

Gene variant databases

sharing information

(*LSDBs*)



Johan den Dunnen



My affiliations



*get all variants/consequences
found easily accessible*



*standards for variant
description and databases*



*software for web-
based gene databases*



DNA diagnostics

..is based on

SHARING what we know on the **relation**
between **variants in genes** & **phenotypes**

without sharing, no DNA diagnostics

..do we share ?

..are databases supported ?

DNA diagnostics

- the work

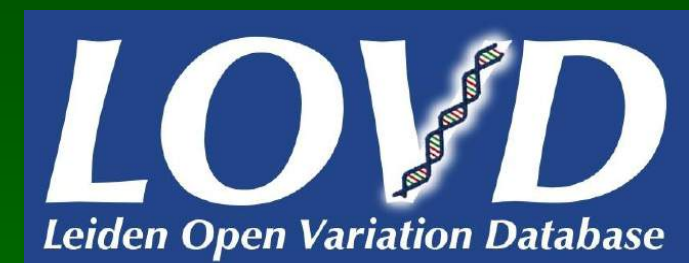
*analyse sample (sequence)
identify variants*

*check what others found
draw initial conclusion*

..perform additional experiments

*RNA, protein, cells, computational, animal model, ..
plan to publish results*

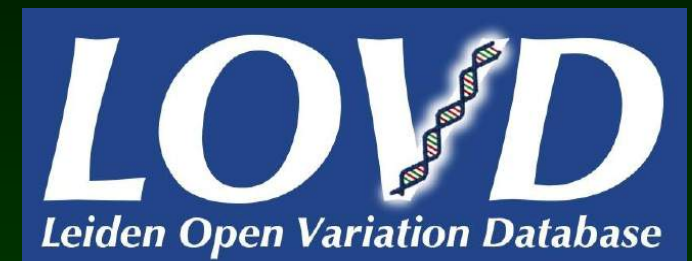
share with colleagues > submit to database



DNA diagnostics

- the work

*analyse sample (sequence)
identify variants*



share with colleagues > submit to database

*check what others found
draw initial conclusion*

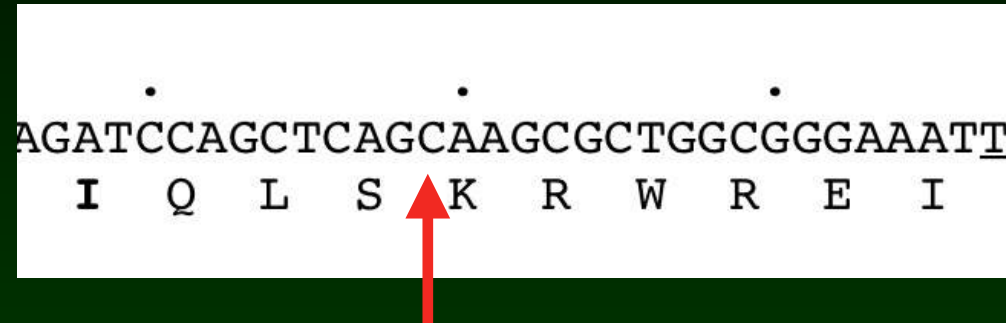
..perform additional experiments

*RNA, protein, cells, computational, animal model, ..
plan to publish results*

It seems so simple...

Example

DMD gene



c.5859C>T r.(?) p(Ser1953=)

found in diagnosis

prenatal

at risk family for DMD

no definite diagnosis

found in diagnosis

WES, trio analysis

male parent

45y, healthy

***you may have life saving information,
do you realize this??***




©John Burn

my data

©Johan vd Leij

...privacy



| | |
|---|--|
| LOVD Leiden Muscular Dystrophy pages | |
| Duchenne Muscular Dystrophy (DMD) | |
| Curator: Johan den Dunnen | |
| LOVD v2.0 Build 26 [Current LOVD status] | |
| Register as submitter Log in | |
| Home Variants Submitters Submit Documentation | |
| DMD homepage Switch gene | |
| LOVD Gene homepage | |
| General information | |
| Gene name | Duchenne Muscular Dystrophy |
| Gene symbol | DMD |
| Chromosome Location | Xp21.2 |
| Database location | www.dmd.nl |
| Curator | Johan den Dunnen |
| PubMed references | View all (unique) PubMed references in the DMD database |
| Date of creation | July 29, 1997 |
| Last update | April 09, 2010 |
| Version | DMD100409 |
| Add sequence variant | Submit a sequence variant |
| First time submitters | Register here |
| Reference sequence | coding DNA reference sequence for describing sequence variants |
| GenBank reference | DMD_N65012232.1.gb |
| Total number of unique DNA variants reported | 2478 |
| Total number of individuals with variant(s) | 22615 |
| Total number of variants reported | 23821 |
| Subscribe to updates of this gene |  |
| Graphical displays and utilities | |
| Summary tables | Summary of all sequence variants in the DMD database, sorted by type of variant (with graphical displays and statistics) |
| Reading-frame checker | The Reading-frame checker generates a prediction of the effect of whole-exon changes |
| UCSC Genome Browser | Show variants in the UCSC Genome Browser (compact view) |
| NCBI Sequence Viewer | Show distribution histogram of variants in the NCBI Sequence Viewer |
| Sequence variant tables | |
| Unique sequence variants | Listing of all unique sequence variants in the DMD database, without patient data |
| Complete sequence variant listing | Listing of all sequence variants in the DMD database |
| Variants with no known pathogenicity | Listing of all DMD variants reported to have no noticeable phenotypic effect (note: excluding |

LMNA : c.?

...we have identified a variant in this gene in a patient with a certain phenotype.

For privacy reasons we are not able to share more information.

For details please contact us.

VUS

Variant of Uninsufficient Sharing

Organisations

- **HVP & HGVS**

Human Variome Project

Human Genome Variation Society

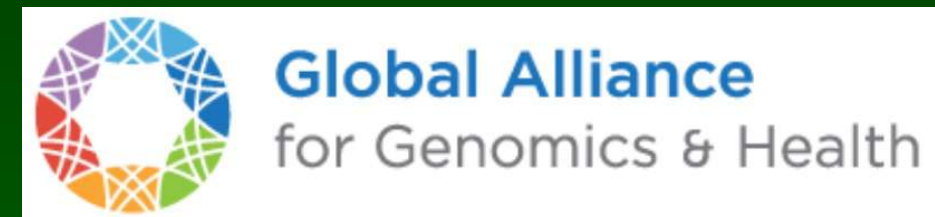
umbrella organisations promoting collecting genome variation & establishing standards



- **GA4GH**

Global Alliance for Genomics and Health

recent initiative, similar goals
active on many aspects



- **EBI & NCBI**

reference sequences
genome browsers
variant databases



Databases require?

- standard to describe phenotypes
HPO (Human Phenotype Ontology)
- standard to describe variants in DNA
HGVS nomenclature
- databases
sharing information



DNA variant DBs

- central databases

inch deep, mile wide

HGMD

*lists first published report > no frequencies
pathogenic only (most)*

OMIM

list firsts report(s) & some interesting cases

dbSNP, EVA

all variants (originally mainly non pathogenic)

many others

COSMIC, DBVar, Decipher, ...

- gene variant databases

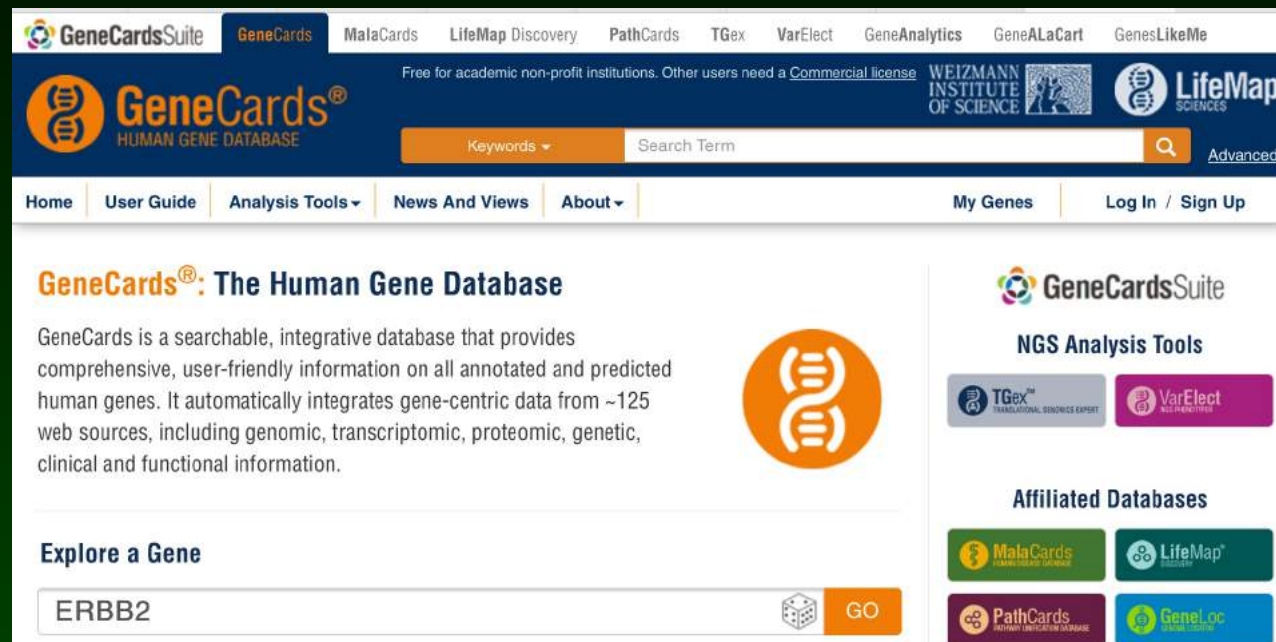
*all details per gene
all variants*

inch wide, mile deep

unpublished data from direct DB submission



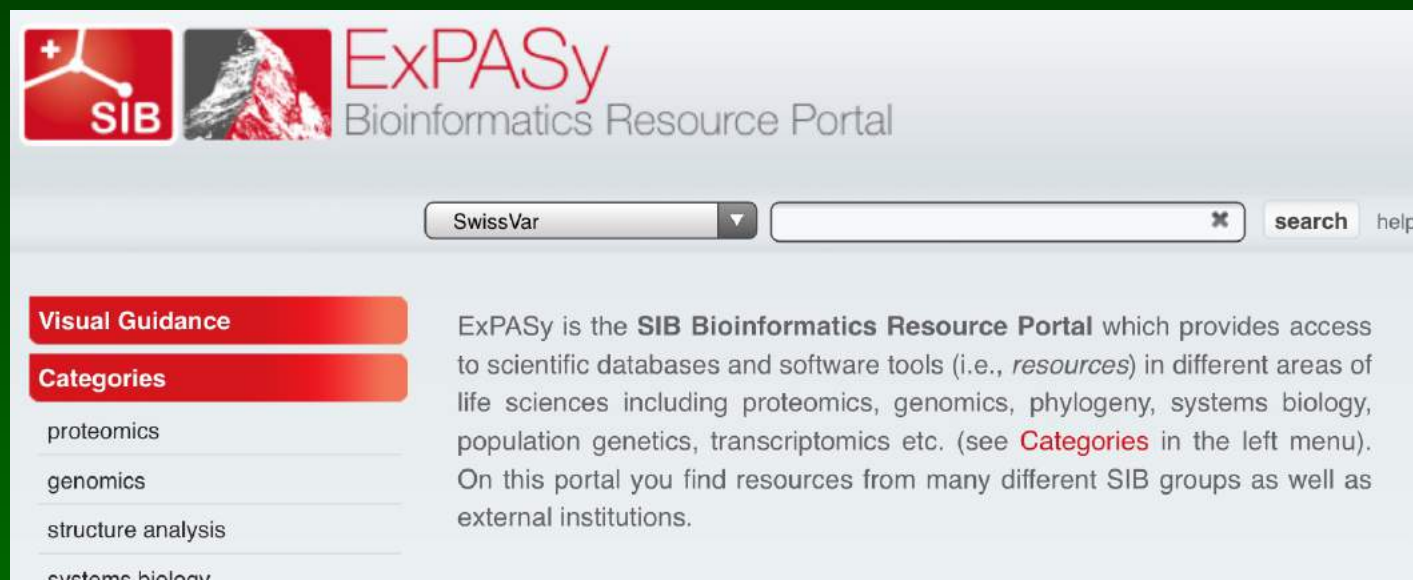
Other databases



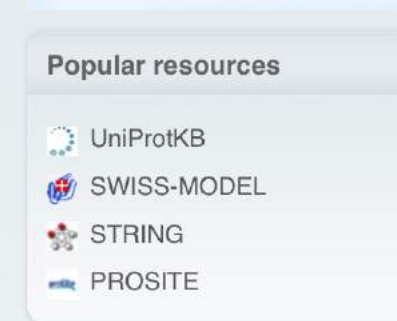
The screenshot shows the GeneCards website, which is part of the GeneCards Suite. The header includes navigation links for GeneCards, MalaCards, LifeMap Discovery, PathCards, TGex, VarElect, GeneAnalytics, GeneALaCart, and GenesLikeMe. A search bar is prominently displayed with the text "Keywords" and "Search Term". Below the header, there is a section titled "GeneCards®: The Human Gene Database" with a description of the database's scope. A sidebar on the right lists "NGS Analysis Tools" (TGex, VarElect) and "Affiliated Databases" (MalaCards, LifeMap, PathCards, GeneLoc). At the bottom, there is a section "Explore a Gene" with a search bar containing "ERBB2" and a "GO" button.



