about these new features, please contact us at clingen@clinicalgenome.org.