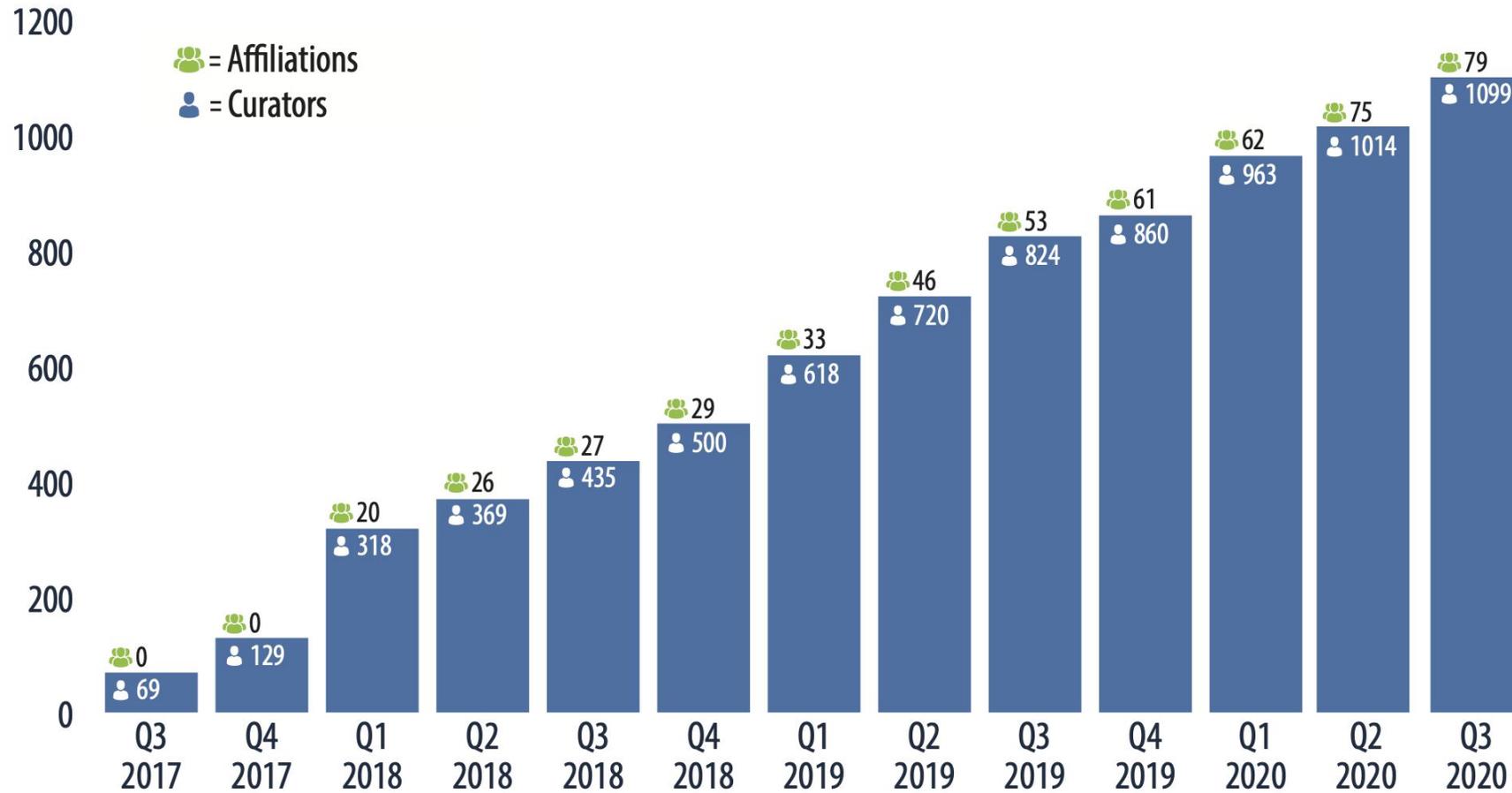


GCI & VCI Platform Rearchitecture

Matt Wright & Christine Preston

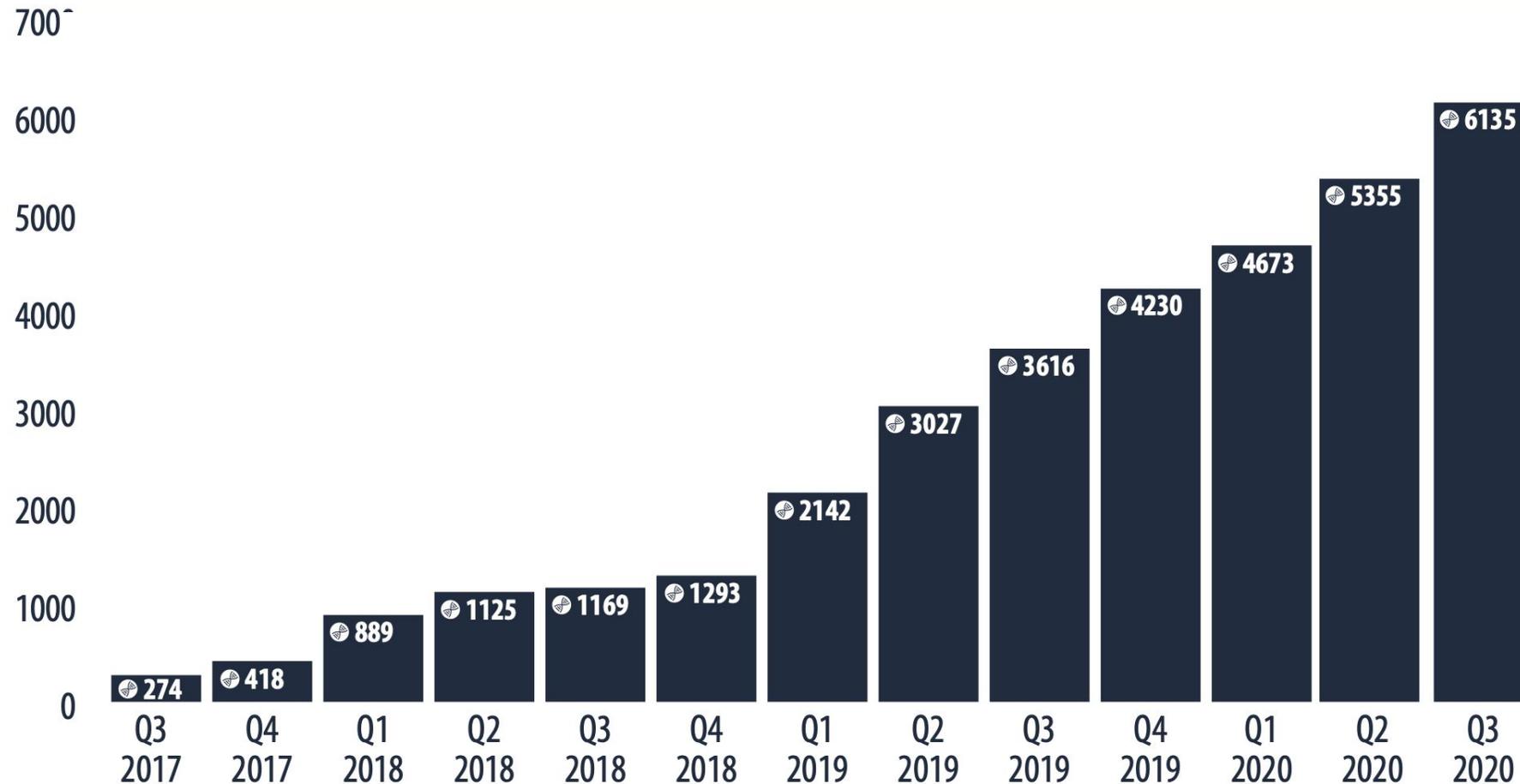
curation.clinicalgenome.org

GCI/VCI: User Growth