The screenshot shows the Orphanet website, described as "The portal for rare diseases and orphan drugs". It features a quote: "Rare diseases are **rare**, but rare disease patients are **numerous**". Below this, there is a section "Access our Services" with a grid of icons and text boxes. The services listed are: "Inventory, classification and encyclopaedia of rare diseases, with genes involved", "Inventory of orphan drugs", "Directory of patient organisations", "Directory of professionals and institutions", "Directory of expert centres", "Directory of medical laboratories providing diagnostic tests", "Directory of ongoing research projects, clinical trials, registries and biobanks", and "Collection of thematic reports: Orphanet Reports Series".



The screenshot shows the ExPASy Bioinformatics Resource Portal. The header includes the SIB logo and the text "ExPASy Bioinformatics Resource Portal". A search bar is present with a dropdown menu showing "SwissVar" and a "search" button. On the left, there is a "Visual Guidance" section with a "Categories" list: proteomics, genomics, structure analysis, and systems biology. The main content area describes ExPASy as the SIB Bioinformatics Resource Portal, providing access to scientific databases and software tools in various life science fields.



This section lists popular resources available on the platform. The resources listed are: UniProtKB, SWISS-MODEL, STRING, and PROSITE.

OMIM[®]

Online Mendelian Inheritance in Man[®]

An Online Catalog of Human Genes and Genetic Disorders

Title

Phenotype-Gen

Rela

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See

References

Title



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OMIM Donation:

Dear OMIM User,

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Thank you in advance for your generous support,
Ada Hamosh, MD, MPH
Scientific Director, OMIM

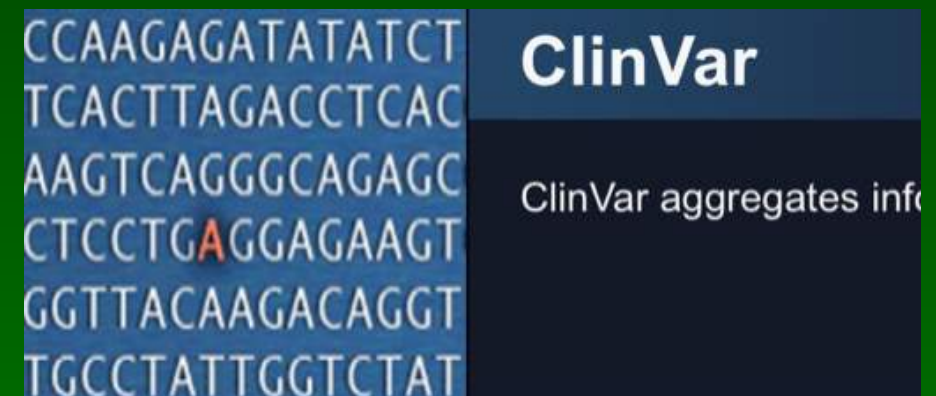
[Donate To OMIM!](#)

Definition

Locus Specific DataBase (LSDB)

A listing of sequence variants in a specific gene causing a Mendelian disorder or a change in phenotype, curated by an expert in that gene

(gene variant database)



LSDBs

- **gene variant databases** (*LSDBs*)

use HGVS description variants

link to other relevant sources

store ALL variants

from publications AND direct submissions

detailed phenotype data (...often limited)

active curator searching, asking, adding, ...

variable formats / quality / updating

*A hit means data on consequences for function
are available*

...but not a DB for all genes

Is there a DB?

try
GeneSymbol.variome.org

Locus Specific Database list [LSDB list](#) | [Log in](#)
Based on various online resources and direct submissions of LSDBs

Locus Specific Mutation Databases

IMPORTANT NOTE: Genes are in order of [HUGO APPROVED GENE DESIGNATION](#), not alias. e.g. "p53" will be found under "TP53" while "CD40L" or "TNFSF5" will be found under "CD40LG" and so on.

If you wish to add a gene you can [do so here](#).

Please select the first letter of the Gene:
A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

Or, specify the HGNC Gene Symbol:

[Go to this gene »](#)

6 public entries

| Gene Symbol | Database | Curators | Software |
|----------------------------------|--|--|----------|
| TP53 tumor protein p53 | Mendelian genes http://grenada.lumc.nl/LOVD2/mendelian_genes/home.php?select_db=TP53 | Curator vacancy ? | LOVD 2.X |
| TP53 tumor protein p53 | IARC TP53 Mutation Database: Human somatic and germline TP53 mutations compiled from the literature http://www-p53.iarc.fr/ | M. Olivier, R. Eeles, M. Hollstein, C. C. Harris, P. Hainaut, IARC, Lyon, France | Unknown |
| TP53 tumor protein p53 | p53 Mutation in Human Cancer http://p53.free.fr/ | T. Soussi; C. Beroud, INSERM, Hopital Necker, Enfants Malades, Paris, France | Unknown |
| TP53 tumor protein p53 | Database of Germline p53 Mutations http://www.lf2.cuni.cz/projects/germline_mut_p53.htm | Zdenek Sedlacek & Marie Trkova, Charles Univ. Prague, Czech Republic | Unknown |
| TP53 tumor protein p53 | p53 Mutation Database Analysis & Search http://p53.genome.ad.jp/ | Human Genome Centre Tokyo, Japan | Unknown |
| TP53 | The UMD TP53 mutation database | Thierry Soussi, France | UMD |

TP53.variome.org

Locus Specific Database list [LSDB list](#) | [Log in](#)
Based on various online resources and direct submissions of LSDBs

Automatic LSDB redirection service

In a few seconds you will be transferred to the CAV3 LSDB list

This service is created with support from:

the Human Genome Variation Society (HGVS)  Leiden University Medical Center 

When this page does not redirect you automatically, please click [here](#)

2 second acknowledgement

always a hit in
LOVD and ClinVar

LOVD [LOVD v2.0 build 29](#) | [Contact LOVD staff](#)

Membrane-Bound Transcription factor Peptidase, site 2 (MBTPS2) [Register as submitter](#) | [Log in](#)

Curator: Emmellen, Alan

[Home](#) [Variants](#) [Submitters](#) [Submit](#) [Documentation](#)

MBTPS2 homepage | Switch gene

LOVD Gene homepage

| General information | |
|--|---|
| Gene name | Membrane-Bound Transcription factor Peptidase, site 2 |
| Gene symbol | MBTPS2 |
| Chromosome Location | 2p22.12-p22.11 |
| Database location | www.LOVD.nl/MB |
| Curator | Emmellen, Alan |
| PubMed references | View all (unique) PubMed |
| Date of creation | August 07, 2009 |
| Last update | October 30, 2010 |
| Version | MBTPS2_101030 |
| Add sequence variant | Submit a sequence variant |
| First time submitters | Register here |
| Reference sequence | coding DNA reference sequence |
| Genbank reference | MBTPS2_HG_012797.1.0 |
| Total number of unique DNA variants reported | 25 |
| Total number of individuals with variant(s) | 94 |
| Total number of variants reported | 109 |

CCAAGAGATATATCT
TCACTTAGACCTCAC
AAGTCAGGGCAGAGC
CTCCTGAGGAGAAGT
GGTTACAAGACAGGT
TGCCTATTGGTCTAT

ClinVar

ClinVar aggregates information

when not ...?

Collaboration

ACTGATGGTATGGGGCCAAGAGATATATCT
CAGGTACGGCTGTCATCACTTAGACCTCAC
CAGGGCTGGGCATAAAAGTCAGGGCAGAGC
CCATGGTGCATCTGACTCCTGAGGAGAAGT
GCAGGTTGGTATCAAGGTTACAAGACAGGT
GGCACTGACTCTCTCTGCCTATTGGTCTAT

ClinVar

ClinVar aggregates information about genomic variation and its relationship to human health.

collaboration initiated, exchange data



approaching other databases to merge their data

Your country ?

xx.LOVD.org

xx = country code

Home Variants in individuals from Malaysia Variants

244 entries on 10 pages. Showing entries 1 - 25.

25 per page Legend << First < Prev 1 2 3 4

| Gene | Transcript | Effect | DNA change (cd |
|--------|-------------|--------|----------------|
| ABCC11 | NM_032583.3 | +/+ | c.538G>A |
| ABCC11 | NM_032583.3 | +/+ | c.538G>A |
| ABCC11 | NM_032583.3 | +/+ | c.538G>A |
| ABCC11 | NM_032583.3 | +/+ | c.538G>A |
| APC | NM_000038.5 | +/+ | c.847C>T |

244 variants

Malaysia DNA Variant Database

Based on:
LOVD
Leiden Open Variation Database

MY

Home Variants in individuals from Malaysia Variants by submitters from Malaysia

This resource automatically retrieves information from our [LOVD3 shared installation](#). The information retrieved is based on the geographic information per country (here for **Malaysia**).

Variants shown are either linked to the country of origin of an *individual* (patient), or to the country of origin of the *submitter* of the variant. Note the difference: data from an *individual* in Germany can be submitted by a *submitter* from Belgium.

Queries can be submitted by using the search boxes in the column's header.

Home Variants in individuals from Malaysia Variants

46 entries on 2 pages. Showing entries 1 - 25.

25 per page Legend << First < Prev 1 2 Next >

| Gene | Transcript | Effect | DNA change (cd |
|-------|-------------|--------|----------------|
| BRCA1 | NM_007294.3 | ?/+ | c.181T>C |
| BRCA1 | NM_007294.3 | +/+ | c.115T>C |
| BRCA1 | NM_007294.3 | +/+ | c.115T>C |
| BRCA1 | NM_007294.3 | -/- | c.2521C>T |
| BRCA1 | NM_007294.3 | ?/+ | c.190T>C |
| BRCA1 | NM_007294.3 | ?/? | c.4211T>G |
| BRCA1 | NM_007294.3 | ?/? | c.5057A>G |
| BRCA1 | NM_007294.3 | ?/? | c.5057A>G |
| BRCA1 | NM_007294.3 | ?/? | c.5072C>A |

46 submissions

Your country ?

xx.LOVD.org

xx = country code

Singapore DNA Variant Database

Based on:
LOVD
Leiden Open Variation Database

SG

Home Variants in individuals from Singapore Variants by submitters from Singapore

This resource automatically retrieves information from our [LOVD3 shared installation](#). The information retrieved is based on the geographic information per country (here for **Singapore**).

Variants shown are either linked to the country of origin of an *individual* (patient), or to the country of origin of the *submitter* of the data. Note the difference: data from an *individual* in Germany can be submitted by a *submitter* from Belgium.

Queries can be submitted by using the search boxes in the column's header.

Home Variants in individuals from Singapore Variants by submitte

78 entries on 4 pages. Showing entries 1 - 25.

