

# Gene Curation Interface

## Help Documentation - October 2017

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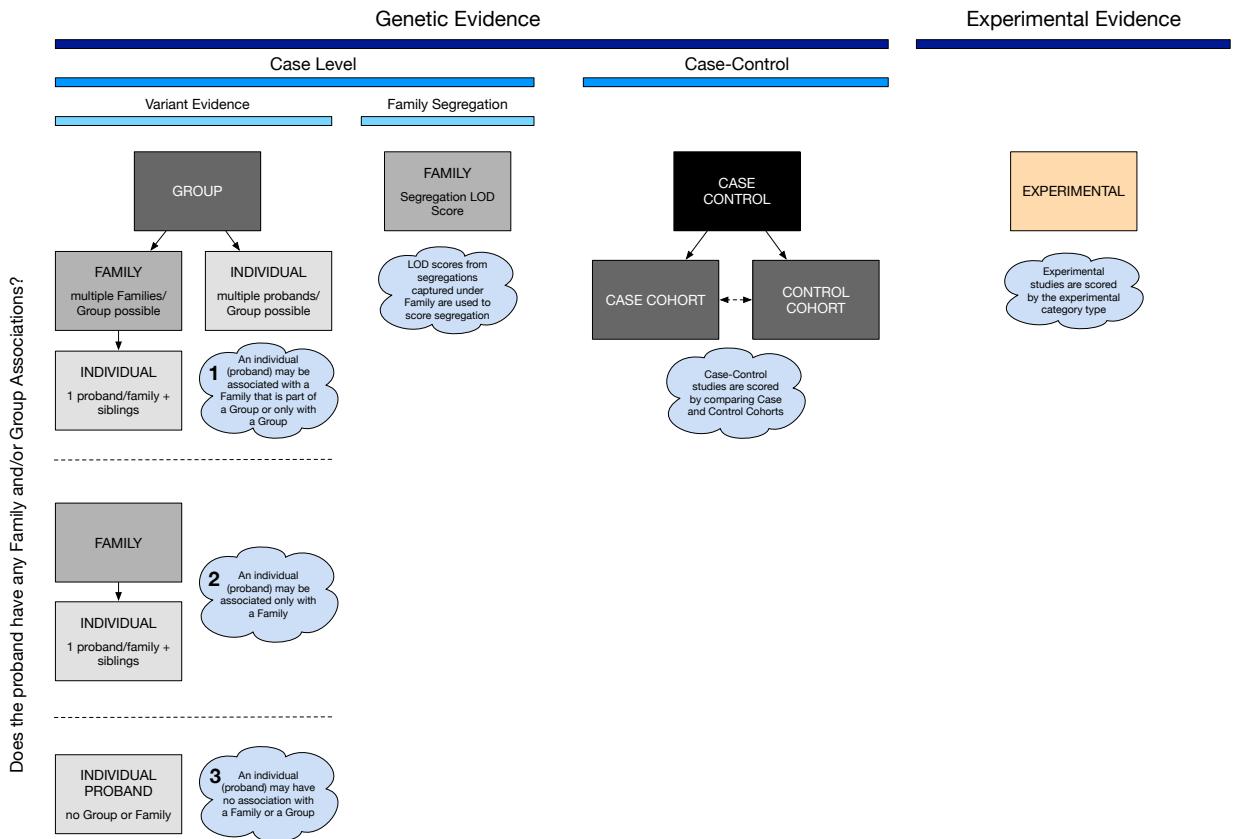
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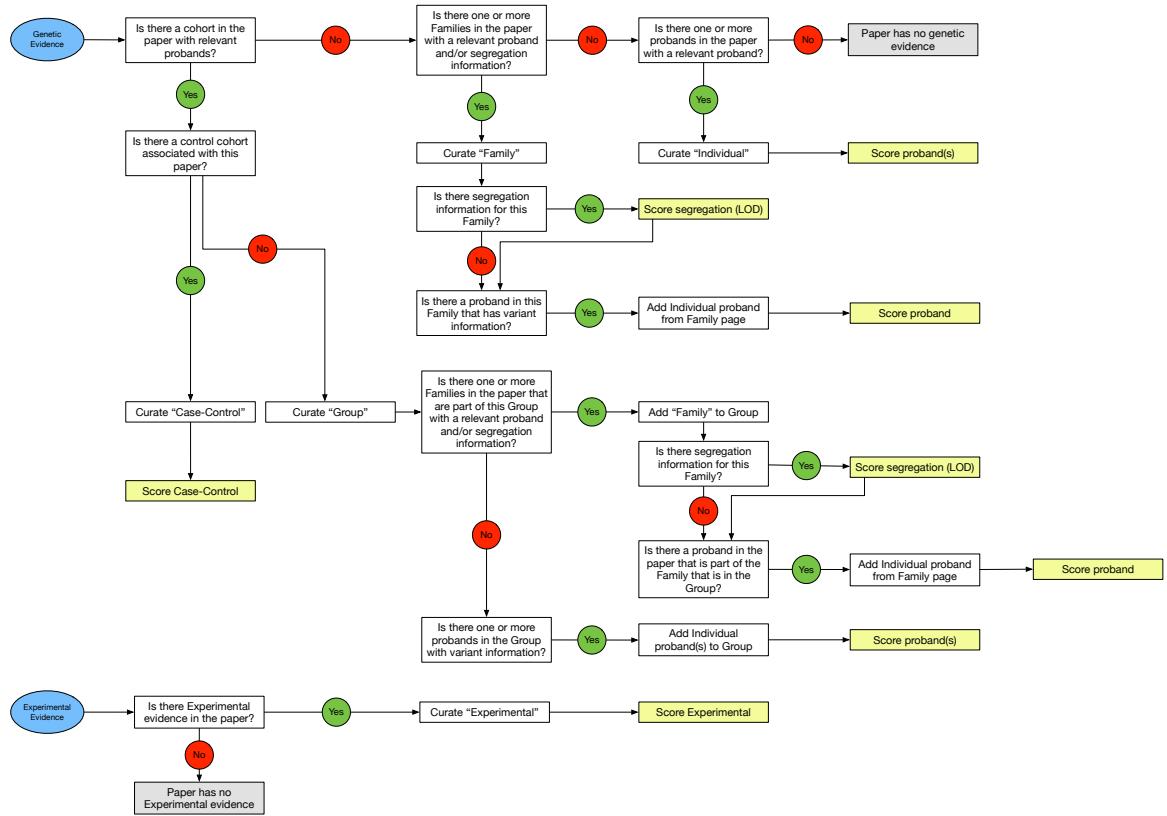
*Feedback / Comments?* Please email us at: [clingen-helpdesk@lists.stanford.edu](mailto:clingen-helpdesk@lists.stanford.edu)

# OVERVIEW OF CURATION

## 1. Quick reference guide



## 2. Curator Workflow



## REGISTRATION

### 1. When to Register

ClinGen curators who would like to access the production version of the ClinGen curation interfaces (<https://curation.clinicalgenome.org/>) will need to register for production interface (see section 2, below, on how to register). Data entered into the production interface is permanently saved, so this interface should only be used for “real” curation.

You can explore the ClinGen test/demo curation interfaces (<https://curation-test.clinicalgenome.org/>) without registering as a ClinGen curator (see ‘Demo Login’ instructions below); however we encourage those who want to explore the interface more thoroughly to register their email with us (see section below for information on how to register). We recommend curators become familiar with the interface by exploring the test interface before curating “real” evidence into the production interface.

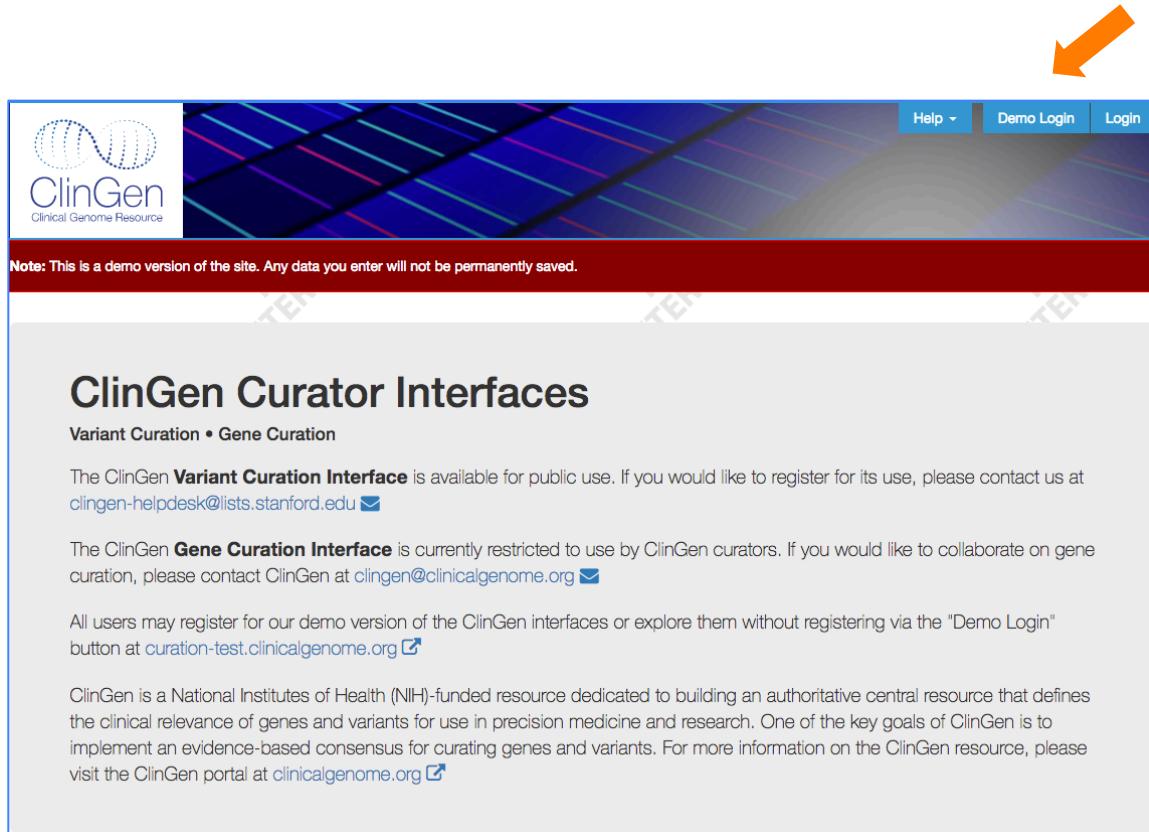
### 2. How to Register

- i. If you are a ClinGen curator, you may request an account by emailing us at [clingen-helpdesk@lists.stanford.edu](mailto:clingen-helpdesk@lists.stanford.edu). The ClinGen **Variant Curation Interface** is available for public use. However, the ClinGen **Gene Curation Interface** is currently restricted to use by ClinGen curators. If you would like to collaborate on gene curation, please contact ClinGen at [clingen@clinicalgenome.org](mailto:clingen@clinicalgenome.org).
- ii. When you write to us please let us know the following:
  - a. Your preferred email address (which you will use to log in to the interfaces)
  - b. Your preferred display name (first and last name)
  - c. Any affiliation you have with ClinGen
- iii. We will write back to you to confirm that your email address has been registered and can be used for logging in to the interfaces.