- Total growth over 3 years: **1493%**
- Average annual growth rate: **217%**

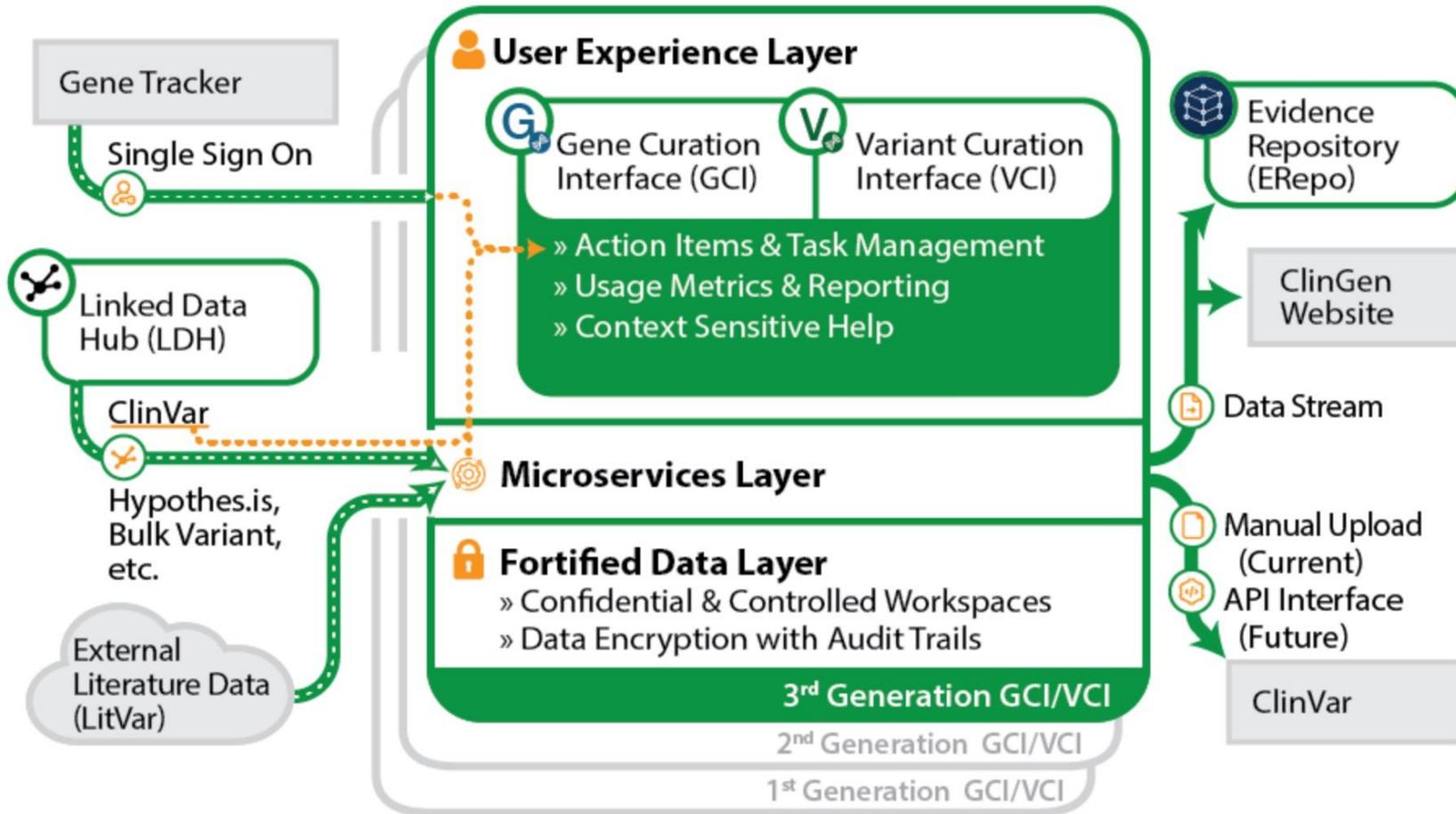
VCI: Classified Variants Growth



- Total growth over 3 years: **2139%**
- Average annual growth rate: **202%**

GCI & VCI Modernization Overview

2.0 release



- Improved User Experience
- Scalability
- Data Accessibility
- Integration
- Reliability
- Maintainability