25 per page Legend << First < Prev 1 2 3 4 Next > Last >

| Gene | Transcript | Effect | DNA change (cDNA) |
|-------|-------------|--------|--------------------------------------|
| APC | NM_000038.5 | +/- | c.1226_1229delinsAAA |
| BRCA1 | NM_007294.3 | +/- | c.(-20+1_-19-1)_(80+1_81-1)del |
| BRCA1 | NM_007294.3 | +/- | c.(4185+1_4186-1)_(4357+1_4358-1)dup |
| BRCA1 | NM_007294.3 | +/- | c.1392del |
| BRCA1 | NM_007294.3 | +/- | c.1405del |

78 variants

Home Variants in individuals from Singapore Variants by su

18 entries on 1 page. Showing entries 1 - 18.

25 per page Legend

| Gene | Transcript | Effect | DNA change (cDNA) |
|------|-------------|--------|----------------------|
| APC | NM_000038.5 | +/- | c.1226_1229delinsAAA |
| LDLR | NM_000527.4 | ?/. | c.1060G>A |
| NPR2 | NM_003995.3 | +?/. | c.1352-1G>A |
| NPR2 | NM_003995.3 | +?/. | c.142G>T |
| NPR2 | NM_003995.3 | +?/. | c.1167G>T |

18 submissions

Your country?

Home

Variants in individuals from Malaysia

Variants

46 entries on 2 pages. Showing entries 1 - 25.

25 per page ▼

Legend

« First

< Prev

1

2

Next >

| Gene | Transcript | Effect | DNA change (cD |
|-------|-------------|--------|----------------|
| BRCA1 | NM_007294.3 | ?/+ | c.181T>C |
| BRCA1 | NM_007294.3 | +/+ | c.115T>C |
| BRCA1 | NM_007294.3 | +/+ | c.115T>C |
| BRCA1 | NM_007294.3 | -/- | c.2521C>T |
| BRCA1 | NM_007294.3 | ?/+ | c.190T>C |
| BRCA1 | NM_007294.3 | ?/? | c.4211T>G |
| BRCA1 | NM_007294.3 | ?/? | c.5057A>G |
| BRCA1 | NM_007294.3 | ?/? | c.5057A>G |
| BRCA1 | NM_007294.3 | ?/? | c.5072C>A |

LSDB-in-a-Box

- **software**

*Open Source, platform independent
freely available > [http:// www.LOVD.nl](http://www.LOVD.nl)
follows existing HGVS guidelines
LSDB content, description of variants*

- **fully WWW-based**

*display of data
data management
access levels incl. manager, curator, submitter*

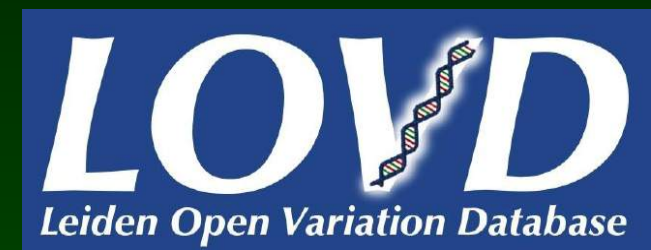
- **runs on any platform**

laptop / PC, intranet, internet

***free hosting
on Leiden servers***

- **make any database**

pre-programmed for DNA / RNA / protein



©Ivo Fokkema

LOVD connections



contact through central site
LSDB list, web service (exome queries)

LOVD is supported by:



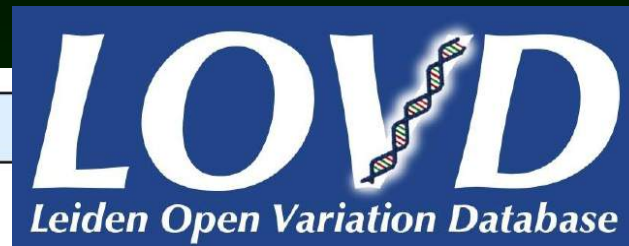
data flow

lab > gene variant database > central repository

LOVDs world-wide

Aug.
2018

| In total: 292,384,028 variants (3,953,852 unique) in 763,965 individuals in 85 LOVD installations. | | | |
|---|--|-------------|-------------------|
| http://bipmed.iqm.unicamp.br/snparray/ | LOVD 3.0-20 | 17391 genes | 902273 unique |
| BIPMed SNP Array | A1BG-AS1,A1CF,A2M,A2M-AS1,A2ML1,A2MP1,A3GALT2,A4GALT,A4GN... | | |
| http://bipmed.iqm.unicamp.br/ | LOVD 3.0-21 | 20930 genes | 66158522 variants |
| BIPMed WES | A1BG,A1BG-AS1,A1CF,A2M,A2M-AS1,A2ML1,A2MP1,A3GALT2,A4GALT... | | 622610 |
| http://databases.lovd.nl/whole_genome/ | LOVD 3.0-20a | 22002 genes | 1998175 |
| Whole genome datasets | A1BG,A1BG-AS1,A1CF,A2M,A2M-AS1,A2ML1,A2MP1,A4GALT,A4GNT,A... | | 1998135 |
| https://databases.lovd.nl/shared/ | LOVD 3.0-21 | 22980 genes | 757275 |
| Global Variome shared LOVD | A1BG,A1BG-AS1,A1CF,A2LD1,A2M,A2M-AS1,A2ML1,A2MP1,A3GALT2,... | | 173628 |
| http://proteomics.bio21.unimelb.edu.au/lovd/ | LOVD 3.0-07 | 14772 genes | 239690 variants |
| LOVD - Leiden Open Variation Database | A1BG,A1BG-AS1,A1CF,A2M,A2ML1,A4GALT,A4GNT,AAAS,AACS,AACSP... | | 152241 |
| http://bipmed.iqm.unicamp.br/cfa/ | LOVD 3.0-21 | 41 genes | 134333 |
| Craniofacial anomalies | APOC2,APOC4-APOC2,AXIN2,BCL3,BMP4,CLPTM1,DVL2,ERBB2,FGF22... | | 257 unique |
| https://ab-openlab.csir.res.in/mitolsdb/ | LOVD 2.0-35 | 37 genes | 112662 variants |
| MitoLSDB | MTATP6,MTATP8,MTCO1,MTCO2,MTCO3,MTCYB,MTND1,MTND2,MTND3,M... | | 4660 unique |
| http://www.insight-database.org/ | LOVD 3.0-21 | 17 genes | 36826 variants |
| International Society for Gastrointestinal Hereditary Tumours Database | APC,BMPR1A,EPCAM,FBXO11,GALNT12,MLH1,MLH3,MSH2,MSH3,MSH6,... | | 5836 unique |
| http://HCI-LOVD.hci.utah.edu | LOVD 2.0-33 | 8 genes | 26167 variants |
| LOVD - human mismatch repair genes | MLH1,MLH1_priors,MSH2,MSH2_priors,MSH6,MSH6_priors,PMS2,P... | | 26167 unique |



Query all LOVDs

LOVD v.3.0 - Leiden Open Variation Database
Online gene-centered collection and display of DNA variations

Home News FAQ Documentation Download Contact Developers Like 728

LOVD 3.0 LOVD 2.0 Public list of LOVD installations Search for a variant Our list of Locus Specific Databases

Query all public LOVD installations

Query all public LOVD instances:

hg19 / GRCh37 genomic HGVS, like chr15:g.40699840C>T Search

Examples: Precise: [chr15:g.40699840C>T](#), Range: [chr13:32936732-32936735](#).

using a position

Query all public LOVD installations

Query all public LOVD instances:

hg19 / GRCh37 chr15:g.40699840C>T Search

Examples: Precise: [chr15:g.40699840C>T](#), Range: [chr13:32936732-32936735](#).

LOVDs currently support only one genome build; if no results are found, you may want to repeat your query using a different genome build.
LOVD contains for hg18 ~1K unique variants, hg19 ~2M unique variants, and hg38 ~1M.
This service queries the variant's location, i.e. results of other variants on the same location will show as well. When searching using a ranged variant in HGVS format, only variants exactly matching that range will be returned. When searching using a range (2nd example above), all variants within that range will be returned (to a max of 50).

| | | |
|---|---------------------------------------|---|
| IVD | NM_001159508.1:c.154-298C>G | (variant effect not shared) |
| http://databases.lovd.nl/whole_genome/ | | Variant location matches your query exactly |
| IVD | NM_002225.3:c.157C>T | Affects function / Probably affects function |
| https://databases.lovd.nl/shared/ | | Variant location matches your query exactly |

LOVDs have an API

Query all public LOVD installations

Query all public LOVD instances:

hg19 / GRCh37 chr13:32936732-32936735 Search

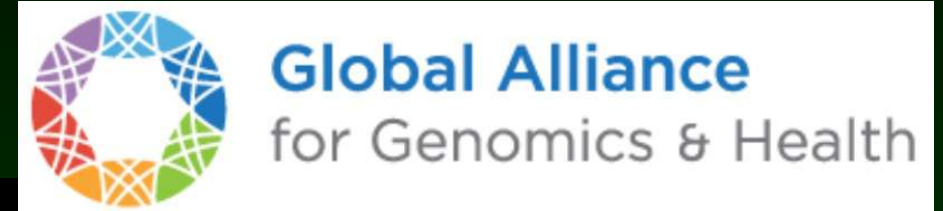
Examples: Precise: [chr15:g.40699840C>T](#), Range: [chr13:32936732-32936735](#).

LOVDs currently support only one genome build; if no results are found, you may want to repeat your query using a different genome build.
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| | | |
|---|-----------------------------------|---|
| BRCA2 | NM_000059.3:c.7878_7881dup | Affects function / Affects function |
| https://databases.lovd.nl/shared/ | | Variant location matches your query exactly |
| BRCA2 | NM_000059.3:c.7878G>A | Affects function / Affects function |
| https://databases.lovd.nl/shared/ | | Variant is within range of your query |
| BRCA2 | NM_000059.3:c.7878G>C | Effect unknown; Probably affects function; Affects function / Affects function |
| https://databases.lovd.nl/shared/ | | Variant is within range of your query |
| BRCA2 | NM_000059.3:c.7879A>T | Effect unknown; Affects function / Affects function |
| https://databases.lovd.nl/shared/ | | Variant is within range of your query |

using a range

Beacons



**A global search engine
for genetic mutations.**

GRCh37 ▾

e.g. 1 : 100,000 A>C

Search

Quickstart: [Search for a BRCA2 variant](#)

Beacon Project

Being implemented on the website of the world's top genomic organizations to test the willingness of international sites to share genetic data.




*there are simply tooooooo
many databases*

brcaexchange.org

BRCA Challenge

The BRCA Challenge aims to advance understanding of the genetic basis of breast and other cancers using data from around the world.




BRCA Exchange

Expert Reviewed

HOME VARIANTS COMMUNITY

search for "c.1105G>A", "brca1" or "IVS7+1037T>C"



BRCA Exchange

a public BRCA variant portal

OPEN


17+ Age

What's New

Followed variant update notifications are now produced through a more robust local background-fetch mechanism, removing the reliance on push notifications. Various small bugfixes and user-interface [more](#)

4mo ago
Version 1.3.12

Preview



This is the BRCA Exchange Clinical Space, and contains only expert-reviewed variant classifications shown here represent the initial set submitted by the ENIGMA consortium, ~1000 (primarily missense BRCA2). The Clinical space will become more fully populated pending additional expert review.

Show All Public Data

Show Filters

2 matching variants of which 1 matched on synonyms

c.1105G>A

| Gene | HGVS Nucleotide | HGVS Protein | Protein Abbrev | BIC Designation | Clinical Significance |
|-------|-----------------|---------------|----------------|-----------------|---------------------------------------|
| BRCA1 | c.1105G>A | p.(Asp369Asn) | D369N | 1224G>A | Benign / Little Clinical Significance |
| BRCA1 | c.993G>C | p.(Arg331Ser) | - | - | Not Yet Classified |

Search

search for "c.1105G>A" or "brc..."

20644 variants [? legend](#)

| Gene | HGVS Nucleotide | |
|-------|--------------------|--|
| BRCA1 | c.4358-2692G>A | |
| BRCA2 | c.775delA | |
| BRCA1 | c.117T>A | |
| BRCA2 | c.7341T>C | |
| BRCA1 | c.134+1508G>A | |
| BRCA2 | c.7544C>T | |
| BRCA1 | c.825_828delCAC... | |
| BRCA2 | c.9118-1G>A | |
| BRCA1 | c.5333-18T>G | |

DMD gene homepage

This database is one of the gene variant databases from the [Leiden Muscular Dystrophy pages](#).