## LOGGING IN

### 1. Demo Login

You can try out the test/demo version of the ClinGen interfaces (<https://curation-test.clinicalgenome.org/>) by simply clicking on the 'Demo Login' button in the header.



The screenshot shows the ClinGen Curator Interfaces demo login page. At the top, there is a navigation bar with the ClinGen logo, a search bar, and buttons for 'Help', 'Demo Login', and 'Login'. A red banner at the bottom of the header states: 'Note: This is a demo version of the site. Any data you enter will not be permanently saved.' Below the header, the main content area has a dark blue background with abstract geometric patterns. It features a large title 'ClinGen Curator Interfaces' and sub-sections for 'Variant Curation • Gene Curation'. Text in this section includes contact information for variant curation and gene curation, a note about demo users, and a brief description of the ClinGen resource. The entire page is framed by a light gray border.

You will be logged in to the test version of the interfaces under a generic “ClinGen Curator” account.

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

Welcome, ClinGen!

Your status: ClinGen Curator

Tools

- Select Variant for Variant Curation [?](#)
- View list of all Variant Interpretations
- Create Gene-Disease Record [?](#)
- View list of all Gene-Disease Records

Your Recent History

You have no activity to display.

Your Variant Interpretations

You have not created any variant interpretations.

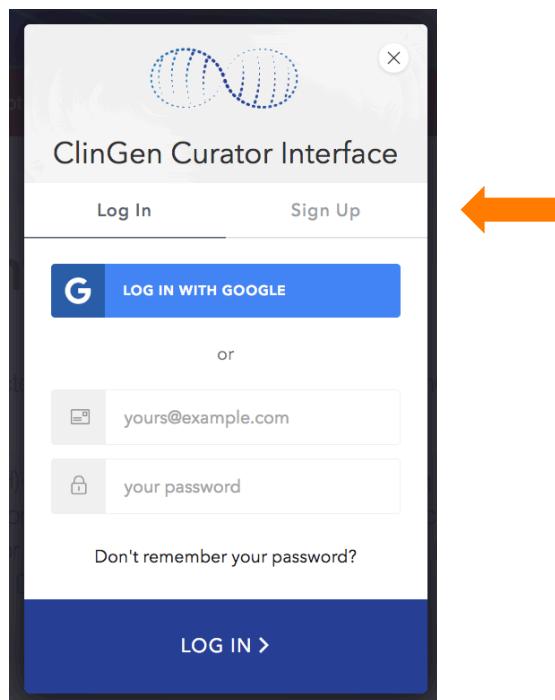
Your Gene-Disease Records

You have not created any Gene-Disease-Mode of Inheritance entries.

## 2. ClinGen Registered User Login

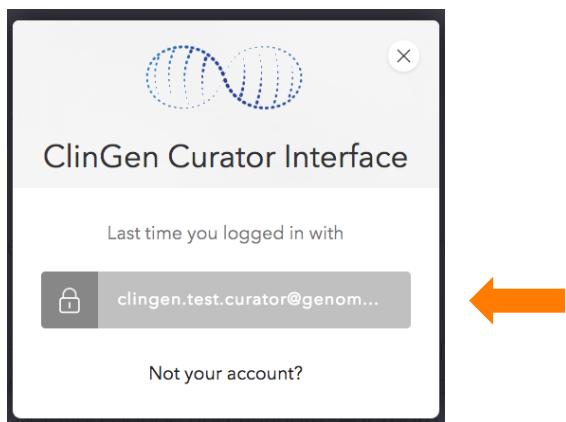
In both the test (<https://curation-test.clinicalgenome.org/>) and production (<https://curation.clinicalgenome.org/>) versions of the ClinGen curation interfaces users who have registered an email address with us can login by clicking the “Login” button in the header. The Auth0 authentication system will now produce a pop-up login window.

- If you are a first time user you will need to go to the “Sign Up” tab and enter your registered email address, enter your desired password, and then click “Sign Up.”



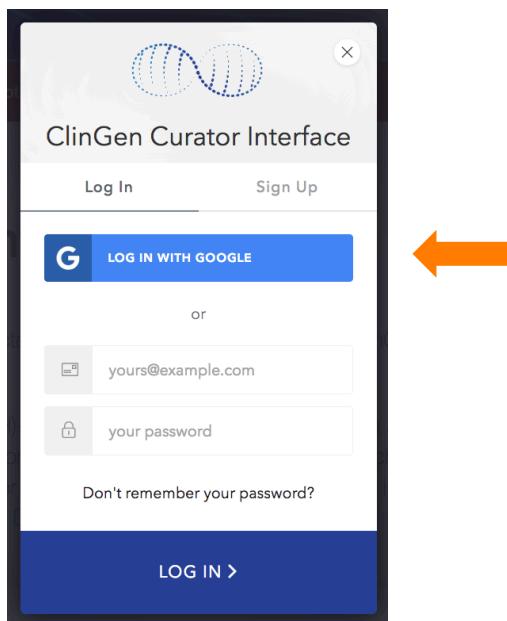
As a first time user, you will also need to be verified by Auth0. When you sign up you will be sent an email in which you need to click the link in order to verify your account. After doing this you should be able to now “log in” using your email and password.

- b. If you are a returning user accessing the interfaces from a different operating system then you will see the pop-up above, in which case you should re-enter your registered email address and your selected password on the “Log In” tab and then click “LOG IN.”
- c. If you are a returning user accessing the interfaces from your usual operating system then your last log in details will likely be saved and you will see the pop-up shown below, in which case you only need to click on your email address to login.



### 3. Google Login

You will note that one of the options on the login window is “LOG-IN WITH GOOGLE.”



You can click this button and log in with a Google email account, however this option is only available for Google emails that have been registered as the preferred email address by a ClinGen curator. You would need to contact us if you wish to change your preferred email to a Google email address.

#### 4. Login Troubleshooting

- i. Have you registered your email address by emailing us at [clingen-helpdesk@lists.stanford.edu](mailto:clingen-helpdesk@lists.stanford.edu)?
- ii. Have you received confirmation from us that your email address has been registered?

## GENERAL NAVIGATION

### 1. Dashboard view

- a Dashboard home – available from all pages
- b Navigating to “Select Variant for Variant Curation” – available from all pages
- c Navigating to “Create Gene-Disease Record” (described below) – available from all pages
- d Navigating to the online Help documentation – available from all pages
- e Navigating to “Select Variant for Variant Curation”
- f View a list of all Variant Interpretations – This list contains all the Interpretations curated to date, along with their status, creator, date created and date last edited.
- g Navigating to “Create Gene-Disease Record” (described below)
- h View a list of all Gene-Disease Records – This list contains all the Gene-Disease Records curated to date, along with their status, creator, date created and date last edited.
- i View of a curator’s recent history – This section provides a chronological history of all edits made by a curator within both the Gene and Variant Curation Interfaces. A curator only views their own history. Each highlighted text is a direct link to the relevant section of the Gene or Variant Curation Interface a curator was previously curating.
- j View of a curator’s current Variant Interpretation curation records – This section provides a list of edits made by a curator within the Variant Curation Interface. A curator only views their own Interpretations. Each highlighted text is a direct link to the variant a curator was previously curating.
- k View of a curator’s current Gene-Disease curation records – This section provides a list of edits made by a curator within the Gene Curation Interface. A curator only views their own Gene-Disease Records. Each highlighted text is a direct link to the Gene-Disease Record a curator was previously curating.
- m Logout – available from all pages

The screenshot shows the ClinGen Test Curator dashboard with several sections and highlighted links:

- Top Navigation:** Help (dropdown), New Variant Curation, New Gene Curation, Home, Logout ClinGen Test Curator.
- Note Bar:** Note: This is a demo version of the site. Any data you enter will not be permanently saved.
- Welcome Section:** Welcome, ClinGen! Your status: ClinGen Curator.
- Tools Section (labeled e):** Select Variant for Variant Curation, View list of all Variant Interpretations, Create Gene-Disease Record, View list of all Gene-Disease Records.
- Your Recent History Section (labeled i):** Family FAMILY1 added to DICER1-Achondroplasia-Autosomal dominant inheritance for PMID:19711917; 2016 Dec 13, 4:47 pm. PMID:5555555 added to DICER1-Achondroplasia-Autosomal dominant inheritance; 2016 Dec 13, 4:46 pm. Disease X-linked non-syndromic intellectual disability associated with Interpretation NM\_020061.5(OPN1LW):c.607T>C (p.Cys203Arg)-X-linked non-syndromic intellectual disability; 2016 Dec 13, 4:46 pm.
- Your Variant Interpretations Section (labeled j):** NM\_020061.5(OPN1LW):c.607T>C (p.Cys203Arg). Disease: X-linked non-syndromic intellectual disability. Mode of Inheritance: None added. Status: Provisional. Creation Date: 2016 Dec 13, 4:45 pm.
- Your Gene-Disease Records Section (labeled k):** DICER1-Achondroplasia-Autosomal dominant inheritance. Status: In Progress. Creation Date: 2016 Dec 13, 4:29 pm.

## CREATING A GENE-DISEASE RECORD

Note: Currently, once a Gene:Disease Record has been created, the disease can be altered up until a PMID has been added. However, the gene, mode of inheritance, and adjective cannot be altered after the record has been created. Please be certain you have selected the desired fields correctly from the beginning.

### 1. Identifying the Gene

A curator is required to identify the specific gene by entering an approved HGNC gene symbol. A link out to HGNC ([www.genenames.org](http://www.genenames.org)) is provided for a curator to look up the correct symbol for their gene.

Enter HGNC gene symbol \* E.G. DICER1

Select disease: \* Search MonDO using OLS Disease +

Mode of Inheritance \* Select

Select an adjective Select

The above options (gene, disease, mode of inheritance, or adjective) can be altered for a Gene:Disease record up until a PMID has been added to the record. This includes adding an adjective to a Gene:Disease:Mode of inheritance record that has already been created or editing an adjective associated with a record.

Submit

### 2. Identifying the Disease

A curator is required to identify the specific disease by entering an MonDO ID. Click on the “Disease +” button to add a disease For additional help in searching for MonDO IDs, please see the “MonDO Search Help” link for further instructions



**Add Disease**

Search MonDO  using the OLS (Ontology Lookup Service).

MonDO Search Help

Enter a MonDO term "id" from MonDO OLS search (Orphanet, DOID, OMIM and NCIt id's allowed). The term "id" can be found in the "Term info" box displayed on the right hand side of the OLS term page (e.g. [Orphanet:93545](#)): \*

Note: We strongly encourage use of an allowed MonDO ontology term and therefore specific database identifier for a disease. If you have searched and there is no appropriate database identifier you may contact us at [clingen-helpdesk@lists.stanford.edu](mailto:clingen-helpdesk@lists.stanford.edu) and/or create a term using free text.

Check this box *only* if you were unable to find a suitable ontology term and need to enter a free text term:

After entering an ID and selecting “Retrieve from OLS,” the term name and definition (if one exists) will be returned. Select “Save” if this is the desired term.