“Like for Like” Functionality

Current UI

NM_000151.4(G6PC1):c.1039C>T (p.Gln347Ter) ⓘ
Evidence View

Variant ID Sources	Variant Genomic Context	My Interpretation
<p>ClinVar VariationID: 12000 ⓘ ClinGen Allele Registry ID: CA256179 ⓘ dbSNP ID: rs80356487 ⓘ Other Names:<ul style="list-style-type: none">• G6PC, GLN347TER• p.Q347*:CAG>TAG• 1118C>T</p>	<p>UCSC [GRCh38/hg38] [GRCh37/hg19] ⓘ Variation Viewer [GRCh38] [GRCh37] ⓘ Ensembl Browser [GRCh38] [GRCh37] ⓘ</p>	

In 2.0 release

NM_000151.4(G6PC1):c.1039C>T (p.Gln347Ter) ⓘ
Evidence View

Variant ID Sources	Links to External Resources	My Interpretation
<p>ClinVar Variation ID: 12000 ⓘ ClinGen Allele Registry ID: CA256179 ⓘ dbSNP ID: rs80356487 ⓘ Other Names:<ul style="list-style-type: none">• G6PC, GLN347TER• p.Q347*:CAG>TAG• 1118C>T</p>	<p>UCSC [GRCh38/hg38] [GRCh37/hg19] ⓘ Variation Viewer [GRCh38] [GRCh37] ⓘ Ensembl Browser [GRCh38] [GRCh37] ⓘ</p>	<p>Interpretation +</p>

“Like for Like”

Current UI

Saved Provisional and Approved Classification(s)

ClinGen Affiliation: Limb Girdle Muscular Dystrophy 
Approved Classification entered by: Brooke Palus
Affiliation Approver: Chris Wehl
Classification Contributors:
Date saved as Approved: 2020 Aug 11, 11:59 am **APPROVED**
Final Approval Date:
Saved Classification: Definitive
Disease: muscular dystrophy-dystroglycanopathy
Mode of Inheritance: Autosomal recessive inheritance [↗](#)
Approver comments:
Contributor comments:
SOP Version: 7

[View Approved Summary](#)

Published by: Brooke Palus (Limb Girdle Muscular Dystrophy GCEP)
Date published: 2020 Aug 11, 12:00 pm **PUBLISHED**
Additional comments:
Link: [FKRP Classification Summary](#) [↗](#)

[Unpublish Summary](#)

In 2.0 release

Saved Provisional and Approved Classification(s)

APPROVED  [Approved Summary](#)

ClinGen Affiliation: Limb Girdle Muscular Dystrophy
Approved Classification entered by: Brooke Palus
Affiliation Approver: Chris Wehl
Classification Contributors:
Date saved as Approved: 2020 Aug 11, 11:59 am
Final Approval Date:

Saved Classification: Definitive
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Approver comments:
Contributor comments:
SOP Version: 7

PUBLISHED
Published by: Brooke Palus (Limb Girdle Muscular Dystrophy GCEP)
Date published: 2020 Aug 11, 12:00 pm
Additional comments:
Link: [FKRP Classification Summary](#) [↗](#)

[Unpublish Summary](#)

Platform Enhancements - Selecting a variant

Current UI

Select Variant by ID type ✓ Select

- ClinVar Variation ID
- ClinGen Allele Registry ID (CA ID)

Note: This version of the interface returns evidence for SNVs (single nucleotide variants) and for some small duplications, insertions, and deletions. We are currently working to optimize the evidence returned for other variant types. However, the interface supports the evaluation/interpretation of any variant.