General information

| | |
|--|---|
| Gene symbol | DMD |
| Gene name | dystrophin |
| Chromosome | X |
| Chromosomal band | p21.2 |
| Imprinted | Unknown |
| Genomic reference | NG_012232.1 |
| Transcript reference | NM_004006.2 |
| Exon/intron information | NM_004006.2 exon/intron table |
| Associated with diseases | all-in-one , BMD , BMD/DMD , CMD-3B , DMD |
| Citation reference(s) | - |
| Refseq URL | Genomic reference sequence |
| Curators (1) | Johan den Dunnen |
| Total number of public variants reported | 15850 |
| Unique public DNA variants reported | 4925 |
| Individuals with public variants | 36693 |
| Hidden variants | 1468 |

Notes

This database is one of the gene variant databases from

Leiden Muscular Dystrophy pages[©]

the:

When referring to this database please cite [Aartsma-Rus et al. \(2006\). Muscle Nerve. 34:135-144](#) and/or [White SJ, den Dunnen JT \(2006\). Cytogenet.Genome Res. 115: 240-246.](#)

| | |
|-------------------|-------------------|
| Date created | July 29, 1997 |
| Date last updated | March 09, 2018 |
| Version | DMD:180309 |

Graphical displays and utilities

| | |
|-------------------------------|---|
| Graphs | Graphs displaying summary information of all variants in the database » |
| Reading frame checker | The Reading-frame checker generates a prediction of the effect of whole-exon changes. Active for: NM_004006.2 . |
| UCSC Genome Browser | Show variants in the UCSC Genome Browser (full view , compact view) |
| Ensembl Genome Browser | Show variants in the Ensembl Genome Browser (full view , compact view) |
| NCBI Sequence Viewer | Show distribution histogram of variants in the NCBI Sequence Viewer |

Links to other resources

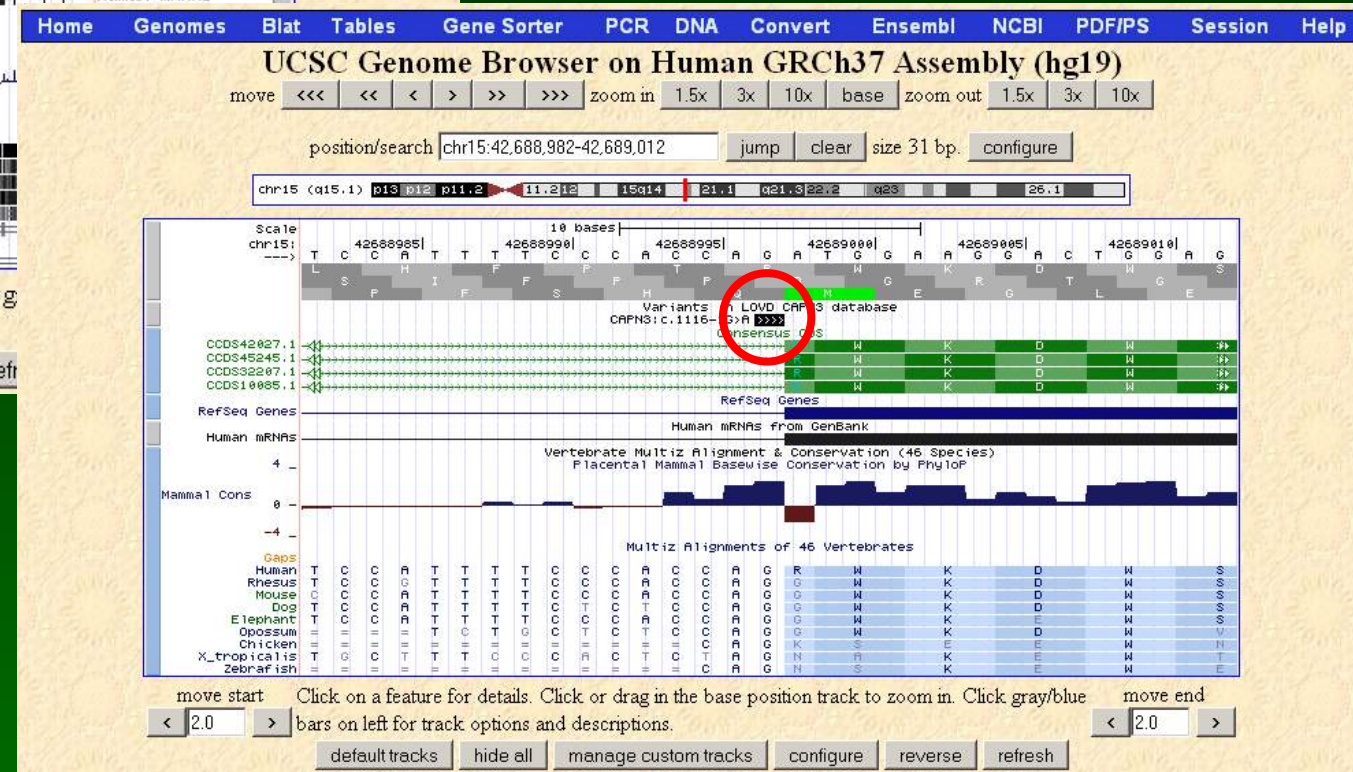
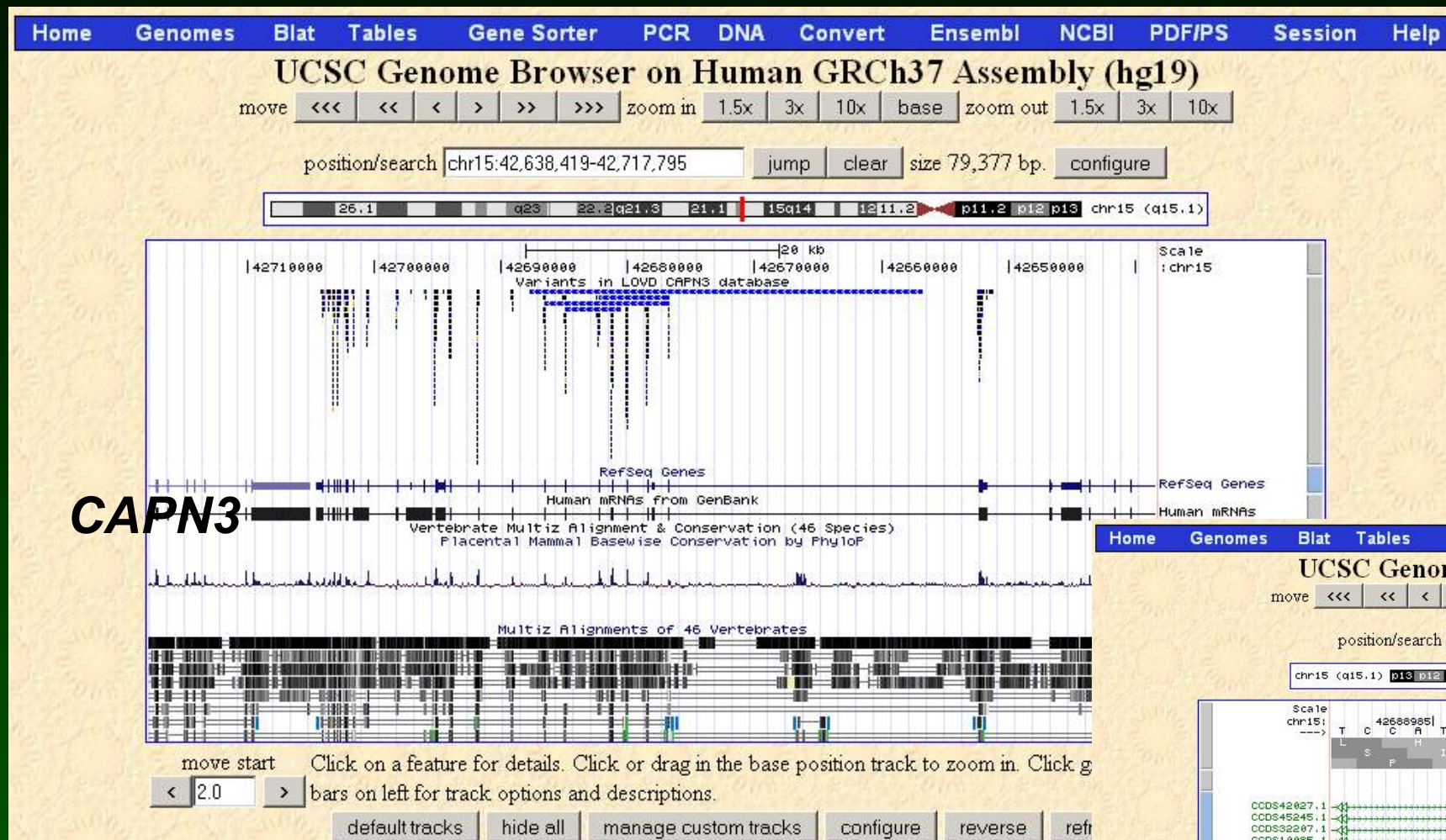
| | |
|------------------------|--|
| Homepage URL | http://www.LOVD.nl/DMD |
| External URL | the Leiden Muscular Dystrophy pages Orphanet |
| HGNC | 2928 |
| Entrez Gene | 1756 |
| PubMed articles | DMD |
| OMIM - Gene | 300377 |
| OMIM - Diseases | BMD (dystrophy, muscular, Becker type (BMD)) CMD-3B (cardiomyopathy, dilated, type 3B (CMD-3B)) DMD (dystrophy, muscular, Duchenne type (DMD)) |
| HGMD | DMD |
| GeneCards | DMD |
| GeneTests | DMD |

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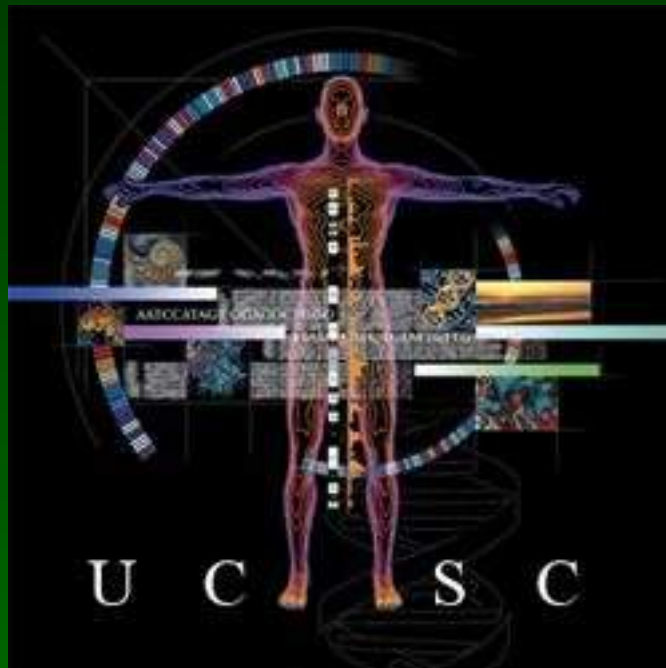
LOVD to genome