**Add Disease**

Search MonDO  using the OLS (Ontology Lookup Service).

MonDO Search Help

Enter a MonDO term "id" from MonDO OLS search (Orphanet, DOID, OMIM and NCIt id's allowed). The term "id" can be found in the "Term info" box displayed on the right hand side of the OLS term page (e.g. [Orphanet:93545](#)): \*

Below are the data from OLS for the ID you submitted. Select "Save" below if it is the correct disease, otherwise revise your search above:

**NGLY1-deficiency** 

A carbohydrate metabolic disorder that has\_material\_basis\_in homozygous or compound heterozygous mutation in the NGLY1 gene on chromosome 1p24. It is characterized by global developmental delay, hypotonia, abnormal involuntary movements, and alacrima or poor tear production.

After entering an ID and saving, the disease term name, ID, and definition (if one exists) will be displayed on the Create GDM page:

The screenshot shows a form for creating a Gene-Disease-Mode of Inheritance record. At the top, there is a field labeled "Enter HGNC gene symbol \*". A yellow highlight box surrounds the input field containing the text "NGLY1". Below this, there is a section titled "Select disease: \*". It includes a search bar "Search MonDO using OLS" and a button "Disease +". To the right of the search bar, the text "NGLY1-deficiency (OMIM:615273)" is displayed. Below this, a detailed "Definition" is provided: "A carbohydrate metabolic disorder that has\_material\_basis\_in homozygous or compound heterozygous mutation in the NGLY1 gene on chromosome 1p24. It is characterized by global developmental delay, hypotonia, abnormal involuntary movements, and alacrima or poor tear production."

### 3. Identifying the Mode of Inheritance

A curator is required to identify the specific Mode of Inheritance by choosing from the selection available in the pull-down.

The screenshot shows the continuation of the form. There is a field "Enter HGNC gene symbol \*" with the placeholder "E.G. DICER1". Below it is a "Select disease: \*" section with a "Disease +" button. The next section is "Mode of Inheritance \*". A dropdown menu is open, showing options: "Select", "Autosomal dominant inheritance (HP:0000006)", "Autosomal recessive inheritance (HP:0000007)", "Mitochondrial inheritance (HP:0001427)", "X-linked inheritance (HP:0001417)", "Other", and "Unknown". An orange arrow points to this dropdown menu. A note below the dropdown says: "The above options (gene, disease, mode of inheritance) can be selected from the dropdown menus. Gene:Disease record up until a PMID has been added to the record. This includes adding an adjective to a Gene:Disease:Mode of inheritance record that has already been created or editing an adjective associated with a record." At the bottom right is a "Submit" button.

#### 4. Free text option for disease

If there is no MonDO term, a free text term may be entered for the disease. *Note: using a disease identifier if highly recommended. If you cannot find an appropriate one, please feel free to contact us at [clingen-helpdesk@lists.stanford.edu](mailto:clingen-helpdesk@lists.stanford.edu) and we will be happy to assist.*

To enter a free text term, verify you click on the checkbox (see arrow below)

The screenshot shows the 'Add Disease' page. At the top, it says 'Search MonDO using the OLS (Ontology Lookup Service)'. Below that is a note about using MonDO IDs from OLS. A text input field contains 'e.g. Orphanet:93545, DOID:0050776, OMIM:100800 OR NCIT:C4089'. A button labeled 'Retrieve from OLS' is next to it. A note below says to use allowed MonDO ontology terms or database identifiers. A checkbox is present with the instruction: 'Check this box only if you were unable to find a suitable ontology term and need to enter a free text term:'. An orange arrow points to this checkbox. At the bottom are 'Cancel' and 'Save' buttons.

This will take you to a page where you can enter a free text term (up to 100 characters in length). You must also provide either a set of HPO terms (preferred) or a Definition for the term you are entering. You may also provide both. *Please remember that if someone else enters a different phrase for the same ID, the interface will not be able to determine they are equivalent.*

**Add Disease**

Search MonDO  using the OLS (Ontology Lookup Service).

[MonDO Search Help](#)

Use of free text could result in different terms being used for the same disease. Please make certain there is no appropriate ontology term before applying a free text disease name.

Disease name: *	<input style="width: 100%; height: 25px; border: 1px solid #ccc; padding: 2px;" type="text"/>
Either HPO term(s) or a definition is required to describe this disease (both fields may be used).	
Phenotype(s) (HPO ID(s)): *	<input style="width: 100%; height: 25px; border: 1px solid #ccc; padding: 2px;" type="text"/> e.g. HP:0010704, HP:0030300
Disease definition: *	<input style="width: 100%; height: 50px; border: 1px solid #ccc; padding: 2px;" type="text"/>

## 5. Selecting an Adjective (optional)

A curator can add an adjective to the Mode of Inheritance by choosing from the selection available in the pull-down.

Enter HGNC  gene symbol \*

Select disease: \*

Search MonDO  using OLS

NGLY1-deficiency (OMIM:615273) Disease 

Definition: A carbohydrate metabolic disorder that has\_material\_basis\_in homozygous or compound heterozygous mutation in the NGLY1 gene on chromosome 1p24. It is characterized by global developmental delay, hypotonia, abnormal involuntary movements, and alacrima or poor tear production.

Mode of Inheritance \*

Autosomal dominant inheritance (HP:0000006) ▼

Select an adjective

Select

- with maternal imprinting
- with paternal imprinting
- sex-limited
- with genetic anticipation
- primarily or exclusively de novo

The above options (gene, disease, mode of inheritance) will be included in the Gene:Disease record up until a PMID has been added. However, the gene, mode of inheritance, and adjective cannot be altered after the record has been created. Please be certain you have selected the desired fields correctly from the beginning.

Note: Currently, once a Gene:Disease Record has been created, the disease can be altered up until a PMID has been added. However, the gene, mode of inheritance, and adjective cannot be altered after the record has been created. Please be certain you have selected the desired fields correctly from the beginning.



## STARTING GENE-DISEASE CURATION

### 1. Curation Central view

This is the landing page/homepage for each Gene-Disease curation.

- a. First line of header shows the Gene Symbol and Disease selected by a curator.
- b. Second line of header shows the Mode of Inheritance selected by a curator. If a curator selected an adjective then this will appear in parentheses.
- c. Curation Central home – available from all pages.
- d. History of the last saved Summary and any Provisional Classifications for the Gene-Disease record.
- e. View Classification Matrix – available from all pages.
- f. Gene symbol and links to HGNC and NCBI Gene.
- g. Disease name and links to disease term and OMIM.
- h. The name of the curator who first created the Gene-Disease record and the timestamp of when they did so.
- i. List of all participants who have made edits to the Gene-Disease record.
- j. Curator name and timestamp for the most recent edit to the Gene-Disease record.

**DICER1 – blue cone monochromacy** **C**  
Autosomal dominant inheritance (with maternal imprinting)

**Classification**  
None **d**

**e** [View Classification Matrix](#)

<b>DICER1</b> <b>f</b> HGNC Symbol: <a href="#">DICER1</a> NCBI Gene ID: <a href="#">23405</a>	<b>blue cone monochromacy</b> <b>g</b> [View definition] Disease ID: <a href="#">OMIM:303700</a> OMIM ID: <a href="#">[Add]</a>	Creator: <a href="#">ClinGen Test Curator</a> — 2017 Oct 11, 4:07 pm <b>h</b> Participants: <a href="#">ClinGen Test Curator</a> <b>i</b> Last edited: <a href="#">ClinGen Test Curator</a> — 2017 Oct 11, 4:11 pm <b>j</b>
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**Add New PMID**

Add papers to this Gene-Disease Record using the **Add New PMID(s)** button; click on any added paper to view its abstract and begin curating evidence from that paper.

### 3. Adding a PubMed article to the Gene-Disease Record

- i. To add a PubMed article to the Gene-Disease record click the “Add New PMID” button .

**DICER1 – blue cone monochromacy** **C**  
Autosomal dominant inheritance (with maternal imprinting)

**Classification**  
None

**View Classification Matrix**

<b>DICER1</b> HGNC Symbol: <a href="#">DICER1</a> NCBI Gene ID: <a href="#">23405</a>	<b>blue cone monochromacy</b> [View definition] Disease ID: <a href="#">OMIM:303700</a> OMIM ID: <a href="#">[Add]</a>	Creator: <a href="#">ClinGen Test Curator</a> — 2017 Oct 11, 4:07 pm Participants: <a href="#">ClinGen Test Curator</a> Last edited: <a href="#">ClinGen Test Curator</a> — 2017 Oct 11, 4:11 pm
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**Add New PMID**

Add papers to this Gene-Disease Record using the **Add New PMID(s)** button; click on any added paper to view its abstract and begin curating evidence from that paper.

- ii. Enter the PMID into the modal that appears and click the “Retrieve PubMed Article” button.

The screenshot shows a modal window titled "Add new PubMed Article". Inside, there is a label "Enter a PMID \*" followed by a text input field containing "10000". Below the input field is a blue button labeled "Retrieve PubMed Article". At the bottom right of the modal are two buttons: "Cancel" and "Add Article". An orange arrow points to the "Add Article" button.

- iii. Based on the PMID entered the authors, title, and citation details will be auto-filled. If these details are correct then a curator can add that PMID to the Gene-Disease Record by clicking the “Add Article” button.

## Add new PubMed Article

Enter a PMID \*

10000

**Retrieve PubMed Article**

Select "Add Article" (below) if the following citation is correct; otherwise, edit the PMID (above) to retrieve a different article.

Baumstark JS, Lee CT, Luby RJ. A new method for the determination of alpha1-protease inhibitor (alpha1-antitrypsin) phenotypes based on the formation of alpha1-protease inhibitor allele product-elastase complexes. *Biochimica et biophysica acta*. 1976 Sep 28;446(1):287-300. PMID:

10000 

**Cancel**

**Add Article**



- iv. The PMID has now been added to the Curation Central view for that Gene-Disease Record.
  - a. All articles that have been added to the record can be found in a scrollable panel on the left-hand side, with the first author, title, citation details, and PMID shown for each article. By default a newly added article will be the one selected for curation in the interface, as shown by a blue border. To select an alternative article for curation, a curator simply needs to click on that article in the left-hand panel.
  - b. The central panel shows more details about the article selected by a curator, including all authors, the title, a link to PubMed, and the full abstract.
  - c. An evidence curation palette on the right-hand side provides now provides access to curation resources for adding Genetic and Experimental Evidence found in the selected article.
  - d. Further articles can be added to the Gene-Disease Record by clicking the "Add New PMID" button.