Instructions (please follow this order to determine correct ID for variant)

1. Search ClinVar [↗](#) for variant.
2. If found in ClinVar, select "ClinVar VariationID" from the pull-down to enter it.
3. If not found in ClinVar, search the ClinGen Allele Registry [↗](#) with a valid HGVS term for that variant.
 - a. If ClinGen Allele Registry [↗](#) returns a ClinVar ID, select "ClinVar VariationID" from the pull-down to enter it.
 - b. If ClinGen Allele Registry [↗](#) does not find a ClinVar ID, register the variant to return a CA ID and then select "ClinGen Allele Registry ID (CA ID)" from the pull-down and enter the CA ID.



ClinVar Variant

Enter ClinVar VariationID *

[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 and View Evidence](#)

In 2.0 release

Search and Select Variant

This version of the interface returns evidence for SNVs (single nucleotide variants) and for some small duplications, insertions, and deletions. [more...](#)

ClinVar Variation ID or ClinGen Allele Registry ID

[Retrieve](#)

Platform Enhancements - Selecting a variant

Current UI

Add Variant: - or -



ClinVar Variant

Enter ClinVar VariationID *

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

In 2.0 release

Add Variant:



Select Variant

Search and Select Variant

ClinVar Variation ID or ClinGen Allele Registry ID

Enter a ClinVar Variation ID or ClinGen Allele Registry ID (CA ID). The Variation ID can be found in the light blue box on a variant page (example: [139214](#)) for variant. The CA ID is returned when you register an allele with the ClinGen Allele Registry (example: [CA003323](#)).

Platform Enhancements - Dashboard tables (VCI)

My Affiliation's Variant Interpretations (3) Download (.CSV)

Search 3 records... Filter By Status Select...

Variant	Disease/Mode of Inheritance	Status	Pathogenicity/Modified	Met Criteria	Date Created	Last Modified
NM_000151.4(G6PC):c.1039 C>T (p.Gln347Ter)	plum allergy (MONDO:0000786) / X-linked inheritance	IN PROGRESS	Uncertain significance - insufficient evidence / --	PM4,BP7	November 4, 2020 8:53 AM PST	November 4, 2020 8:55 AM PST
NM_002294.3(LAMP2):c.86 5-3C>A	peach allergy (MONDO:0000785) / Autosomal recessive inheritance	PROVISIONAL	Likely pathogenic / Likely pathogenic	PM2,PP3,PP4,PS1	November 4, 2020 8:52 AM PST	November 4, 2020 8:53 AM PST
NM_001065.4(TNFRSF1A):c.295T>A (p.Cys99Ser)	tomato allergy (MONDO:0000787) / Autosomal dominant inheritance	APPROVED	Benign / Benign	BA1,BP4,BS4	November 4, 2020 8:45 AM PST	November 4, 2020 8:51 AM PST

<< < Page 1 of 1 > >> Go to page: 1 Show 10

Platform Enhancements - Dashboard tables (GCI)

My Affiliation's Gene-Disease Records (41) [Download \(.CSV\)](#)

Search 41 records... Filter By Status Select...