Genome browsers

*genome browsers start to accept
HGVS descriptions*

immediately jumping to position/change in genome



| Request: | Genome Browser Response: |
|---|--|
| chr7 | Displays all of chromosome 7 |
| chrUn_gl000212 | Displays all of the unplaced contig gl000212 |
| 20p13 | Displays region for band p13 on chr 20 |
| chr3:1-1000000 | Displays first million bases of chr 3, counting from p-arm telomere |
| chr3:1000000+2000 | Displays a region of chr3 that spans 2000 bases, starting with position 1000000 |
| RH18061;RH80175 15q11;15q13 rs1042522;rs1800370 | Displays region between genome landmarks, such as the STS markers RH18061 and RH80175, or chromosome bands 15q11 to 15q13, or SNPs rs1042522 and rs1800370. This syntax may also be used for other range queries, such as between uniquely determined ESTs, mRNAs, refSeqs, etc. |
| D16S3046 | Displays region around STS marker D16S3046 from the Genethon/Marshfield maps. Includes 100,000 bases on each side as well. |
| AA205474 | Displays region of EST with GenBank accession AA205474 in BRCA1 cancer gene on chr 17 |
| AC008101 | Displays region of clone with GenBank accession AC008101 |
| AF083811 | Displays region of mRNA with GenBank accession number AF083811 |
| PRNP | Displays region of genome with HUGO Gene Nomenclature Committee identifier PRNP |
| NM_017414 | Displays the region of genome with RefSeq identifier NM_017414 |
| NP_059110 | Displays the region of genome with protein accession number NP_059110 |
| pseudogene mRNA | Lists transcribed pseudogenes, but not cDNAs |
| homeobox caudal | Lists mRNAs for caudal homeobox genes |
| zinc finger | Lists many zinc finger mRNAs |
| kruppel zinc finger | Lists only kruppel-like zinc fingers |
| huntington | Lists candidate genes associated with Huntington's disease |
| zahler | Lists mRNAs deposited by scientist named Zahler |
| Evans,J.E. | Lists mRNAs deposited by co-author J.E. Evans |

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visitor

[GHR homepage](#) [Switch gene](#)

[Home](#) [Variants](#) [Submitters](#) [Submit](#) [Documentation](#)

submitter *colleague*

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curator *collaborator*



Configuration



Switch gene



Curate



Find & Replace



Add column



Edit columns



Edit gene db



Empty gene db



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DB manager



Setup



Settings



Add col



Edit cols



New col



All cols



New link



Edit links



Scan



Modules



New gene



Edit genes



New user



Edit users



New sub



Edit subs

Lo

LOVD Setup

Leiden Open Variation Database

Installed:2008-06-12 Updated:2008-09-01

Statistics

Users:12 Submitters:8 Genes:5 Log entries:395

Variants

Total:92 Submitted:24 Non public:2 Marked:8 Public

Show your data

Leiden, Netherlands

Carli Tops

Leiden University Medical Center

Clinical Genetics

84 entries in MLH1

| Path. | Exon | DNA change | DNA_reported | RNA change | Protein |
|-------|------|----------------|--------------|------------|-----------------|
| +/? | 01 | c.18_34del17 | - | r.(?) | p.Val7_ArgfsX18 |
| +/? | 01 | c.18_34del17 | - | r.(?) | p.Val7_ArgfsX18 |
| +/? | 01 | c.18_34del17 | - | r.(?) | p.Val7_ArgfsX18 |
| ??/? | 01 | c.102_103delGA | - | r.(?) | p.Glu34AspfsX3 |

You have not sent any submissions to the MLH3 gene database yet!

60 entries in MSH2

| Path. | Exon | DNA change | DNA_reported | RNA change | Protein |
|-------|------|-----------------|---|------------|---------|
| ??/? | 00 | c.(?-68)_*+?del | del 1_16 | - | p.0? |
| ??/? | 00 | c.(?-68)_*+?del | del MSH2 ex1_16, delTACSTD1-15,-27, del MSH6 | - | p.0? |
| ??/? | 00 | c.(?-68)_*+?del | del 1_16 | - | p.0? |

62 entries in MSH6

| Path. | Exon | DNA change | DNA_reported | RNA change | Protein | Codon_nr |
|-------|------|----------------------------|---|------------|------------------------|----------|
| ??/? | 00 | c.1-?_*+?del + MSH2 (1) | del MSH2 ex1_16, delTACSTD1-15,-27, del MSH6 | - | p.0? | - |
| ??/? | 01 | c.1-18G>T | - | - | p.? | - |
| ??/? | 01 | c.1-?_457+?del | deletion of 21.6 kb around exon 1+2 | - | p.Met1_Gly153>ValfsX21 | - |

You have not sent any submissions to the PMS1 gene database yet!

9 entries in PMS2

| Path. | Exon | DNA change | DNA_reported | RNA change | Protein |
|-------|------|---|----------------------|------------|------------------|
| +/? | 03 | c.219_220dup + MLH1 (2) | - | r.(?) | p.Gly74ValfsX3 |
| ??/? | 07i | c.? | g.46227+?_47919-?ins | r.(?) | - |
| ??/? | 08 | c.861_864delACAG + c.1688G>T, MLH1 (1) | c.856delG | r.(?) | p.Arg287SerfsX19 |

4 databases in 1

- **Individuals**
*details on the Individual
fields fixed per database installation*
- **Phenotypes**
*details on Phenotype(s) per Individual
one Individual can have several Phenotypes
fields variable per Phenotype*
- **Screenings**
*details on Screening(s) performed
fields fixed per database installation*
- **Variants**
*details on Variant(s) identified
fields variable per Gene*



LOVD 3 LOVD 3.0 shared installation
Leiden Open Variation Database FBN3 (fibrillin 3)
Curator: LOVD-team, but with Curator vacancy

Genes Transcripts Variants Individuals Diseases Screenings

View individual #00100621

| | |
|---------------|------------------------------------|
| Individual_ID | @VED |
| Reference | - |
| Remarks | - |
| Gender | F |
| Consanguinity | no |
| Country | Italy |
| Population | White |
| Age of death | - |
| VIP | 0 |
| Data_av | - |
| Treatment | Surgery of cranial posterior fossa |
| Panel size | 3 |
| Diseases | CM-1 |
| Owner name | Patrizia De Marco |

Phenotypes

malformation, Chiari, type I (CM-1) (CM-1) Add phenotype for this disease

| Phenotype ID | Phenotype details | Inheritance |
|--------------|-------------------|------------------------------|
| 0000078872 | - | Familial, autosomal dominant |

Screenings

| Screening ID | Template | Technique | Tissue | Genes screened |
|--------------|----------|-----------|--------|-----------------------|
| 0000101037 | DNA | SEQ-NG-I | blood | DDK1, FBN3, ITGA10, M |

Variants

4 entries on 1 page. Showing entries 1 - 4.
100 per page Legend

| Chr | Allele | DNA change (genomic) (hg19) | Published as |
|-----|----------------------|-----------------------------|---------------------|
| 1 | Paternal (confirmed) | g.145534176C>G | hg38 g.145900900G>C |
| 2 | Paternal (confirmed) | g.20205769C>A | g.11687G>T |
| 10 | Paternal (confirmed) | g.54074315G>A | hg38 g.52314555G>A |
| 19 | Paternal (confirmed) | g.8212222C>T | - |

4 in 1: Individual

[Genes](#) [Transcripts](#) [Variants](#) [Individuals](#) [Diseases](#) [Screenings](#) [Submit](#)

Individual #00054908

[Variants](#) [Individuals](#) [Diseases](#) [Screenings](#) [Submit](#)

| | |
|----------------------|--|
| Individual_ID | - |
| Reference | Journal: O'Rawe 2015 |
| Remarks | 2-generation family, 3 affected brothers, unaffected heterozygous carrier mother |
| Gender | M |
| Consanguinity | - |
| Country | Colombia |
| Population | - |
| Age/Death | >9y (later than 9 years) |
| VIP | 0 |
| Data_av | - |
| Treatment | - |
| Panel size | 3 |
| Diseases | ID |
| Owner name | Johan den Dunnen |

4 in 1: Phenotype

Phenotype #0000041575

| | |
|---------------------------|--|
| Individual ID | 00054908 |
| Associated disease | ID |
| Diagnosis/Initial | intellectual disability |
| Diagnosis/Definite | MRXS-33 |
| Inheritance | Familial, X-linked recessive |
| Age/Examination | 09y (9 years) |
| Birth_Details | 36w, caesarian section (HP:0011410), weight 4480 (1.85), height 52 (0.48), OFC 36.5 (1.02) |
| Age/Diagnosis | - |
| Age/Onset | - |
| Phenotype/Onset | - |
| Phenotype details | seizures (4 hours after birth), lactic acidosis.; postnatal growth retardation (HP:0008897); delayed gross motor development (HP:0002194); delayed speech and language development (HP:0000750); oral-pharyngeal dysphagia (HP:0200136); prominent supraorbital ridges (HP:0000336); downslanted palpebral fissures (HP:0000494); prominent forehead (HP:0011220); sagging cheeks; long philtrum (HP:0000343); low-set ears (HP:0000369); protruding ear (HP:0000411); thickened helices (large earlobe HP:0009748); long face (HP:0000276); high arched palate (high palate HP:0000218); thin upper lip (thin upper lip vermilion HP:0000219); pointed chin (HP:0000307); broad upturned nose (anteverted nares HP:0000463); hypertelorism (HP:0000316); sacral dimple (HP:0000960); hirsutism (HP:0001007); frequent dermatitis & eczema (eczema HP:0000964); toenail dysplasia (HP:0100797); hearing impairment (HP:0000365); chronic otitis media (HP:0000389); strabismus (HP:0000486); constipation (HP:0002019); gastroesophageal reflux (HP:0002020); microcephaly (HP:0000252); cerebellar atrophy (low cerebral white matter volume); hypoplasia of the corpus callosum (HP:0002079); seizures (HP:0001250); generalized hypotonia (HP:0001290); non-ambulatory; sleep-wake cycle disturbance (HP:0006979); osteopenia (HP:0000938); unusual gluteal crease with sacral caudal remnant/sacral dimple (abnormal sacral segmentatino, HP:0008468), prominent protruding coccyx (HP:0008472); distal joint hypermobility (HP:0001382); kyphosis (HP:0002808); scoliosis (HP:0002650); short neck (HP:0000470); hydronephrosis; autistic behaviors (HP:0000729); intellectual disability (HP:0001249); not present -HP:0000490, -HP:0000496, -HP:0000579, -HP:0000739, -HP:0001057, -HP:0001251, -HP:0001257, -HP:0001264, -HP:0001511, -HP:0002119, -HP:0002141, -HP:0007018, -HP:0007375 |
| Intellectual_dis | - |
| Speech | - |
| Development | - |
| Owner name | Johan den Dunnen |

Variants

Individuals

Diseases

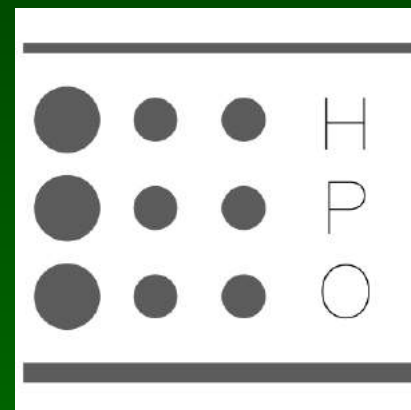
Screenings

HPO

HP:

-HP:

?HP:



links to files
- internet
- local

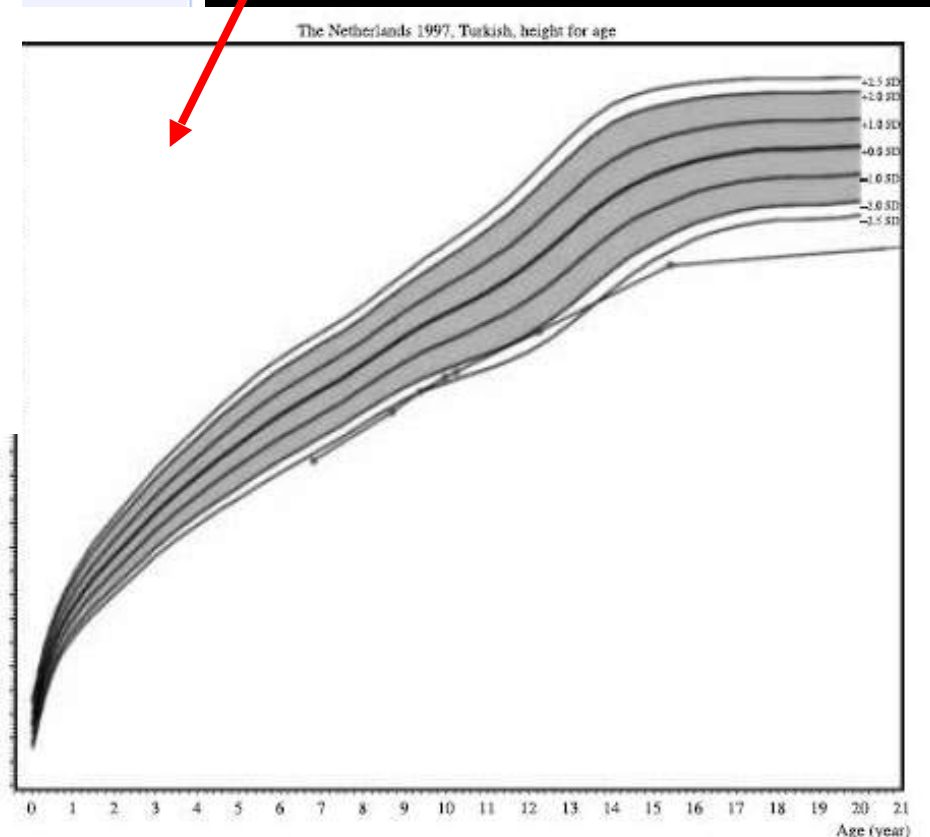
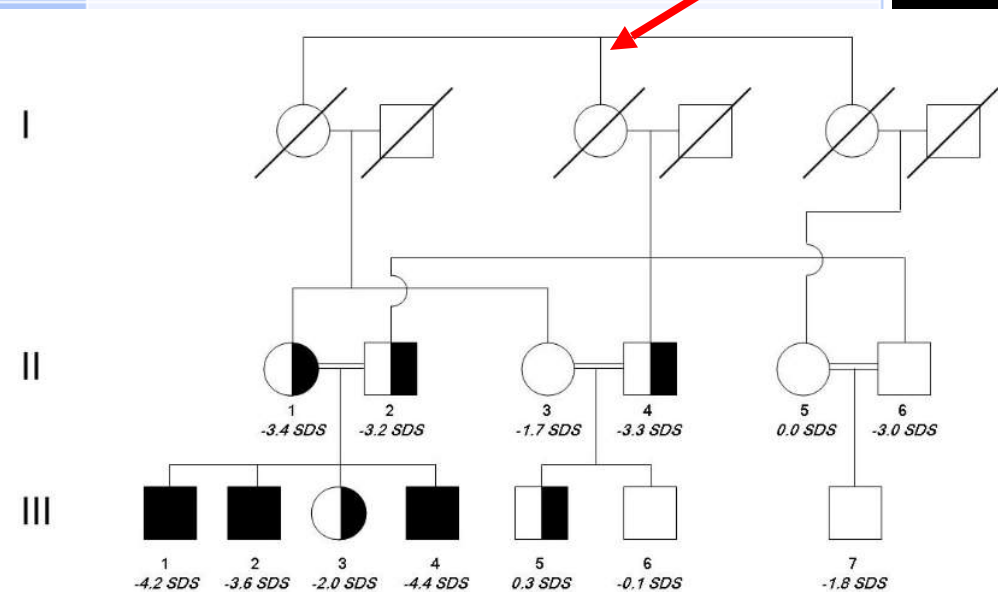
LOVD - Variant listings

Patient data (#0000070)

| | | |
|------------------|------------------------------------|---------|
| Patient ID | p.A | |
| Reference | Netherlands:Leiden | |
| Date_Of_Birth | - | |
| Gender | F | |
| Origin/Geograph | Father/Birth | - |
| Origin/Ethnic | Father/Adult | ?,184.7 |
| Residence/Count | Father/Head | - |
| Referring_doctor | Father/Puberty | unknown |
| Visit_1st/Date_a | Father/Clinical | no |
| Visit_1st/Comple | Mother/Birth | - |
| Neonatal/Gestat | Mother/Adult | ?,176.6 |

| | |
|-------------------|---|
| Patient ID | 18463107.III2 |
| Disease | - |
| Remarks | 3 siblings 3 generation family (III-2) , growth curve |
| Reference | Nederland:Leiden |
| # Reported | 1 |
| Geographic origin | - |
| Ethnic origin | Kurdish |
| Date Of Birth | 1985-12-28 |

| | |
|------------------|--------------------|
| Length/Curve | Skeletal |
| Length/SitStand | Protein |
| Length/SitStandF | Protein |
| Weight_BMI | Protein |
| Weight_BMIRef | Protein |
| Head | Protein/GH_stim2 |
| HeadRef | Protein/IGF_gen1 |
| Dysmorphism/Fa | Protein/IGF_gen2 |
| Dysmorphism/Ot | Protein/IGF_gen3 |
| Neuro | Treatment_GH |
| Syndrome | Treatment_IGF1 |
| Radiology | Carbohydrate_metab |
| Skeletal | Carbohydrate_OGTT |
| Bone/BMDyoung | Bone/BMDyoung |
| Bone/BMDadult | Bone/BMDadult |
| Remarks | |



W.A. Ester et al, table 1 shows the and after GH therapy.
Patient A also had delayed dentition and hypocanthal folds.

4 in 1: Screening

Genes

Transcripts

Variants

Individuals

Diseases

Screenings

Submit

Documentation

Screening #0000054861

| | |
|-----------------|------------------|
| Individual ID | 00054908 |
| Template | DNA |
| Technique | SEQ;SEQ-NG |
| Tissue | - |
| Remarks | WES |
| Variants found? | 1 |
| Owner name | Johan den Dunnen |

Genes screened

| Symbol | Gene | Chr | Band | Transcript |
|--------|--|-----|-------|------------|
| TAF1 | TAF1 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 250kDa | X | q13.1 | |

Variants found

1 entry on 1 page. Showing entry 1.

100 per page Legend

| Chr | Allele | DNA change (genomic) (hg19) | DNA change (hg38) | Published as |
|-----|----------------------|-----------------------------|-------------------|--------------|
| X | Maternal (confirmed) | g.70602671C>T | - | - |

100 per page Legend

4 in 1: Variants

| | | | | | | | |
|-------|-------------|-----------------|-------------|----------|------------|--------|---------------|
| Genes | Transcripts | Variants | Individuals | Diseases | Screenings | Submit | Documentation |
|-------|-------------|-----------------|-------------|----------|------------|--------|---------------|

Genomic variant #0000084884

| | |
|--|--|
| Individual ID | 00054908 |
| Chromosome | X |
| Allele | Maternal (confirmed) |
| Affects function (as reported) | Affects function |
| Affects function (by curator) | Not classified |
| DNA change (genomic) (Relative to hg19 / GRCh37) | g.70602671C>T |
| DNA change (hg38) | - |
| Published as | - |
| ISCN | - |
| DB-ID | TAF1_000024 See all 4 reported entries |
| Variant remarks | - |
| Reference | Journal: O'Rawe 2015 |
| ClinVar ID | - |
| dbSNP ID | - |
| Germline/De novo/Somatic | Germline |
| Segregation | yes |
| Frequency | - |
| Re-site | - |
| VIP | 0 |
| Methylation | - |
| Average frequency (large NGS studies) | Variant not found in online data sets |
| Owner | Johan den Dunnen |

| | | | | |
|-----------------|-------------|----------|------------|---|
| Variants | Individuals | Diseases | Screenings | S |
|-----------------|-------------|----------|------------|---|

| | |
|--------------------------------|-----------------------------|
| Gene | TAF1 |
| Transcript ID | NM_004606.3 |
| Affects function (as reported) | Affects function |
| Affects function (by curator) | Not classified |
| Exon | 12 |
| DNA change (cDNA) | c.1786C>T |
| Class. | - |
| RNA change | r.(?) |
| Protein | p.(Pro596Ser) |

1 individual / many variants

Curators: [Andrea Gaedigk](#) and [Lisa Kalman](#)

[Genes](#) [Transcripts](#) [Variants](#) [Individuals](#) [Diseases](#) [Screening](#)

Individual #00074429

| | |
|---------------|--|
| Individual_ID | - |
| Reference | PubMed: Buermans 2017 , Journal: Buermans 2017 |
| Remarks | - |
| Gender | - |
| Consanguinity | no |
| Country | Netherlands |
| Population | - |
| Age/Death | - |
| VIP | 0 |
| Data_av | - |
| Treatment | - |
| Panel size | 1 |
| Diseases | DMB-i |
| Owner name | Henk Buermans |

23 entries on 1 page. Showing entries 1 - 23.

| Chr | Allele | DNA change (genomic) (hg19) | DNA change (hg38) |
|-----|-------------------|-----------------------------|-----------------------------|
| 22 | Parent #2 | g.42522071C= | g.42126069A>C |
| 22 | Parent #2 | g.42522071C= | g.42126069A>C |
| 22 | Parent #2 | g.42522613C>G | g.42126611C>G |
| 22 | Parent #2 | g.42523003G>A | g.42127001G>A |
| 22 | Parent #2 | g.42523209C>T | g.42127207C>T |
| 22 | Parent #2 | g.42523409G= | g.42127407T>G |
| 22 | Parent #2 | g.42523943A= | g.42127941G>A |
| 22 | Parent #2 | g.42525132G= | g.42129130C>G |
| 22 | Parent #1 | g.42525625C>T | g.42129623C>T |
| 22 | Parent #2 | g.42525772G>A | g.42129770G>A |
| 22 | Both (homozygous) | g.42525952C= | g.42129950A>C |
| 22 | Parent #2 | g.42526484A= | g.42130482C>A |
| 22 | Parent #2 | g.42526549C= | g.42130547T>C |
| 22 | Parent #2 | g.42526561_42526562= | g.[42130559T>G;42130560C>G] |
| 22 | Parent #2 | g.42526567G= | g.42130565A>G |
| 22 | Parent #2 | g.42526571C= | g.42130569G>C |
| 22 | Parent #2 | g.42526573T= | g.42130571G>T |
| 22 | Parent #2 | g.42526580G= | g.42130578C>G |
| 22 | Parent #2 | g.42527533G= | g.42131531G>A |
| 22 | Parent #1 | g.42527887delT | g.42131885delT |
| 22 | Parent #2 | g.42528028C= | g.42132026T>C |
| 22 | Parent #1 | g.42528030T[21] | g.42132049delT |
| 22 | Parent #2 | g.42528030T[25] | g.42132047_42132049dup |

Databases and RNA

RNA ?

NCBI Resources How To

ClinVar ClinVar Advanced

Home About Data use and maintenance Using the website

NM_033337.2(CAV3):c.158G>A (p.Ser53Asn)
NM_033337.2(CAV3):c.158G>A (p.Ser53Asn)

Variant type: single nucleotide variant

Cytogenetic location: 3p25

Genomic location: Chr3:8745569 (on Assembly GRCh38)
Chr3:8787255 (on Assembly GRCh37)

Protein change: S53N

HGVS: NG_008797.2:g.16760G>A
NM_033337.2:c.158G>A
NC_000003.12:g.8745569G>A
NC_000003.11:g.8787255G>A
[...more](#)

Links: Leiden Muscular Dystrophy (CAV3): [CAV3_00054](#)
dbSNP: [199476326](#)

NCBI 1000 Genomes Browser: [rs199476326](#)

Molecular consequence: NM_033337.2:c.158G>A: missense variant [Sequence Ontology SO:0001583]

Functional consequence: unknown functional consequence

HGV Database

managed by Human Genome Variation powered by figshare

The HGV database is a fully searchable online database of genome variations published in peer-reviewed Data Reports in **Human Genome Variation** (ISSN 2054-345X). You can search and filter by different variables, including specific disease, gene, population or region.

| | |
|--------------------------|--|
| Gene name | KRT5 |
| Gene/Locus MIM number | 148040 |
| Mutation type | missense |
| Disease / Phenotype | Epidermolysis Bullosa Simplex Koebner type |
| Phenotype MIM number | 131900 |
| GenBank accession number | NM_000424.3 |
| Mutation (HGVS format) | c.T974A |
| Protein alteration | p.L325H |
| Codon / Base change | CTC-CAC |
| Chromosome | 12q13.13 |