**DICER1 – blue cone monochromacy** 

Autosomal dominant inheritance (with maternal imprinting)

<b>Classification</b> None		<a href="#">View Classification Matrix</a>
<b>DICER1</b> HGNC Symbol: <a href="#">DICER1</a>  NCBI Gene ID: 23405 	<b>blue cone monochromacy</b> <a href="#">[View definition]</a> Disease ID: OMIM:303700  OMIM  ID: <a href="#">[Add]</a>	Creator: ClinGen Test Curator — 2017 Oct 11, 4:07 pm Participants: ClinGen Test Curator Last edited: ClinGen Test Curator — 2017 Oct 11, 4:11 pm
<b>Add New PMID</b>  <b>d</b>  <div style="border: 1px solid #ccc; padding: 5px; margin-bottom: 10px;">           Baumstark JS et al. A new method for the determination of alpha1-protease inhibitor (alpha1-antitrypsin) phenotypes based on the formation of alpha1-protease inhibitor allele product-elastase complexes. <b>1976 Sep 28</b>;446(1):287-300.   <b>PMID: 10000</b>  </div> <div style="border: 1px solid #ccc; padding: 5px; margin-bottom: 10px;">           Carlsson E et al. [Receptor pharmacology (4): beta adrenoreceptor blocker effect in cardiovascular diseases]. <b>1978 Nov 01</b>;75(44):4028-33.   <b>PMID: 30000</b>  </div> <div style="border: 1px solid #ccc; padding: 5px; margin-bottom: 10px;">           Laxenaire MC et al. [Pharmacology of nitrous oxide]. <b>1977 Jul 19</b>;18(3):1E-6E.         </div>		<b>Evidence for PMID:10000</b>  <b>c</b>  <b>Genetic Evidence</b> > Case Level <ul style="list-style-type: none"> <li><b>Group</b>  </li> <li><b>Family</b>  </li> <li><b>Individual</b>  </li> </ul> > Case-Control <ul style="list-style-type: none"> <li><b>Case-Control</b>  </li> </ul> <b>Experimental Evidence</b> <b>Experimental Data</b>   <b>Associated Variants</b>

### 3. Starting Evidence Collection

The gene curation palette on the right-hand side is the starting point for adding evidence for a selected article. To begin curation a curator clicks the ‘+’ sign next to specific type of evidence they wish to curate.

## ADDING GENETIC EVIDENCE

### 1. Curate Group Information

Evidence for PMID:10000

Genetic Evidence

Case Level

Group

Family

Individual

Case-Control

Case-Control

Experimental Evidence

Experimental Data

Associated Variants

The top of the landing page to Curate Group Information shows the authors, title, and citation details for the selected PubMed article in a yellow box below the header. A curator is required to enter a label for the Group, if possible using a label described in the paper.

Baumstark JS, Lee CT, Luby RJ. A new method for the determination of alpha1-protease inhibitor (alpha1-antitrypsin) phenotypes based on the formation of alpha1-protease inhibitor allele product-elastase complexes. *Biochimica et biophysica acta*. 1976 Sep 28;446(1):287-300. PMID: 10000

Curate Group Information

Group EXAMPLE-GROUP-LABEL1

Group Label: \* EXAMPLE-GROUP-LABEL1

Please enter a label to help you keep track of this Group within the interface - if possible, please use the label described in the paper.

The rest of the Curate Group Information page is split into relevant sections based on the type of evidence:

#### i. Group – Common Disease(s) & Phenotype(s)

A curator is required to enter at least one of the following to describe disease(s)/phenotype(s) common to the group:

- a) MonDO ID (or free text)
- b) HPO ID(s)
- c) Phenotype free text

Please enter a disease term and/or phenotype(s); phenotypes may be entered using HPO ID(s) (preferred) or free text when there is no appropriate HPO ID.

**Disease(s) in Common:**  
Search [MonDO](#) using OLS

**Phenotype(s) in Common (HPO ID(s)):**

**Phenotype(s) in Common (free text):**

- or -

## ii. Group – Demographics

Enter information about the demographics of the group.

**Group – Demographics**

# males:	<input type="text"/>
# females:	<input type="text"/>
Country of Origin:	<input type="text"/>
Ethnicity:	<input type="text"/>
Race:	<input type="text"/>
<b>Age Range</b>	
Type:	<input type="text"/>
Value:	<input type="text"/> to <input type="text"/>
Unit:	<input type="text"/>

## iii. Group – Information

Enter information about the individuals in the group. A curator is required to enter the total number of individuals in the group.

**Group – Information**

Total number individuals in group: \*

# individuals with family information:

# individuals WITHOUT family information:

# individuals with variant in gene being curated:

# individuals without variant in gene being curated:

# individuals with variant found in other gene:

Other genes found to have variants in them (HGNC symbol):  E.G. DICER1, SMAD3



#### iv. Group – Methods

Enter information about the methods used to obtain genetic data for the Group.

**Group – Methods**

Previous Testing:  No Selection

Description of Previous Testing:

Were genome-wide analysis methods used to identify the variant(s) described in this publication?:  No Selection

**Genotyping Method**

Method 1:  No Selection

Method 2:  No Selection

Entire gene sequenced?:  No Selection

Copy number assessed?:  No Selection

Specific mutations genotyped?:  No Selection

Description of genotyping method:

#### v. Group – Additional Information

Enter any additional information about the Group.

**Group – Additional Information**

Additional Information about Group:

Enter PMID(s) that report evidence about this same Group:

e.g. 12089445, 21217753

Note: Any variants associated with probands that will be counted towards the Classification are not captured at the Group level - variants and their association with probands are required to be captured at the Family or Individual level. Once you submit the Group information, you will be prompted to enter Family/Individual information.

#### vi. Cancel/Save buttons

- Clicking the “Cancel” button, found at the bottom of the Curate Group Information page, will return a curator to the Record Curation page without saving any entered data.
- Clicking the “Save” button, found at the bottom of the Curate Group Information page, is the only way to save all the Group data added by a curator. Navigating away from this page without saving will result in the loss of any entered data.
- After clicking the “Save” button if any of the required fields (described above) are not filled in, then a red text warning will appear next to the buttons.

Please fix errors on the form and resubmit.

- Additionally, a red text warning will appear next to the required fields that need to be curated before the page can be saved.

Total number individuals in group: \*

Required

## 2. Curate Family Information

If the Family to be entered is part of a Group already curated in this Gene-Disease Record then it can be added when prompted after saving a Group by selecting ‘Yes’ from the pull-down, and then ‘Add New Family for this Group’:

**Do any of the probands or other individuals in this Group have Family Information?**

Yes

**Note:** Family Information includes any information about a proband in the group that is part of family and any relatives of the proband (e.g. average age of onset, race, family ethnicity, etc.) and information about segregation of phenotype(s) and variant(s).

Any variant associated with a proband in a Family is captured at the Family level.

To associate segregation, variant, or any other information for a family, **Add New Family for this Group.**

[Add New Family for this Group](#)

If you have previously created an entry for this Family, **Return to Record Curation page** to add this Family to the newly created Group.

OR

[Return to Record Curation page](#)

It can also be added directly from that Group in the curation palette on the Record page.

**Evidence for PMID:10000**

**Genetic Evidence**

Case Level

Group +

**EXAMPLE-GROUP-LABEL**  
ClinGen Test Curator  
2017 Jan 06, 2:51 pm  
[View](#) | [Edit](#)

[Add new Family to this Group](#)  
[Add new Individual to this Group](#)



To add a new Family that is not associated with a Group, click the Family '+' in the curation palette.

**Evidence for PMID:10000**

**Genetic Evidence**

> Case Level

- Group** +
- Family** +
- Individual** +

> Case-Control

- Case-Control** +

**Experimental Evidence**

- Experimental Data** +

**Associated Variants**



The top of the landing page to Curate Family Information shows the authors, title, and citation details for the selected PubMed article in a yellow box below the header. A curator is required to enter a label for the Family, if possible using a label described in the paper.

Baumstark JS, Lee CT, Luby RJ. A new method for the determination of alpha1-protease inhibitor (alpha1-antitrypsin) phenotypes based on the formation of alpha1-protease inhibitor allele product-elastase complexes. *Biochimica et biophysica acta*. 1976 Sep 28;446(1):287-300. PMID: 10000 ↗

**Curate Family Information**

Group EXAMPLE-GROUP-LABEL // No entry

Family Label: \*

Please enter a label to help you keep track of this Family within the interface - if possible, please use the label described in the paper.



The rest of the Curate Family Information page is split into relevant sections based on the type of evidence. The first three sections are in a similar format to the same sections in the Curate Group Information:

- i. Family – Disease(s) & Phenotype(s)
- ii. Family – Demographics
- iii. Family – Methods

iv. Family – Segregation. This section is split into two separate sections for adding information on tested individuals and LOD score respectively.

Fields for entering information on Tested Individuals within a Family:

- a) For a Dominant and Recessive disease/phenotype a curator is required to enter the total number of AFFECTED individuals in the Family WITH the genotype for that disease/phenotype.
- b) For a Recessive disease/phenotype a curator is required to enter the total number of UNAFFECTED individuals in the Family WITHOUT the biallelic genotype for that disease/phenotype.
- c) Enter the total number of segregations reported for the Family.
- d) If there are any inconsistent segregations amongst the TESTED Individuals then 'Yes' should be selected from the pull-down. If not, then select 'No'.
- e) If 'Yes' is selected in the prior field then optional free text can be added here to describe the inconsistent segregations.
- f) If the Family is consanguineous then 'Yes' should be selected from the pull-down. If not, then select 'No'. If this is unknown then selected 'Not Specified'.
- g) If a pedigree was provided in the publication, then optional free text can be added here to describe the location of the pedigree within the paper.

**Family – Segregation**

**Tested Individuals**

For Dominant AND Recessive inheritance: a Number only  
Number of AFFECTED Individuals *WITH* genotype? \*

For Recessive inheritance only: b Number only  
Number of UNAFFECTED individuals *WITHOUT* the biallelic genotype? (required for Recessive inheritance)

Number of segregations reported for this Family: c Number only  
(required for calculating an estimated LOD score for Dominant inheritance)

Were there any inconsistent segregations amongst TESTED individuals? (i.e. affected individuals *WITHOUT* the genotype or unaffected individuals *WITH* the genotype)? d No Selection

please provide explanation: e (optional)

Is this family consanguineous?: f No Selection

If pedigree provided in publication, please indicate location: g e.g. Figure 3A

For entering information on a LOD Score for the Family, there are two separate scenarios based on whether the LOD score was published in the paper or not.

## Published LOD Score

Select 'Yes' from the pull-down.

➤ LOD Score (select one to include as score):

Published LOD score?:	<input checked="" type="checkbox"/> No Selection <input type="checkbox"/> Yes <input type="checkbox"/> No
-----------------------	---



Enter the value of the published LOD score.

➤ LOD Score (select one to include as score):

Published LOD score?:	<input type="text" value="Yes"/>
Published Calculated LOD score:	<input type="text" value="0.72"/>



If the entered published LOD score should be included in the final aggregate calculation then 'Yes' must be selected from the pull-down.

If the entered published LOD score should NOT be included in the final aggregate calculation then 'NO' should be selected from the pull-down.

A box is provided to add free text to 'Explain reasoning' behind this decision. A further free text box allows 'Additional Segregation Information' to be entered.

➤ LOD Score (select one to include as score):

Published LOD score?:	<input type="text" value="Yes"/>
Published Calculated LOD score:	<input type="text" value="0.72"/>
Include LOD score in final aggregate calculation?	<input checked="" type="checkbox"/> No Selection <input type="checkbox"/> Yes <input type="checkbox"/> No
Explain reasoning:	<input type="text"/>
Additional Segregation Information:	<input type="text"/>



### Estimated LOD Score

If there is no Published LOD Score then Select 'No' from the pull-down. If the required Tested Individual fields (above) have been entered then the Estimated LOD score will be calculated automatically within the interface.