Gene	Disease/Mode of Inheritance	Status	Classification/Modified	Date Created	Last Modified
DES	dilated cardiomyopathy (MONDO:0005021) / Autosomal dominant inheritance	IN PROGRESS	Strong / Definitive	August 6, 2020 7:44 AM PST	September 13, 2020 3:07 AM PST
PKP2	dilated cardiomyopathy (MONDO:0005021) / Autosomal dominant inheritance	IN PROGRESS	Limited / No Modification	September 10, 2020 9:33 AM PST	September 10, 2020 12:16 PM PST
LMNA	dilated cardiomyopathy (MONDO:0005021) / Autosomal dominant inheritance	IN PROGRESS	Limited / No Modification	August 13, 2020 11:04 AM PST	September 8, 2020 12:36 PM PST
TPM1	dilated cardiomyopathy 1Y (MONDO:0012744) / Autosomal dominant inheritance	IN PROGRESS	Strong / No Modification	September 7, 2020 3:13 AM PST	September 7, 2020 9:25 AM PST
FLNC	dilated cardiomyopathy (MONDO:0005021) / Autosomal dominant inheritance	IN PROGRESS	-- / --	September 7, 2020 2:08 AM PST	September 7, 2020 8:27 AM PST
JPH2	dilated cardiomyopathy (MONDO:0005021) / Semidominant inheritance	IN PROGRESS	Moderate / No Modification	August 12, 2020 6:15 AM PST	September 4, 2020 8:35 AM PST
VCL	dilated cardiomyopathy (MONDO:0005021) / Autosomal dominant inheritance	IN PROGRESS	Moderate / No Modification	March 24, 2020 6:22 AM PST	September 4, 2020 3:37 AM PST
NEBL	dilated cardiomyopathy (MONDO:0005021) / Autosomal dominant inheritance	IN PROGRESS	No Known Disease Relationship / No Modification	February 13, 2020 6:33 AM PST	September 3, 2020 11:36 AM PST
ANKRD1	dilated cardiomyopathy (MONDO:0005021) / Autosomal dominant inheritance	APPROVED PUBLISHED	Limited / No Modification	February 14, 2020 4:07 AM PST	September 3, 2020 8:17 AM PST
TNNT2	dilated cardiomyopathy (MONDO:0005021) / Autosomal dominant inheritance	PROVISIONAL	Definitive / No Modification	June 10, 2020 11:32 AM PST	August 27, 2020 11:23 AM PST

<< < Page 1 of 5 > >> Go to page: 1 Show 10

Platform Enhancements - Splice tool links (VCI)

In 2.0 release

Splice Site Predictors

[Analyze using MaxEntScan](#)

[Analyze using NNSPLICE](#)

[Analyze using HumanSplicingFinder](#)



SpliceAI



varSEAK



Platform Enhancements - Medaka (GCI)

Model Systems

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

Non-human model organism: *

Description of gene alteration: *

Phenotype(s) observed in model system ([HPO](#) or MP ID): *

Phenotype(s) observed in model system (free text): *

- ✓ No Selection
- Budding yeast (*Saccharomyces cerevisiae*) 4932
- Cat (*Felis catus*) 9685
- Chicken (*Gallus gallus*) 9031
- Chimpanzee (*Pan troglodytes*) 9598
- Chlamydomonas (*Chlamydomonas reinhardtii*) 3055
- Cow (*Bos taurus*) 9913
- Dog (*Canis lupus familiaris*) 9615
- Fission yeast (*Schizosaccharomyces pombe*) 4896
- Frog (*Xenopus*) 262014
- Fruit fly (*Drosophila*) 7215
- Gerbil (*Gerbillinae*) 10045
- Guinea pig (*Cavia porcellus*) 10141
- Hamster (*Cricetinae*) 10026
- Macaque (*Macaca*) 9539
- Medaka (*Oryzias latipes*) 8090**
- Mouse (*Mus musculus*) 10090
- Pig (*Sus scrofa*) 9823
- Rabbit (*Oryctolagus cuniculus*) 9986
- Rat (*Rattus norvegicus*) 10116
- Round worm (*Caenorhabditis elegans*) 6239
- Sheep (*Ovis aries*) 9940
- Zebra finch (*Taeniopygia guttata*) 59729
- Zebrafish (*Danio rerio*) 7955

Platform Enhancements - SOP v8 (GCI)

Approval Modal

Approve Classification

ClinGen Affiliation: General Gene Curation
Entered by:
Current curator's name will be entered upon submission

Select Approver:

Final Approval Date:

SOP Version:

[Acknowledge Other Contributors](#) ⓘ

[Preview Approval](#)

Evidence Summary

ELMO1 – Atlantic cod allergy – *Autosomal dominant inheritance*

Classification owner: General Gene Curation

Calculated classification: No Known Disease Relationship

Modified classification: No Modification

Reason for modified classification: None

SOP: [Gene Clinical Validity Standard Operating Procedures \(SOP\), Version 8](#) ↗

Classification status: **PROVISIONAL**

Date classification saved: 2020 Nov 10, 9:26 pm

Replication Over Time: No

Contradictory Evidence? Proband: **No**, Experimental: **No**

Disease: [Atlantic cod allergy](#) ↗

Platform Enhancements - Summary Text (GCI)

In 2.0 release, will become required!