ClinVar DMD

| | | | | | |
|--------------------------|--|---------------------|---------------------------|---|-------------------------------------|
| <input type="checkbox"/> | NM_004006.2(DMD):c.3637A>G (p.Lys1213Glu) | DMD | not specified | Uncertain significance (Feb 1, 2016) | criteria provided, single submitter |
| 825. | GRCh37: ChrX:32466722 GRCh38: ChrX:32448605 | | | | |
| <input type="checkbox"/> | NM_004006.2(DMD):c.3631G>T (p.Glu1211Ter) | DMD | Becker muscular dystrophy | Pathogenic (Nov 1, 1997) | no assertion criteria provided |
| 826. | GRCh37: ChrX:32466728 GRCh38: ChrX:32448611 | | | | |
| <input type="checkbox"/> | NM_004006.2(DMD):c.3604-12T>A | DMD | not specified | Likely benign (Aug 12, 2016) | |
| 827. | GRCh37: ChrX:32466767 GRCh38: ChrX:32448650 | | | | |
| <input type="checkbox"/> | NM_004006.2(DMD):c.3604-14T>C | DMD | not specified | Likely benign (Nov 16, 2016) | |
| 828. | GRCh37: ChrX:32466769 GRCh38: ChrX:32448652 | | | | |
| <input type="checkbox"/> | NM_004006.2(DMD):c.3603+15dupA | DMD | not specified | Likely benign (Apr 28, 2015) | |
| 829. | GRCh37: ChrX:32472764 GRCh38: ChrX:32454647 | | | | |

NCBI Resources How To

ClinVar ClinVar Search ClinVar for gene symbols, HGVS expression
Advanced

Home About Access Help Submit Statistics FTP

NM_004006.2(DMD):c.3631G>T (p.Glu1211Ter)

Variation ID: 11280
Review status: (0/4) no assertion criteria provided

Interpretation Go to: ^

Clinical significance: [Pathogenic](#)
Last evaluated: Nov 1, 1997
Number of submission(s): 1
Condition(s): [Becker muscular dystrophy](#) [MedGen - Orphanet - OMIM]
[See supporting ClinVar records](#)

Allele(s) Go to: ^

NM_004006.2(DMD):c.3631G>T (p.Glu1211Ter)

LOVD DMD

| | | | | |
|----|---------------------------------|---|---|--|
| 27 | c.3628_3665del | - | r.3628_3665del | p.Lys1210* |
| 27 | c.3630delA | - | r.(?) | p.(Glu1211Lysfs*4) |
| 27 | c.3631G>T | 3839G>T | r.[3631g>u, 3604_3786del, 3604_4071del] | p.[Glu1211*; Arg1202_1262del; Arg1202_1357del] |
| 27 | c.3679C>T | - | r.(?) | p.(Gln1227*) |
| 27 | c.3697delC | Patient data (#0006974) Phenotype muscular dystrophy, Becker (BMD) Phenotype additional - Reference Japan:Kobe Remarks - Geographic origin Japan Ethnic origin - Gender M Inheritance unknown Consanguinity - Fam_Pat - # reported 1 CK level - Protein data - Submitter Masafumi Matsuo | | p.(Gln1233Lysfs*4) |
| 27 | c.3700G>T | | | p.(Glu1234*) |
| 27 | c.3705C>T (Reported 2 times) | | | p.(=) |

| Variant data | |
|--------------------------------|--|
| Allele | Parent #1 |
| Reported pathogenicity | Pathogenic |
| Concluded pathogenicity | Unknown |
| Exon | 27 |
| DNA change | c.3631G>T (View in UCSC Genome Browser , Ensembl) |
| Var_pub_as | 3839G>T |
| RNA change | r.[3631g>u, 3604_3786del, 3604_4071del] |
| Protein change | p.[Glu1211*; Arg1202_1262del; Arg1202_1357del] |
| DB-ID | DMD_00074 |
| Variant remarks | 10% diff.splice |
| Genet_ori | germline (inherited) |
| Segregation | - |
| Reference | Shiga, Takeshima 2010, (OMIM 0074) |
| Template | DNA, RNA |
| Technique | RT-PCR, SEQ, SSCA |
| Frequency | - |
| RE-site | - |

| | | | | | |
|------|--|-----|---------------------------|--------------------------------------|-------------------------------------|
| 825. | NM_004006.2(DMD):c.3637A>G (p.Lys1213Glu) GRCh37: ChrX:32466722 GRCh38: ChrX:32448605 | DMD | not specified | Uncertain significance (Feb 1, 2016) | criteria provided, single submitter |
| 826. | NM_004006.2(DMD):c.3631G>T (p.Glu1211Ter) GRCh37: ChrX:32466728 GRCh38: ChrX:32448611 | DMD | Becker muscular dystrophy | Pathogenic (Nov 1, 1997) | no assertion criteria provided |
| 827. | NM_004006.2(DMD):c.3604-12T>A GRCh37: ChrX:32466767 GRCh38: ChrX:32448650 | DMD | not specified | Likely benign (Aug 12, 2016) | criteria provided, single submitter |
| 828. | NM_004006.2(DMD):c.3604-14T>C GRCh37: ChrX:32466769 GRCh38: ChrX:32448652 | DMD | not specified | Likely benign (Nov 16, 2016) | criteria provided, single submitter |
| 829. | NM_004006.2(DMD):c.3603+15dupA GRCh37: ChrX:32472764 GRCh38: ChrX:32454647 | DMD | not specified | Likely benign (Apr 28, 2015) | criteria provided, single submitter |

POMGNT1 database

| | | | | | | |
|------|----|------------|---|--------------|------------------|---------------|
| +/. | 7 | c.594C>G | - | r.(?) | p.(Ser198Arg) | g.46660574G>C |
| +/. | 7 | c.630G>T | - | r.(?) | p.(Trp210Cys) | g.46660538C>A |
| +/? | 7 | c.636C>T | - | r.spl | p.? | g.46660532G>A |
| +/. | 7 | c.636C>T | - | r.535_652del | p.Asp179Valfs*23 | g.46660532G>A |
| +/. | 7 | c.636C>T | - | r.(?) | p.(=) | g.46660532G>A |
| +/. | 7 | c.636C>T | - | r.535_652del | p.Asp179Valfs*23 | g.46660532G>A |
| +/. | 7 | c.636C>T | - | r.(=) | p.(=) | g.46660532G>A |
| +/. | 7 | c.643C>T | - | r.535_652del | p.Asp179Valfs*23 | g.46660525G>A |
| +/? | 7 | c.643C>T | - | r.535_652del | p.Asp179Valfs*23 | g.46660525G>A |
| +?/? | 7i | c.652+1G>A | - | r.spl | p.? | g.46660515C>T |
| +/. | 7i | c.652+1G>A | - | r.spl? | p.? | g.46660515C>T |

dbSNP POMGNT1 variant

NCBI dbSNP Short Genetic Variations

Re-designed RefSNP Report page! NEW

Search small variations in dbSNP or large structural variations in dbVar

Reference SNP (refSNP) Cluster Report: rs19057175

Organism: human (Homo sapiens)

Molecule Type: Genomic

Created/Updated in build: 135/150

Map to Genome Build: hg19/hg19.1

Validation Status:

Allele

Variation Class: SNV

RefSNP Alleles: A/G (FWD)

Allele Origin: Ancestral Allele: G

Clinical Significance: With Pathogenic allele (ClinVar)

MAF/MinnorAlleleCounts: A=0.000212 (EAC) A=0.000211 (1000 Genomes) A=0.000311 (TOPMED)

Integrated Maps (click on 'Chr Pos' to see variant in the new NCBI variation viewer)

Assembly: GRCh38.p7

Annotation Release: 108

Chr: 1

Chr Pos: 81,320,713

Contig: NT_813207.2

Contig Pos: 81320713

SNP No: Chr: 1

Contig: chr1

Contig Pos: 81,320,713




Ref: G

Alt: A



Map Method: RefSeq

No effect at protein level?!

In vitro record

| <div>   <div> Shared database BRCA1 (breast cancer 1, early onset) </div> </div> <div> LOVD is supported by:  LOVD v.3.0 Build 21 [Curr Register as st </div> | | | | | | |
|--|-------|----------------------------------|------------|-----------------|--------------------------|---|
| Effect | Exon | DNA change (cDNA) | RNA change | Protein | Germline/De novo/Somatic | Functional Analysis/Technique |
| +/. | 1i_3i | c.(-20+1_-19-1)_(134+1_135-1)del | r.spl | p.Met1_Cys47del | In vitro (cloned) | mRNA analysis (RT-PCR) |
| -?/. | 1i | c.-19-22_-19-21dup | r.= | ? | In vitro (cloned) | Splicing reporter minigene |
| -?/. | 1i | c.-19-10T>C | r.= | ? | In vitro (cloned) | Splicing reporter minigene |
| -/. | 1i | c.-19-10T>C | r.= | ? | In vitro (cloned) | mRNA analysis (RT-PCR) |
| ?/. | 2 | c.-3G>C | ? | ? | In vitro (cloned) | ? |
| -/. | 2 | c.19C>T | - | p.Arg7Cys | In vitro (cloned) | E3 Ub-ligase activity assay BRCA1/RING-BARD1 |
| -/. | 2 | c.32T>C | - | p.Val11Ala | In vitro (cloned) | E3 Ub-ligase activity assay BRCA1/RING-BARD1 |
| ?/. | 2 | c.32T>C | ? | p.Val11Ala | In vitro (cloned) | ? |
| ?/. | 2 | c.32T>C | - | p.Val11Ala | In vitro (cloned) | peptide binding ability BRCA1/RING-BARD1 |
| -/. | 2 | c.43A>C | - | p.Ile15Leu | In vitro (cloned) | evolutionary conservation analysis |
| -/. | 2 | c.43A>C | - | p.Ile15Leu | In vitro (cloned) | E3 Ub-ligase activity assay BRCA1/RING-BARD1 |
| +/. | 2 | c.44T>C | - | p.Ile15Thr | In vitro (cloned) | evolutionary conservation analysis |
| ?/. | 2 | c.44T>C | - | p.Ile15Thr | In vitro (cloned) | E3 Ub-ligase activity assay BRCA1/RING-BARD1 |
| -/. | 2 | c.44T>C | - | p.Ile15Thr | In vitro (cloned) | peptide binding ability BRCA1/RING-BARD1 |

BRCA1 variants tested in in vitro functional assays

| Installation (early onset)  | | LOVD is supported by:  | | LOVD v.3.0 Build 19a [Current LOVD 3.0] Register as submitter | |
|--|---|---|--|---|--|
| to encode protein | ENIGMA classification criteria | - | | SUMMARY record | |
| to encode protein | ENIGMA classification criteria | - | | SUMMARY record | |
| to encode protein | ENIGMA classification criteria | - | | SUMMARY record | |
| terior torial holds for | ENIGMA classification criteria, {ENIGMA:BRCA[1] [c.1001C%3ET]}, PubMed: Lindor 2012 | - | | SUMMARY record | |
| ss 1 based y = | | | | | |
| to encode al protein | ENIGMA classification criteria | - | | SUMMARY record | |
| to encode al protein | ENIGMA classification criteria | - | | SUMMARY record | |
| to encode al protein | ENIGMA classification criteria | - | | SUMMARY record | |
| to encode al protein | ENIGMA classification criteria | - | | SUMMARY record | |
| to encode al protein | ENIGMA classification criteria | - | | SUMMARY record | |

[illegible]

CLASSIFICATION record

View genomic variant #0000146002

| | |
|--|---------------------------------------|
| Chromosome | 1 |
| Allele | Parent #1 |
| Affects function (reported) | Effect unknown |
| Affects function (concluded) | Not classified |
| DNA change (genomic) (Relative to hg19 / GRCh37) | g.898757G>C |
| Published as | - |
| ISCN | - |
| DB-ID | KLHL17_000001 |
| Variant remarks | - |
| Reference | - |
| dbSNP ID | - |
| Germline/Somatic/De novo | CLASSIFICATION record |
| Segregation | - |
| Frequency | - |
| Re-site | - |
| VIP | 0 |
| Methylation | - |
| Average frequency (large NGS studies) | Variant not found in online data sets |
| Owner | VKGL-NL_Leiden |

VKGL initiative

*no data on
Individual
(disease)*

Germline/Somatic/De novo
CLASSIFICATION



| Owner |
|-------------------|
| VKGL |
| VKGL-NL_AMC |
| VKGL-NL_Groningen |
| VKGL-NL_Rotterdam |
| VKGL-NL_Utrecht |
| VKGL-NL_AMC |
| VKGL-NL_Utrecht |
| VKGL-NL_Groningen |
| VKGL-NL_Leiden |

Variant on transcripts

| Gene | Transcript | Affects function | Exon | DNA change (cDNA) | Class. | RNA change | Protein |
|--------|-------------|------------------|------|-------------------|--------|------------|---------------|
| KLHL17 | NM_198317.2 | ?/. | 8 | c.1228G>C | - | r.(?) | p.(Asp410His) |

| Effect | Exon | DNA change (cDNA) | Owner |
|--------|------|-------------------|-------------------|
| -/. | 14 | c.1635A>G | VKGL-NL_Utrecht |
| -/. | 14 | c.1635A>G | VKGL-NL_AMC |
| -/. | 14 | c.1635A>G | VKGL-NL_Groningen |

*Dutch clinical labs sharing all
variants and their classification*



VKGL initiative

LOVD³ Shared database
Leiden Open Variation Database
DMD (dystrophin)

LOVD is supported by: LOVD v.3.0 Build 21 [Current LOVD status]
Register as submitter | Log out

48 entries on 1 page. Showing entries 1 - 48.