› LOD Score (select one to include as score):

Published LOD score?:	No
Estimated LOD score: <small>(optional, and only if no published LOD score)</small>	0.3



If the estimated LOD score should be included in the final aggregate calculation then 'Yes' must be selected from the pull-down.

If the estimated LOD score should NOT be included in the final aggregate calculation then 'NO' should be selected from the pull-down.

A box is provided to add free text to 'Explain reasoning' behind this decision. A further free text box allows 'Additional Segregation Information' to be entered.

› LOD Score (select one to include as score):

Published LOD score?:	No
Estimated LOD score: <small>(optional, and only if no published LOD score)</small>	0.3

Include LOD score in final aggregate calculation?

✓ No Selection

Yes  
No

Explain reasoning:

Additional Segregation Information:



#### v. Family – Variant(s) Segregating with Proband

To score the proband for a Family then, in addition to the LOD score for the segregation, an Individual proband will need to be created including adding their associated variant(s).

- a. A curator is required to enter a label for the Proband, if possible using a label described in the paper. A real name should not be entered.

- b. The disease ID(s) for the disease(s) associated with the Family automatically shown.
- c. Enter the disease ID(s) for the disease(s) associated with the Individual.
- d. Click this button to automatically copy the disease ID(s) for the disease(s) associated with the Family to the field above for the Individual.
- e. Check this box if the Individual is homozygous.
- f. Check this box if the Individual is hemizygous.
- g. Click this button to add the first variant associated with the Individual via a ClinVar ID
- h. Click this button to add the first variant associated with the Individual via a ClinGen Allele Registry CA ID.
- i. Click this button to add a second variant (where appropriate) associated with the Individual via a ClinVar ID.
- j. Click this button to add a second variant (where appropriate) associated with the Individual via a ClinGen Allele Registry CA ID.

**Family – Variant(s) Segregating with Proband**

If you would like to score the proband for this family in addition to the LOD score for segregation, you need to create the individual proband, including adding their associated variant(s). Please follow the steps below -- you will be able to add additional information about the proband following submission of Family information.

Note: Probands are indicated by the following icon: 

Once this Family page is saved, an option to score and add additional information about the proband (e.g. demographics, phenotypes) will appear.

Proband Label \* **a** EXAMPLE-PROBAND

Note: Do not enter real names in this field. Please enter a label to help you keep track of this individual within the interface - if possible, please use the label described in the paper.

Orphanet Disease(s) Associated with Family: **b** ORPHA777

Orphanet Disease(s) for Individual \* **c** E.G. ORPHA15

**d** Copy Orphanet IDs from Family

Check here if homozygous: **e**   
(Note: If homozygous, enter only 1 variant below)

Check here if hemizygous: **f**

Add Variant: **g** Add ClinVar ID - or - **h** Add CA ID

Add Variant: **i** Add ClinVar ID - or - **j** Add CA ID

## Adding Variants

When adding a Variant associated with an Individual via the 'Add ClinVar ID' or 'Add CA ID' buttons, a pop-up window will appear. Enter the ClinVar ID or CA ID into the window

and click the 'Retrieve from ClinVar' or 'Retrieve from ClinGen Allele Registry' button respectively.

ClinVar Variant

Enter ClinVar VariationID \*

37644

Retrieve from ClinVar

Enter a ClinVar VariationID. The VariationID can be found in the light blue box on a variant page (example: 139214).

Cancel Save

Check the evidence retrieved for either the ClinVar ID or CA ID you have entered and once you are convinced the ID you have entered represents the correct variant, Select 'Save' to add that variant to the Individual.

ClinVar Variant

Enter ClinVar VariationID \*

10505

Retrieve from ClinVar

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

NM\_020061.5(OPN1LW):c.607T>C (p.Cys203Arg)

ClinVar Variant ID    10505

HGVS terms

NC_000023.11:g.154154602T>C (GRCh38)
NC_000023.10:g.153420077T>C (GRCh37)
NG_009105.2:g.15352T>C
NM_020061.5:c.607T>C
NP_064445.2:p.Cys203Arg
NG_009105.1:g.15353T>C
NM_020061.4:c.607T>C
NP_064445.1:p.Cys203Arg

Cancel Save

The variants added via the ClinVar and/or CA IDs can now be seen associated with the Proband:

- a. ClinVar Variation ID with linkout to ClinVar.
  - b. ClinVar Preferred Title for the variant.
  - c. Link within the Interface to ‘Curate Variant Information’ so that curator can enter the gene impact for that variant. [Please note: this feature was removed, but will be added back shortly]
- Note: A variant's gene impact should be specified in order to score the Proband.**
- d. Link within the Interfaces to the ‘Evidence View’ in the Variant Curation Interface so that curator can view all known evidence (both programmatic and manually entered from papers) for that variant.
  - e. Clear the selected variant.
  - f. ClinGen Allele Registry ID with linkout to the ClinGen Allele Registry.
  - g. HGVS Title for the current genome build. Shown only of for novel variant that cannot be found in ClinVar.

ClinVar Variation ID: **a** [10505](#)

ClinVar Preferred Title: **b** NM\_020061.5(OPN1LW):c.607T>C (p.Cys203Arg)

Note: a variant's gene impact must be specified in order to score this proband.

**c** Curate variant's gene impact  
**d** View variant evidence in Variant Curation Interface

Clear Variant Selection: **e** [Clear](#)

---

ClinGen Allele Registry ID: **f** [CA2289129](#)

Genomic HGVS Title: **g** NC\_000003.12:g.25729211\_25729214del (GRCh38)

Note: a variant's gene impact must be specified in order to score this proband.

[Curate variant's gene impact](#)  
[View variant evidence in Variant Curation Interface](#)

Clear Variant Selection: [Clear](#)

Once variants have been saved to a Gene Record they will appear in the Gene Record page under the header in a Gene-Disease Records Variants section. There is an individual blue box for each variant containing the name for each variant. Each box is a link to a page for curating the variant's gene impact.

**Gene-Disease Record Variants**

Click a variant to View, Curate, or Edit it. The icon indicates curation by one or more curators.

NM\_007294.3(BRCA1):c.536delA (p.Tyr179Serfs)

NC\_000003.12:g.25729211\_25729214del

vi. Family – Cancel/Save buttons

- Clicking the “Cancel” button, found at the bottom of the Curate Family Information page, will return a curator to the Record Curation page without saving any entered data.
- Clicking the “Save” button, found at the bottom of the Curate Family Information page, is the only way to save all the Family data added by a curator. Navigating away from this page without saving will result in the loss of any entered data.
- After clicking the “Save” button if any of the required fields (described above) are not filled in, then a red text warning will appear next to the buttons.

Please fix errors on the form and resubmit.

Cancel      Save

- A red text warning will appear next to the missing required field.

For Dominant AND Recessive inheritance:

Number of AFFECTED individuals WITH genotype? \*

Number only

Required

### 3. Curate Individual Information

A Proband Individual can be associated with a Family during the Curate Family Information process (as shown above). Upon saving the Family you can:

- Score and/or Add information about the Proband entered with the Family ('Scoring Probands' discussed later)
- Add a non-proband Individual to this Family.
- Return to Record Curation page.

An Individual entry for the proband **EXAMPLE-PROBAND1** and its associated variant(s) has been created.

You can score and add additional information about this proband, create an entry for a non-proband in this Family, or return to the Record Curation page.

**Note:** Individual information includes associated variant(s), phenotypes, sex, etc. For a proband, variant information can only be added or edited on the Family page as it is associated with segregation information.

a Score / Add information about proband      b Add non-proband Individual

c Return to Record Curation page

Information about Individuals can also be entered at any time from the Curation palette on the Record Curation page:

- a. If the Individual to be entered is part of a Group already curated in this Gene-Disease Record then it can be added from this link within that Group.
- b. If the Individual to be entered is part of a Family already curated in this Gene-Disease Record then it can be added from this link within that Family.
- c. To add a new Individual that is not associated with an existing Group or Family, click the Individual '+' in the curation palette.
- d. To Edit the Information already added for an existing Individual.

The screenshot shows the 'Genetic Evidence' Curation palette with three main sections:

- Group**: Contains 'EXAMPLE-GROUP-LABEL' (Curated by ClinGen Test Curator on 2017 Jan 17, 4:28 pm). It includes links to 'View | Edit', 'Add new Family to this Group', and 'Add new Individual to this Group' (marked with a red letter 'a').
- Family**: Contains 'EXAMPLE-FAMILY1' (Curated by ClinGen Test Curator on 2017 Jan 17, 5:19 pm). It includes links to 'View | Edit' and 'Add new Individual to this Family' (marked with a red letter 'b').
- Individual**: Contains 'EXAMPLE-PROBAND1' (Curated by ClinGen Test Curator on 2017 Jan 17, 5:19 pm). It includes links to 'View/Score | Edit' (marked with a red letter 'd') and a red letter 'c'.

The top of the landing page to Curate Individual Information shows the authors, title, and citation details for the selected PubMed article in a yellow box below the header.

- a. A curator is required to enter a label for the Individual, if possible using a label described in the paper. If Editing a pre-existing Individual then this Label will already be filled in but can be changed here.
- b. A curator must then select 'Yes' if the Individual is a proband and 'No' if the Individual is a non-proband.
- c. Selecting 'Yes' will make the disease field a required field.

Baumstark JS, Lee CT, Luby RJ. A new method for the determination of alpha1-protease inhibitor (alpha1-antitrypsin) phenotypes based on the formation of alpha1-protease inhibitor allele product-elastase complexes. *Biochimica et biophysica acta*. 1976 Sep 28;446(1):287-300. PMID: 10000

## Curate Individual Information

📁 // Individual EXAMPLE-PROBAND2

If this Individual is part of a Family or a Group, please curate that Group or Family first and then add the Individual as a member.

Individual Label: \* **a** EXAMPLE-PROBAND2

Note: Do not enter real names in this field. Please enter a label to help you keep track of this Individual within the interface - if possible, please use the label described in the paper.

No Selection

Is this Individual a proband: \* **b** ✓ Yes  
No

Note: Probands are indicated by the following icon: 🚩

**Individual – Disease & Phenotype(s)**

Orphanet 🌐 Disease for Individual: \* **C** E.G. ORPHA15

The Curate Individual Information page is split into relevant sections based on the type of evidence:

- i. Individual – Disease & Phenotype(s)
- ii. Individual – Demographics

Enter information about the demographics of the group. The 'Sex' of an Individual is a required field; extensive options are via a pull-down.

**Individual – Demographics**

The screenshot shows a dropdown menu for 'Sex: \*' with the following options:

- No Selection (selected)
- Male
- Female
- Intersex
- MTF/Transwoman/Transgender Female
- FTM/Transman/Transgender Male
- Ambiguous
- Unknown
- Other

- iii. Individual – Methods
- iv. Individual – Associated Variant(s)

See the section ‘Adding Variants’ above, which describes how to add Variants using either a ClinVar Variation ID(s) and/or ClinGen Allele Registry CA ID(s).