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	0	0	<input type="checkbox"/>
Calculated Classification	No Known Disease Relationship		No Scored Genetic Evidence & No Contradictory Evidence	
	LIMITED		0.1-6	
	MODERATE		7-11	
	STRONG		12-18	
	DEFINITIVE		12-18 & Replicated Over Time	
Contradictory Evidence?	Proband: No Experimental: No			
Modify Calculated Clinical Validity Classification:	<input type="text" value="Definitive"/>		Evidence Summary (optional): Rationale for the clinical validity classification	
Explain Reason(s) for Change: *	<p>Note: This text will appear on ClinGen's website if you publish this Classification.</p>		<p>Note: This text will appear on ClinGen's website if you publish this Classification.</p>	
			View Example Evidence Summary Text 	
Last Saved Summary Classification	Definitive (2020 Nov 10, 10:37 am)			

 Click Save to save the Calculated Classification (highlighted in blue) without modification, or modify the Classification value in the pull-down and hit Save. Once it is saved, you will have the opportunity to edit the saved Classification, view the Evidence Summary for the saved Classification, and save it as Provisional.

Platform Enhancements - MONDO ID editing (GCI)

In 2.0 release or shortly after, ability to change MONDO IDs on GCI entries

Note: This is a demo version of the site. Data entered will be deleted once per month upon release of updated versions. clingen-helpdesk@lists.stanford.edu

Edit Disease

Enter a MONDO ID below. To find the desired MONDO ID:

1. Search for the desired MONDO term using the [OLS MONDO](#) Search [\[Help\]](#).
2. Once you have selected the term, enter its MONDO ID (the "id" at the bottom of the "Term info" box on the right hand side of the OLS term page (e.g. [MONDO:0016587](#)).

[Retrieve from OLS](#)

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

[peach allergy](#)

Unable to find a suitable ontology? [Add free text term](#)

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 and/or create a term using free text.

[Close](#) [Save](#)

ClinGen
Clinical Genome Resource

ELMO1 - peach allergy
Autosomal dominant inheritance

ELMO1
HGNC Symbol: [ELMO1](#)
NCBI Gene ID: [9844](#)

All classifications for this disease

My classification
You haven't created a classification

Dashboard Help Log Out
change your affiliation, go to
Disease
Classification Matrix
Nov 11, 2020 10:14
14 AM PST

Enabled Future Enhancements - GCI & VCI

- Bulk curation workflow (variant prioritization, semi-automated evaluation)
- Data access (full data provenance, complex searches, comprehensive outputs)
- Task management (automatic alerts, tagging)
- Coordinator support (affiliation management, reports)
- Training support (training instances)
- Curation efficiency/usability (refactor UI)
- Integration with other ClinGen systems (e.g. GeneTracker)

GCI & VCI 2.0 Release Schedule

Milestone	Details	Allowed Users	Date
Beta Release	2.0 Beta version of Demo site (no production data)	Volunteer registered users	11/13/2020
Official 2.0 Release	Production & Demo sites switch over to 2.0	All registered users	12/11/2020

GCI & VCI 2.0 testing to release process



Type of testing	Purpose	Testers
Pre-alpha testing	Internal testing of specific features	Stanford Biocurators
Alpha testing	Internal full testing	
Beta testing	External users acceptance testing	20 VCI/GCI curators
Beta release	Final check for bugs, provide public access to the new platform	Volunteer VCI/GCI users