100 per page Legend

| Effect | Reported | Exon | DNA change (cDNA) | Class. | RNA change | Protein | DNA change (genomic) (hg38) | DNA change (hg38) |
|-----------|----------|-------|-------------------|-----------------------|--------------|---------------|-----------------------------|-------------------|
| ? | | 2 6 | c.434G>A | VUS | r.(?) | p.(Arg145Gln) | g.32834681C>T | g.32816564C>T |
| -/-, -?/. | | 3 8i | c.832-18C>G | benign, likely benign | r.(?) | p.(=) | g.32716133G>C | g.32698016G>C |
| -/-, -?/. | | 3 8i | c.832-17C>A | benign, likely benign | r.(?) | p.(=) | g.32716132G>T | g.32698015G>T |
| -?/., ?/. | | 2 9 | c.842G>C | likely benign, VUS | r.(?) | p.(Ser281Thr) | g.32716105C>G | g.32697988C>G |
| -?/. | | 2 10 | c.1095A>C | likely benign | r.(?) | p.(Gln365His) | g.32663135T>G | g.32645018T>G |
| -/- | | 3 14 | c.1635A>G | benign | r.(?) | p.(=) | g.32591931T>C | g.32573814T>C |
| ? | | 2 16 | c.1945C>T | VUS | r.(?) | p.(Arg649Trp) | g.32583866G>A | g.32565749G>A |
| -/- | | 2 17 | c.2143A>T | benign | r.(?) | p.(Thr715Ser) | g.32563301T>A | g.32545184T>A |
| -/- | | 2 17i | c.2168+13T>C | benign | r.(?) | p.(=) | g.32563263A>G | g.32545146A>G |
| -?/., -/- | | 6 20 | c.2391T>G | likely benign, benign | r.(?) | p.(Asn797Lys) | g.32509625A>C | g.32491508A>C |
| -?/. | | 2 20 | c.2490C>T | likely benign | r.(?) | p.(=) | g.32509526G>A | g.32491508A>C |
| -/-, -?/. | | 3 20i | c.2623-11C>G | benign, likely benign | r.(?), r.(=) | p.(=) | g.32503227G>C | g.32491508A>C |

| Effect | Exon | DNA change (cDNA) | Class. | RNA change | Protein |
|--------|------|-------------------|---------------|------------|---------|
| -?/. | 26i | c.3603+15dup | likely benign | r.(?) | p.(=) |
| -/- | 26i | c.3603+15dup | benign | r.(?) | p.(=) |
| -/- | 26i | c.3603+15dup | benign | r.(?) | p.(=) |
| -/- | 26i | c.3603+15dup | benign | r.(?) | p.(=) |
| -/- | 26i | c.3603+15dup | benign | r.(?) | p.(=) |

| DNA change (hg38) | Published as |
|-------------------|---------------------|
| g.32454647dup | 3603+15_3603+16insA |
| g.32454647dup | 3234+15_3234+16insA |
| g.32454647dup | 3234+14_3234+15insA |
| g.32454647dup | 3234+13_3234+14insA |
| g.32454647dup | 3603+2_3603+3insA |



VKGL initiative

LOVD³ Leiden Open Variation Database
Shared database DMD (dystrophin)
Curator: **Johan den Dunnen**

Genes Transcripts **Variants** Individuals Diseases

All genomic variants

28122 entries on 282 pages. Showing entries 1 - 100.

100 per page Legend << First < Prev 1 2 3 4 5 6

| Variant ID | Effect | Chr | DNA change (genomic) (hg19) |
|------------|--------|-----|-----------------------------|
| 0000280965 | -?/. | 1 | g.1961469C>A |
| 0000284534 | -?/. | 1 | g.1961469C>A |
| 0000299488 | -?/. | 1 | g.2160390C>G |
| 0000302119 | -?/. | 1 | g.2160390C>G |

public: 28,122

LOVD³ Leiden Open Variation Database
Shared database DMD (dystrophin)

Genes Transcripts **Variants** Individuals Diseases

All genomic variants

105780 entries on 1058 pages. Showing entries 1 - 100.

100 per page Legend << First < Prev 1 2 3 4 5 6 7

| Variant ID | Effect | Chr | DNA change (genomic) (hg19) |
|------------|--------|-----|-----------------------------|
| 0000245460 | -?/. | 1 | g.69270A>G |
| 0000343193 | ?/. | 1 | g.879375C>T |
| 0000304227 | -?/. | 1 | g.881627G>A |
| 0000320401 | ?/. | 1 | g.898757G>C |

total: 105,780

*Dutch clinical labs sharing all variants
and their **consensus** classification*

1139 variants no consensus
29 variants opposite classification

Minimal reporting

LOVD Leiden Muscular Dystrophy pages
Protein O-Mannosyltransferase 1 (POMT1)

Home Variants Submitters Submit Documentation

View unique variants Search unique variants View all contents Full database search Variant listing based on patient origin Database statistics Switch gene

LOVD - Variant listings

Unhide all columns

291 public entries
100 entries per page

| Exon | DNA change | Disease | Reference | Geographic origin |
|------|--|-----------|--|-------------------|
| 00 | c.? | LIS-II | JdD | (FR) |
| 02 | + c.1790_1791del | | | |
| 02 | c.-6T>G + c.752G>A, c.942C>T, c.2110dupG, c.*41C>T | WWS | JdD | IT |
| 02 | c.78G>A + c.1148+16G>A, c.2234G>A | MDC | United States:Marshfield, WI | - |
| 02 | c.85A>C + c.1864C>T | MDC | United States:Iowa City | US |
| 02 | c.122-5dupT | - | JdD | - |
| 02 | c.122+5G>A + c.2115G>A | LIS-II | JdD | (FR) |
| 02 | c.122+417GT(15_23) | - | JdD | - |
| 03 | c.123-5dupT + 18 others | FCMD, MEB | Portugal:Porto | PT |
| 03 | c.129C>T | - | JdD | - |
| 03 | c.145_146ins290145_160dup | WWS | JdD | FR |

variant + contact details

How improve sharing?

- ...make variant submission obligatory

for publication

for approved grants

for clinical lab

*as part of QC
to get accreditation*

...to get a sample sequenced



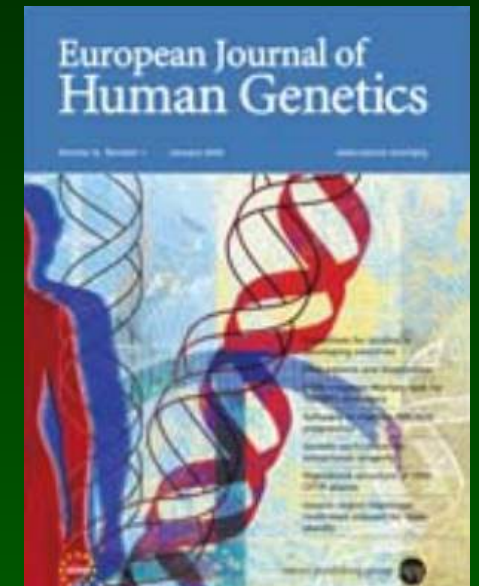
+ QC standards for LSDBs

Journals

Human Mutation
Variation, Informatics, and Disease



- **Human Mutation**
first to demand using HGVS nomenclature
first to demand database submission
before accepting a paper for publication
- **European Journal of Human Genetics**
demanding HGVS nomenclature & DB submission
...and checking every paper !!



collaboration with



Adopt a gene !

CV

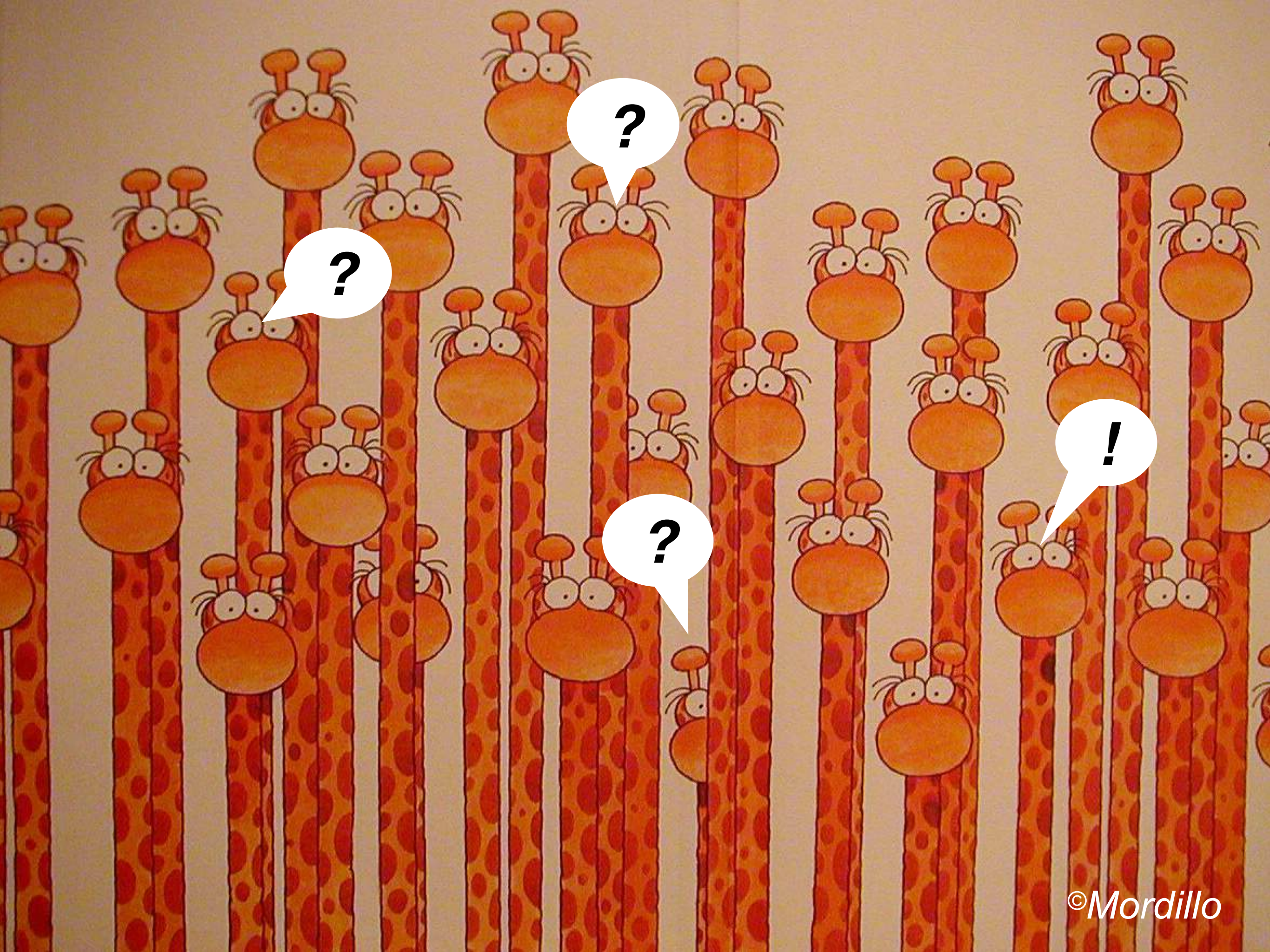
Curator for the ... gene variant database.



many orphan genes

become a
foster parent
database curator





?

?

?

!