- v. Individual – Additional Information
- vi. Individual – Score Proband

### Scoring Probands

In order to score a proband, a curator must:

- a. Associate the proband with at least one variant in the ‘Individual – Associated Variant(s)’ section above.
- b. Specify the gene impact for each variant associate with the proband. To do so, the curator should click on the ‘Curate variant’s gene impact’ link under the variant.

ClinVar Variation ID: 50505

ClinVar Preferred Title: NM\_001256240.1(PGAP2):c.46C>T (p.Arg16Trp)

Genomic HGVS Title: NC\_000011.10:g.3811305C>T (GRCh38)

Note: a variant's gene impact must be specified in order to score this proband.

Curate variant's gene impact



- h. After following the link, a curator is required to select the gene impact for the variant from the pull-down. [Please note: this feature was removed, but will be added back shortly]

**Evaluation of Pathogenicity**

Select gene impact for variant:  
(Note: Required for score calculation)

[View evidence](#)

No Selection  
Predicted or observed null  
Other variant with gene impact  
Insufficient evidence for gene impact

- c. Each variant that has had its gene impact assessed is marked with a white box next to its variant name in the Gene-Disease Records Variants section of the Record Curation page.

**Gene-Disease Record Variants**

Click a variant to View, Curate, or Edit it. The icon indicates curation by one or more curators.

NM\_007294.3(BRCA1):c.1669A>G (p.Thr557Ala)   NM\_007294.3(BRCA1):c.538delA (p.Tyr179Serfs)   NM\_004646.3(NPHS1):c.1234G>T (p.Gly412Cys)



- d. Upon saving the gene impact for all the variants associated with a proband, you can return to the Edit Individual Information page and will now be able to Score the proband via a pull-down selection (Score, Review or Contradicts).

**Individual — Score Proband**

The gene impact for each variant associated with this proband must be specified in order to score this proband (see variant(s) and links to curating their gene impact in variant section for this individual, above).

Select Status:

No Selection  
Score  
Review  
Contradicts

- e. The case type must then be confirmed from the pull-down. Note: The default score and range of choice if choosing a different score will change depending on this case type choice.

**Individual — Score Proband**

The gene impact for each variant associated with this proband must be specified in order to score this proband (see variant(s) and links to curating their gene impact in variant section for this individual, above).

Select Status:

No Selection  
Proband with other variant type with some evidence of gene impact  
Proband with predicted or proven null variant  
Variant is de novo

Confirm Case Information type:

Default Score: 2

Select a score different from default score: (optional) 1

Explain reason(s) for change: (required for selecting different score)

Note: If you selected a score different from the default score, you must provide a reason for the change here.

- f. If a curator chooses a different score from the default score then they are required to explain their reasoning in the box provided.

Default Score: 1.5

Select a score different from default score:  
(optional)

Explain reason(s) for change:  
(required for selecting different score)

Note: If you selected a score different from the default score, you must provide a reason for the change here.

A reason is required for the changed score.

#### 4. Curate Case Control Information

To add Case Control data to a record click on the '+' in the curation palette on the Record Curation page.

Evidence for PMID:10000

遗传证据

Case Level

Group +

Family +

Individual +

Case-Control +

实验证据

Experimental Data +

Associated Variants

The top of the landing page to Curate Group Information shows the authors, title, and citation details for the selected PubMed article in a yellow box below the header. A curator is required to enter a label for the Case-Control, the Case Cohort and the Control Cohort.

Case-Control Label

Case-Control Label \* CASE-CONTROL

Case Cohort

Case Cohort Label: \* CASE1

Control Cohort

Control Cohort Label: \* CONTROL1

Upon saving the gene impact for all the variants associated with a proband, you can return to the Edit Individual Information page and will now be able to Score the proband via a pull

i. Case Cohort – Disease(s) and Phenotype(s)

A curator is required to enter at least one of the following to describe disease(s)/phenotype(s) common to the Case Cohort:

- a) MonDO ID(s)
- b) HPO ID(s)
- c) Phenotype free text

For the following sections, there is a split screen where Case Cohort information can be entered in the left panel and Control Cohort information can be entered in the right panel.

- ii. Case Cohort/ Control Cohort – Demographics
- iii. Case Cohort/ Control Cohort – Methods
- iv. Case Cohort/ Control Cohort – Power
- v. Case Cohort/ Control Cohort – Additional Information

For instance:

<p><b>Demographics CASE</b></p> <p>Number of males: <input type="text"/></p> <p>Number of females: <input type="text"/></p> <p>Country of Origin: <input type="text"/> No Selection</p> <p>Ethnicity: <input type="text"/> No Selection</p> <p>Race: <input type="text"/> No Selection</p> <p><b>Age Range</b></p> <p>Type: <input type="text"/> No Selection</p> <p>Value: <input type="text"/> to <input type="text"/></p> <p>Unit: <input type="text"/> No Selection</p>	<p><b>Demographics CONTROL</b></p> <p>Number of males: <input type="text"/></p> <p>Number of females: <input type="text"/></p> <p>Country of Origin: <input type="text"/> No Selection</p> <p>Ethnicity: <input type="text"/> No Selection</p> <p>Race: <input type="text"/> No Selection</p> <p><b>Age Range</b></p> <p>Value: <input type="text"/> to <input type="text"/></p> <p>Unit: <input type="text"/> No Selection</p>
---	---

Then the Case Control Evaluation section is for evaluating the evidence on the Case Control group as a whole.

- vi. Case Control Evaluation – Statistics
- vii. Case Control Evaluation – Bias Category
- viii. Case Control Evaluation – Comments
- ix. Case Control – Score

#### Scoring Case Control

In order to score Case Control, a curator must select a Score from the pull-down and the click Save.

<p><b>Case-Control Score</b></p> <p>Score: <input type="text"/></p>	<p>No Selection</p> <p>0 0.5 1 1.5 ✓ 2 2.5 3 3.5 4 4.5 5 5.5</p> <p style="text-align: right;">Save</p>
---	---

## ADDING EXPERIMENTAL EVIDENCE

To add Experimental data to a record click on the '+' in the curation palette on the Record Curation page.

The screenshot shows the 'Evidence for PMID:10000' interface. It includes sections for 'Genetic Evidence' (Case Level: Group, Family, Individual) and 'Case-Control' (Case-Control). Below these is the 'Experimental Evidence' section, which contains a blue button labeled 'Experimental Data' with a white plus sign. An orange arrow points to this button from the left.

A curator is first required to select the Experiment Type from a pull-down:

The screenshot shows a dropdown menu titled 'Experiment type: \*'. The menu lists the following options:

- No Selection
- Biochemical Function
- Protein Interactions
- Expression
- Functional Alteration
- Model Systems
- Rescue

There are six different curation experiences dependent on the Experiment Type selected by the curator.

- i. Experimental – Biochemical Function (A) and (B)

The 'Biochemical Function' option has two separate options, A and B, provided in a pull-down.

Experiment type: \* Biochemical Function

A. The gene product performs a biochemical function shared with other known genes in the disease of interest

B. The gene product is consistent with the observed phenotype(s)

Please select which one (A or B) you would like to curate \*

No Selection

A. Gene(s) with same function implicated in same disease  
B. Gene function consistent with phenotype(s)

Both have a number of required fields, shown with an asterisk next to the field. One of these required fields is for adding the Gene Ontology (GO) ID that best defines the function of the gene in the Record.

**A. Biochemical Function**

Please enter the gene's molecular function or biological process term (**required**) using the Gene Ontology (GO) term wherever possible (e.g. GO:2001284). If you are unable to find an appropriate GO term, use the free text box instead. Please email [clingen-helpdesk@lists.stanford.edu](mailto:clingen-helpdesk@lists.stanford.edu) for any ontology support.

View existing GO annotations for this gene [in UniProt](#).  
 Search [GO](#) using the OLS.  
 Search for existing or new terms using [QuickGO](#).

Identified function of gene in this record (GO ID): \* E.G. GO:2001284

Identified function of gene in this record (free text): \* Use free text descriptions only after verifying no appropriate ontology term exists

Evidence for above function: \*

Notes on where evidence found in paper:



### Adding GO IDs

In order to aid the curator in searching for the correct GO ID, there are 3 links provided – one to view existing GO annotations for the gene, one that links to the OLS GO Search, and one that links to Quick GO

- a) Only choose either “Molecular Function” or “Biological Process”
- b) Only choose manual experimental evidence, e.g. codes IDA, IMP, IGI, IPI and IEP. Other codes may be inferred, e.g. IEA which is ‘Inferred by electronic annotation’

- c) As you go down a GO tree the terms become more specific, only go down the tree as far as you feel secure in your decision.
- d) If you are not sure which specific GO term to add then go back up the tree until you find a general term that fits your knowledge.

### Scoring Experimental Evidence

Experimental data can be scored via a pull-down selection (Score, Review or Contradicts) in Experimental Data Score sections found at the foot of every Curate Experimental Data Information page.

The screenshot shows a 'Select Status:' dropdown menu open, displaying three options: 'No Selection', 'Score', 'Review', and 'Contradicts'. The 'Score' option is selected. Other fields visible include 'Default Score: 0.5' and a note about explaining a score change if it's different from the default.

The default score and range of choice if choosing a different score will change depending on the experimental data type.

If a curator chooses a different score from the default score then they are required to explain their reasoning in the box provided.

The screenshot shows a 'Select a score different from default score:' dropdown menu open, displaying the value '1'. A red arrow points to the 'Note' box below, which contains the text: 'Note: If you selected a score different from the default score, you must provide a reason for the change here.' Other fields visible include 'Default Score: 0.5' and a note about explaining a score change if it's different from the default.

#### ii. Experimental – Protein Interactions

Has a number of required fields, shown with an asterisk next to the field.

#### iii. Experimental – Expression (A and B)

The 'Expression' option has two separate options, A and B, provided in a pull-down.

Please select which one (A or B) you would like to curate \*

No Selection

✓ A. Gene normally expressed in tissue relevant to the disease  
B. Altered expression in Patients

Both have a number of required fields, shown with an asterisk next to the field. One of these required fields is for adding an anatomical structure Ontology (UBERON) ID that best defines the organ or tissue relevant to the gene expression evidence. A link out to UBERON has been provided to aid in searching for the correct ID.

Search [Uberon](#) for an organ type (e.g. heart = UBERON\_0015228)

Organ of tissue relevant to disease, in which gene expression is examined in patient ([Uberon](#) ID): \*

E.G. UBERON\_0015228

#### iv. Experimental – Functional Alteration

Has a number of required fields, shown with an asterisk next to the field.

Includes section for adding variant(s) associated with this data type. Simply click on “Add variant associated with Experimental data”. A pop-up window will appear whereby variants can be added via either a ClinVar VariationID or a ClinGen Allele Registry CA ID.

If your Experimental data is about one or more variants, please add these variant(s) below

Add variant associated with Experimental data



Variants can then be added via either a ClinVar Variation ID or a ClinGen Allele Registry CA ID.

Add Variant:

Add ClinVar ID - or - Add CA ID

#### v. Experimental – Model Systems

Has a number of required fields, shown with an asterisk next to the field.