VCI & GCI 2.0 Beta Testers

VCI

Steven Harrison

Xi Luo

Megan Frone

Emily Groopman

Jessi Mester

Diane Zastrow

VCI & GCI

Jenny Goldstein

Shannon McNulty

Shruthi Mohan

Mayher Patel

Justyne Ross

Emma Wilcox

GCI

Erin Riggs

Marina Distefano

Courtney Thaxton

May Flowers

Madeline Hughes

Alicia Byrne

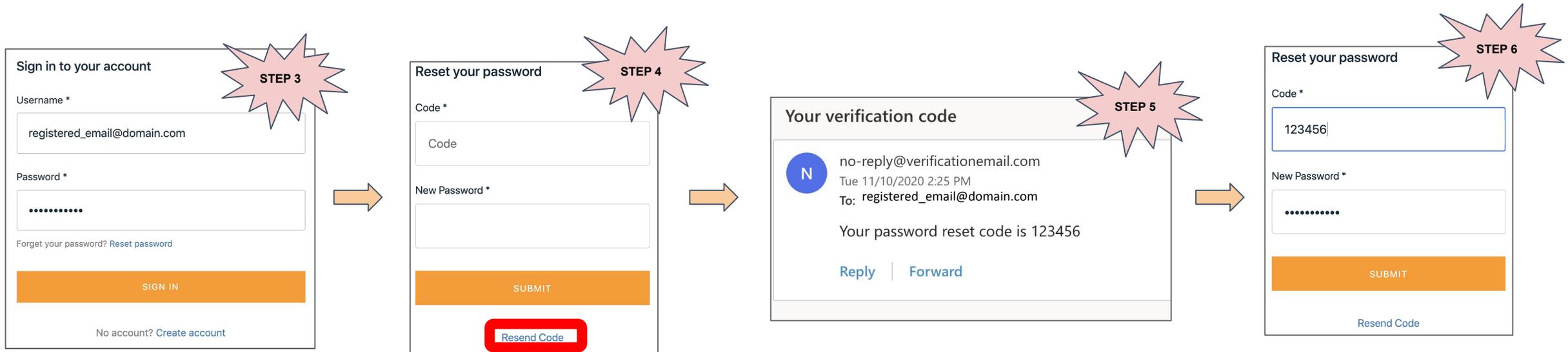
Hannah McCurry

Taylor Bingaman

Thank you!

Access to the Beta Release - for registered users

1. Navigate to <https://curation-beta.clinicalgenome.org/>
2. Click “login” in the upper right corner
3. Enter the VCI/GCI registered email as “Username”
 - a. Enter any text into the password field - it does not need to be your current VCI/GCI password
 - b. You’ll be re-directed to the “Reset your password” modal
4. Click on “Resend Code”
5. Check email for the sent code
6. Enter code and choose a password
 - a. Note: This process will not affect your VCI/GCI production access or password
7. You should now have access to the beta release



Beta release access - troubleshooting and feedback

Troubleshooting

1. Issues seeing the dashboard once you've logged in?
 - a. Refresh your web browser and clear the browser cache.
2. Issues receiving the code in the email?
 - a. Check your spam email folder >10 minutes after clicking "send code" for the code.
 - b. Resending the code by clicking the "send code" button.
3. Contact us at clingen-helpdesk@lists.stanford.edu

Feedback

1. Fill out feedback on the beta release site on this public spreadsheet
 - a. [Feedback Spreadsheet](#)
2. Contact us directly at clingen-helpdesk@lists.stanford.edu

GCI & VCI 2.0 Rearchitecture Team

Software Engineering



Shaung Cheng



Gloria Cheung



Rao Madhavrao



Mark Mandell



Howard Tong



Bryan Wulf

Product Management / Biocuration



Christine Preston



Matt Wright

Variant and Gene Curation Interfaces (VCI/GCI)

Production: curation.clinicalgenome.org
Demo: curation-test.clinicalgenome.org

Help desk: clingen-helpdesk@lists.stanford.edu

Thank you!