Including selecting whether it is a non-human model organism or cell culture model, and the associated ‘Description of gene alteration’.

**Model Systems**

Non-human model organism or cell culture model?: \*

Description of gene alteration: \*

No Selection  
Non-human model organism  
Cell culture model

If 'Cell culture model' is selected then cell culture model type/line becomes a required field. This field can accept either an Experimental Factor Ontology (EFO) ID or a Cell Ontology (CL) ID. Links out to EFO and CL ontologies within the ontology lookup service (OLS) have been provided to aid in searching for the correct ID.

Search the [EFO](#) or [Cell Ontology \(CL\)](#) using the OLS.

Cell culture model type/line (EFO or CL ID): \*  
E.G. EFO\_0001187, OR CL\_0000057 (IF AN EFO TERM IS UNAVAILABLE)

Also includes section for adding variant(s) associated with this data type.

vi. Experimental – Rescue

Has a number of required fields, shown with an asterisk next to the field. For instance:

**Rescue**

Rescue observed in human, non-human model organism, cell culture model, or patient cells?: \*

Description of gene alteration: \*

No Selection  
Human  
Non-human model organism  
Cell culture model  
Patient cells

Includes section for adding variant(s) associated with this data type.

# THE CLASSIFICATION MATRIX

## 1. Viewing the Classification Matrix

To view the Classification Matrix click on the ‘View Classification Matrix’ button found in the left upper header on each page. This will generate the Matrix for the **current** saved evidence and scores:

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

DICER1 – blue cone monochromacy

Autosomal dominant inheritance (with maternal imprinting)

Classification  
None

**View Classification Matrix**

The resulting page contains two tables:

1. Automated upper Calculated Classification Matrix (note: **this matrix represents the saved evidence and scores at the time you clicked the “View Classification Matrix button”**)
2. Beneath that is a Save Classification panel where you can save the Classification based on the data in the Matrix, either with the Calculated Classification value or with a Modified value

**Calculated Classification Matrix**

		Evidence Type	Count	Total Points	Points Counted
Genetic Evidence	Case-Level	Autosomal Dominant OR X-linked Disorder	0	0	0
		Proband with other variant type with some evidence of gene impact	0	0	0
		Proband with predicted or proven null variant	0	0	0
	Variant is <i>de novo</i>	0	0	0	
Autosomal Recessive Disorder	Two variants (not predicted/proven null) with some evidence of gene impact in trans	0	0	0	
	Two variants in trans and at least one <i>de novo</i> or a predicted/proven null variant	0	0	0	
Experimental Evidence	Case-Control	Segregation	0	0 (0)	0
		Case-Control Total	0	0	0
		Genetic Evidence Total	0.00		
	Functional	Biological Functions	0	0	0
Protein Interactions		0	0	0	
Expression		0	0	0	
Functional Alteration		Patient cells	0	0	0
		Non-patient cells	0	0	0
		Non-human model organism	0	0	0
Models		Cell culture model	0	0	0
		Rescue in human	0	0	0
		Rescue in non-human model organism	0	0	0
		Rescue in cell culture model	0	0	0
Rescue	Rescue in patient cells	0	0	0	
	Experimental Evidence Total	0.00			
	Total Points	0.00			

– Combined LOD Score

The above Classification Matrix was calculated based on the current evidence and accompanying scores saved in the database when you clicked the “View Classification Matrix” button to navigate to this page. To save a new Classification based on this current evidence, please fill in the fields below and click “Save”. Otherwise, click “Cancel”.

**Gene/Disease Pair**

Assertion Criteria	Genetic Evidence (0-12 points)	Experimental Evidence (0-6 points)	Total Points (0-18 points)	Replication Over Time (Yes/No)
Assigned Points	0.00	0.00	0.00	<input type="checkbox"/>
				LIMITED 1-6
				MODERATE 7-11
				STRONG 12-18
				DEFINITIVE 12-18 & Replicated Over Time

Calculated Classification

Contradictory Evidence?  Proband: No Experimental: No

Modify Calculated Clinical Validity Classification:  No Modification  Moderate  Strong  Definitive

Mark status as “Provisional Classification” (optional):

Explain Reason(s) for Change

Evidence Summary:

Last Saved Summary Classification  None

The above Classification Matrix was calculated based on the current evidence and accompanying scores saved in the database when you clicked the “View Classification Matrix” button to navigate to this page. To save a new Classification based on this current evidence, please fill in the fields above and click “Save”. Otherwise, click “Cancel”.

## 2. Classification Matrix Features

For each specific evidence type there are the following columns rows (see graphic on next page to see where each item, below, is found in the matrix):

- a. Evidence Type – brief description of types of evidence scored upon.
- b. Count - total number of pieces of evidence scored for the Evidence Type listed
- c. Total Points – the total number of points for all the pieces of evidence scored for that Evidence Type; *if the maximum points allowed is reached, the number of points displayed will be the maximum value*
- d. Points Counted – the total of all the scores added together for each section; *if the maximum points allowed is reached, the number of points displayed will be the maximum value* (for each specific type of evidence there is a maximum number of points allowable, see the SOP for allowed max scores).

Each specific evidence type is shown in rows (see graphic on next page to see where each item, below, is found in the matrix):

- e. Variant/proband scores, if curating an autosomal dominant disease or an X-linked disorder
- f. Variant/proband scores, if curating an autosomal recessive disease.
- g. Case level segregation scores
- h. Case Control scores
- i. Genetic Evidence Total. The total number of allowable points for genetic evidence. Calculated by adding the ‘Points Counted’ for each of the genetic evidence types  
Note: Maximum points allowed for this field is 12
- j. Experimental (functional) scores
  - a. Biochemical Functions
  - b. Protein Interactions
  - c. Expression
- k. Experimental (functional alteration) scores
  - a. Patient cells
  - b. Non-patient cells
- l. Experimental (model) scores
  - a. Non-human model organism
  - b. Cell culture model
- m. Experimental (rescue) scores
  - a. Rescue in human
  - b. Rescue in non-human model organism
  - c. Rescue in cell culture model
  - d. Rescue in patient cells
- n. Experimental Evidence Total. The total number of allowable points for experimental evidence. Calculated by adding the ‘Points Counted’ for each of the experimental evidence types
- o. Total Points. The sum of the Genetic Evidence Total and Experimental Evidence Total.

a	b	c	d	
Evidence Type		Count	Total Points	Points Counted
Genetic Evidence	e Autosomal Dominant OR X-linked Disorder	Proband with other variant type with some evidence of gene impact	2	1.6
		Proband with predicted or proven null variant	1	1.5
		Variant is <i>de novo</i>	2	4.5
	f Autosomal Recessive Disorder	Two variants (not predicted/proven null) with some evidence of gene impact in <i>trans</i>	0	0
		Two variants in <i>trans</i> and at least one <i>de novo</i> or a predicted/proven null variant	0	0
	g Segregation	4	7 (7.77*)	7
Experimental Evidence	h Case-Control	1	0.5	0.5
	i Genetic Evidence Total			12
	j Functional	Biochemical Functions	2	2
		Protein Interactions	1	1.5
		Expression	0	0
	k Functional Alteration	Patient cells	1	0.5
		Non-patient cells	0	0
	l Models	Non-human model organism	1	2
		Cell culture model	1	0.5
		Rescue in human	1	0.5
	m Rescue	Rescue in non-human model organism	1	0.5
		Rescue in cell culture model	1	1
		Rescue in patient cells	1	1
	n Experimental Evidence Total			6
	o Total Points			18.00

\* – Combined LOD Score

For Segregation Evidence, the Total Points field additionally contains the LOD score in parentheses. If the LOD score has been generated by summing multiple LOD scores then it will have an asterisk.

Segregation	4	7 (9.05*)	7
-------------	---	-----------	---



2. Modifying a Classification (see graphic on next page to see where each item, below, is found on the Save Classification panel)
  - a. Genetic Evidence Total assigned points.
  - b. Experimental Evidence Total assigned points
  - c. Total Points
  - d. Replication Over Time. Tickbox to identify whether the evidence has been replicated over time. Tick for 'Yes', leave blank for 'No'. (*Note: this can change the Calculated Classification; to upgrade a 12-18 Total Points from a Strong to Definitive classification then 'Yes' must have been selected for Replication Over Time.*)
  - e. Calculated Classification is automatically filled in based on the Total Points, including your answer to "Replication Over Time?" The calculated classification is highlighted in blue.
  - f. Contradictory Evidence. If a Proband or Experimental evidence has been scored as Contradictory by the curator then it will have a red 'Yes', if not it will have a black 'No'.
  - g. Curators can modify the Calculated Clinical Validity Classification by selecting an alternative Classification from the pull-down options.

- h. If the curator has modified the Classification then they are required to explain their reasoning here.
- i. Change status to “Provisional Classification” – this tick box allows curators to change the status of their Classification to “Provisional”.
- j. Evidence Summary – this free text box allows curators to summarize their evidence and provide a rationale for the clinical validity.
- k. Last Saved Summary Classification (i.e. Classification value saved previously, before clicking “Save”)
- l. Timestamp when current Last Saved Summary Classification was saved.

Gene/Disease Pair												
Assertion Criteria	Genetic Evidence (0-12 points)	Experimental Evidence (0-6 points)	Total Points (0-18 points)	Replication Over Time (Yes/No)								
Assigned Points	<b>a 12</b>	<b>b 6</b>	<b>C 18.00</b>	<b>d</b> <input type="checkbox"/>								
<b>e Calculated Classification</b>												
<table border="1" style="margin-left: auto; margin-right: auto; border-collapse: collapse;"> <tr> <td>LIMITED</td> <td>1-6</td> </tr> <tr> <td>MODERATE</td> <td>7-11</td> </tr> <tr> <td>STRONG</td> <td>12-18</td> </tr> <tr> <td>DEFINITIVE</td> <td>12-18 &amp; Replicated Over Time</td> </tr> </table>					LIMITED	1-6	MODERATE	7-11	STRONG	12-18	DEFINITIVE	12-18 & Replicated Over Time
LIMITED	1-6											
MODERATE	7-11											
STRONG	12-18											
DEFINITIVE	12-18 & Replicated Over Time											
<b>f Contradictory Evidence?</b>	Proband: Yes Experimental: No											
Modify Clinical Validity Classification:	<b>g</b> Limited		Mark status as "Provisional Classification" (optional): <input checked="" type="checkbox"/> <b>i</b>									
Explain Reason(s) for Change *	<b>h</b> Because because because ...		<b>j</b> Summary of the evidence and rationale for the clinical validity classification (optional).									
Last Saved Summary Classification	<b>k</b> Limited (2017 Oct 11, 3:41 pm)											

### 3. Saving a Classification

Clicking the “Save” button at the bottom of the Save Classification table will save the Classification. The Calculated Classification will be saved by default as the Classification, unless a modification has been selected.

Gene/Disease Pair												
Assertion Criteria	Genetic Evidence (0-12 points)	Experimental Evidence (0-6 points)	Total Points (0-18 points)	Replication Over Time (Yes/No)								
Assigned Points	3.00	0.00	3.00	<input type="checkbox"/>								
Calculated Classification												
<table border="1" style="margin-left: auto; margin-right: auto; border-collapse: collapse;"> <tr> <td>LIMITED</td> <td>1-6</td> </tr> <tr> <td>MODERATE</td> <td>7-11</td> </tr> <tr> <td>STRONG</td> <td>12-18</td> </tr> <tr> <td>DEFINITIVE</td> <td>12-18 &amp; Replicated Over Time</td> </tr> </table>					LIMITED	1-6	MODERATE	7-11	STRONG	12-18	DEFINITIVE	12-18 & Replicated Over Time
LIMITED	1-6											
MODERATE	7-11											
STRONG	12-18											
DEFINITIVE	12-18 & Replicated Over Time											
<b>Contradictory Evidence?</b>	Proband: No Experimental: No											
Modify Calculated Clinical Validity Classification:	No Modification		Mark status as "Provisional Classification" (optional): <input type="checkbox"/>									
Explain Reason(s) for Change			<b>Evidence Summary:</b> Summary of the evidence and rationale for the clinical validity classification (optional).									
Last Saved Summary Classification	None											
<small>The above Classification Matrix was calculated based on the current evidence and accompanying scores saved in the database when you clicked the “View Classification Matrix” button to navigate to this page. To save a new Classification based on this current evidence, please fill in the fields above and click “Save”. Otherwise, click “Cancel”.</small>												
<input type="button" value="Cancel"/> <input type="button" value="Save"/>												



Upon saving the bottom of the page will be updated to a View only option to reflect the saved options. Check that everything looks correct

- a. Classification value just saved (when “Save” was clicked).
- b. Timestamp for the Classification value (a).
- c. Link back to the Record Curation page.
- d. Option to unlock the Save Classification section for re-editing (i.e. to change the modification, update the reason(s) for change text, mark as provisional, and/or update the evidence summary text).
- e. View the Evidence Summary for this saved Classification for the Gene:Disease record.

Gene/Disease Pair				
Assertion Criteria	Genetic Evidence (0-12 points)	Experimental Evidence (0-6 points)	Total Points (0-18 points)	Replication Over Time (Yes/No)
Assigned Points	3.00	0.00	3.00	No
Calculated Classification		LIMITED	1-6	
		MODERATE	7-11	
		STRONG	12-18	
		DEFINITIVE	12-18 & Replicated Over Time	
Contradictory Evidence?	Proband: No Experimental: No			
Modify Calculated Clinical Validity Classification: No Modification		Mark status as "Provisional Classification" (optional): No		
Explain Reason(s) for Change:		Evidence Summary:		
Last Saved Summary Classification	Limited <b>a</b> (2017 Oct 11, 10:11 pm) <b>b</b>			

**c** Select “Edit Classification” to edit the Last Saved Classification or click “Evidence Summary” to view all evidence associated with the saved Classification. If you don’t wish to save, click “Record Curation page” to add more evidence.

[Record Curation page](#)
[Edit Classification](#)
[Evidence Summary](#)

#### 4. Saving a Classification as Provisional

If the “Provisional Classification” checkbox was checked before saving...

Mark status as "Provisional Classification" (optional):

... then upon saving the Classification will be saved as “Provisional”

Mark status as "Provisional Classification" (optional): Yes

When a curator saves a new Provisional Classification it will now appear in the banner under the header on each page (see **b** below).

- a. Name of Curator who saved the Classification.
- b. Last Saved status for the Classification.

- c. Calculated Total points (plus Classification, including consideration of “Replication over time), based on current saved Classification.
- d. Modified Classification, based on a saved modification to classification.
- e. Timestamp when current Last Saved Summary Classification was saved.
- f. Click here to View the Classification Matrix for the current evidence and its scores

**DICER1 – red-green color blindness**   
Autosomal dominant inheritance

<b>Classification</b>	Curator: Matt Wright <b>a</b>	Calculated Classification: 18 (Definitive) <b>c</b>
	Status: Provisional <b>b</b>	Modified Classification: No Modification <b>d</b>
		Last Saved: 2017 Oct 11, 6:20 pm <b>e</b>
		<b>f</b> <a href="#">View Classification Matrix</a>

## 5. Revisiting the Classification Matrix

Every time a curator visits the Classification Matrix all the scores in the upper Calculated Classification table are recalculated based on the current set of saved evidence and associated saved scores. You will see a yellow box below that table that explains this.

Calculated Classification Matrix							
Genetic Evidence	Case-Level	Variant	Evidence Type	Count	Total Points	Points Counted	
			Proband with other variant type with some evidence of gene impact	0	0	0	
Autosomal Dominant OR X-linked Disorder			Proband with predicted or proven null variant	0	0	0	
			Variant is <i>de novo</i>	0	0	0	
			Two variants (not predicted/proven null) with some evidence of gene impact in <i>trans</i>	0	0	0	
			Two variants in <i>trans</i> and at least one <i>de novo</i> or a predicted/proven null variant	0	0		
			<b>Segregation</b>	0	0 (0*)	0	
Autosomal Recessive Disorder	<b>Case-Control</b>			1	6	6	
	<b>Genetic Evidence Total</b>			<b>6.00</b>			
	Functional		Biochemical Functions	0	0	0	
			Protein Interactions	0	0		
			Expression	0	0		
	Functional Alteration		Patient cells	0	0	0	
			Non-patient cells	0	0		
	Models		Non-human model organism	0	0	0	
			Cell culture model	0	0		
			Rescue in human	0	0		
Experimental Evidence	Rescue		Rescue in non-human model organism	0	0	0	
			Rescue in cell culture model	0	0		
			Rescue in patient cells	0	0		
			<b>Experimental Evidence Total</b>	<b>0.00</b>			
			<b>Total Points</b>	<b>6.00</b>			

\* – Combined LOD Score

The Total Points shown above are based on the set of saved evidence and accompanying scores existing when the "View Classification Matrix" button was clicked. To save a Classification for this Gene Disease Record based on this evidence, please see the section below.



With every visit the four editable fields in the lower Save Classification table are available to be edited again (i.e. to change the modification based on any new Calculated Classification, update the reason(s) for change text, mark as provisional, and/or update the evidence summary text).

**Note: The Save button must be clicked to save any edits to the Current Classification value.**

Gene/Disease Pair				
Assertion Criteria	Genetic Evidence (0-12 points)	Experimental Evidence (0-6 points)	Total Points (0-18 points)	Replication Over Time (Yes/No)
Assigned Points	12	6	18.00	<input checked="" type="checkbox"/>
Calculated Classification			LIMITED	1-6
			MODERATE	7-11
			STRONG	12-18
			DEFINITIVE	12-18 & Replicated Over Time
Contradictory Evidence?		Proband: Yes Experimental: No		
Modify Calculated Clinical Validity Classification:		No Modification	Mark status as "Provisional Classification" (optional): <input checked="" type="checkbox"/>	
Explain Reason(s) for Change		Because because because ...	Evidence Summary: Summary of the evidence and rationale for the clinical validity classification (optional).	
Last Saved Summary Classification		Definitive (2017 Oct 11, 6:20 pm)		
<p>Click Save to save the Calculated Classification (highlighted in blue) without modification, or modify the Classification value in the pull-down and hit Save. You may also choose to mark your Classification as Provisional.</p>				

Cancel **Save**



If the new calculated Total Points now suggests a calculated Classification that is the same as a Modification saved on the last visit, then that Modification will be reset to “No Modification” and there will be a red warning message to explain this.

Gene/Disease Pair				
Assertion Criteria	Genetic Evidence (0-12 points)	Experimental Evidence (0-6 points)	Total Points (0-18 points)	Replication Over Time (Yes/No)
Assigned Points	6.00	2.00	8.00	<input type="checkbox"/>
Calculated Classification			LIMITED	1-6
			MODERATE	7-11
			STRONG	12-18
			DEFINITIVE	12-18 & Replicated Over Time
Contradictory Evidence?		Proband: No Experimental: No		
Modify Calculated Clinical Validity Classification:		No Modification	Mark status as "Provisional Classification" (optional): <input checked="" type="checkbox"/>	
Explain Reason(s) for Change		because because because	Evidence Summary: Summary of the evidence and rationale for the clinical validity classification (optional).	
<p>⚠ This value has been reset to "No Modification" as the Calculated Classification based on the new Total Points is now equivalent to your last saved Classification value. Click "Save" to save the Calculated Classification value, or modify to a new value and click "Save."</p>				
Last Saved Summary Classification		Moderate (2017 Oct 12, 9:52 am)		

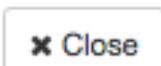
## EVIDENCE SUMMARY

### 1. Evidence Summary Header:

Upon saving a Classification, you have the option of viewing the summary of the evidence for this Classification by clicking on the “Evidence Summary” button at the bottom of the page.



The Evidence Summary will pop up as a new tab or window. **Be sure to close it when you are finished.** There is a close button at the top of the page as well as the bottom, just so you do not get confused the next time you generate an Evidence Summary:



The Evidence Summary table header contains a summary of information about the saved Classification:

Evidence Summary	
CDGE – blue cone monochromacy – Autosomal dominant inheritance (with maternal imprinting)	Classification status: Provisional Date classification saved: 2017 Oct 12, 11:00 pm Disease: blue cone monochromacy ♂
Classification owner: Matt Wright Calculated classification: Strong Modified classification: Definitive Reason for modified classification: Reason(s) Reason(s) Reason(s) Reason(s) Reason(s) Reason(s) Reason(s) Reason(s)	
Evidence Summary	
Rationale	

### 2. Evidence Summary tables

The Evidence Summary summarizes and sorts all the evidence for the saved Classification into tables according the evidence types (Case Level, Case Level for segregation evidence when there is no associated proband, Case-Control, and Experimental). Note that evidence that has a score status of “Score,” “Review,” or “Contradicts” is shown. For the total points shown at the bottom of each evidence table, only those rows of evidence where the score status was set as “Score” are included in the calculation.

See next page for the various tables of evidence in the Evidence Summary

## Case Level Data:

## Case Control Data:

Genetic Evidence: Case-Control											
Reference (PMID)	Disease (Case)	Study type	Detection method (Case)	Power		Bias confounding	Statistics				
				# of cases genotyped/sequenced	# of controls genotyped/sequenced		Cases with variant in gene / all cases genotyped/sequenced	Controls with variant in gene / all cases genotyped/sequenced	Test statistic: value	p-value	Confidence interval
Gamkema JS, Lee CT, Luby RJ. <b>1976</b> . PMID: 10000002	blue cone monochromacy (OMIM:303700)					comments					3.5
Toya S, Shizawa H, Isaka Y, Shiobara R, Ichikizaki K. <b>1977</b> . PMID: 7000002	blue cone monochromacy (OMIM:303700)	Single variant analysis				comments comments comments comments	3	3	Odds Ratio: 0.79		1

## Experimental Data:

3. Printing Evidence Summary & Saving as PDF. When printing this view, we recommend the following print settings:

- "Landscape" for layout,
- 50% for Scale,
- "Minimum" for Margins
- Select "Background graphics"

You can also use your Print dialogue box to save your classification as a PDF.

*Feedback and Comments?*

Please email us at: [clingen-helpdesk@lists.stanford.edu](mailto:clingen-helpdesk@lists.stanford.edu)