Security

To protect all data, LOVD has various built-in security measures. LOVD implements techniques to prevent brute force attacks, SQL injection, XSS attacks and local and remote file inclusion. When desired, access of authorized users can be limited to specific IP addresses making access to LOVD, even with the right login/password combination, impossible from other computers or from outside your institution.

Brute force attacks are prevented by locking submitter, curator and manager accounts after three failed login attempts. In addition, LOVD has a system log allowing the tracking of attempts to break security by authorized as well as external users.

To protect the data consistency in the MySQL database, the InnoDB table type has been chosen as the default table type.

Did you know:

- · We offer everybody the possibility to set up, with or without our help, their databases on our LOVD server free of charge. For more information see www.LOVD.nl.
- · LOVD was the first software package to receive the "recommended system" status from the Human Variome Project.
- · >95% of all gene variant databases world-wide are using LOVD, and LOVD has been cited in >1000 scientific papers.
- There are 90 LOVD installations publicly sharing gene variant information for all human genes, with information from more than 170,000 individuals, together harboring more than 2,100,000 unique variants submitted by over 2000 registered submitters.
- · Over 350 volunteer database curators quard individual gene variant databases.
- The LOVD databases hosted in Leiden have >10,000 unique visitors each month, viewing 350,000 pages.

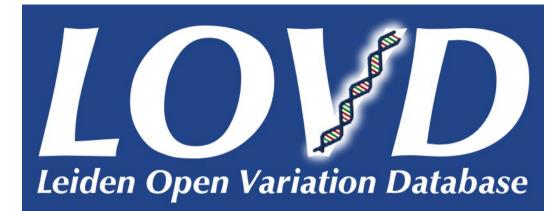
Some LOVD installations (also see www.lovd.nl):

- · Leiden Muscular Dystrophy pages (DMD, Sarcoglycans, LMNA, CAPN3, DYSF, ...)
- · http://www.dmd.nl/nmdb/
- · Osteogenesis Imperfecta (COL1A1, COL1A2, LEPRE1, ...)
- http://oi.gene.le.ac.uk/
- · InSiGHT Colon Cancer (MLH1, MSH6, MUTYH, ...)
- http://chromium.liacs.nl/LOVD2/colon_cancer/
- · X-linked Mental Retardation
- · http://grenada.lumc.nl/LOVD2/MR/
- · LOVD 3.0 shared installation with VIP-variants and VIP-phenotypes (22,000 genes)
- · http://databases.lovd.nl/shared/
- · Whole genome analysis (22,000 genes)
- · http://databases.lovd.nl/whole genome/

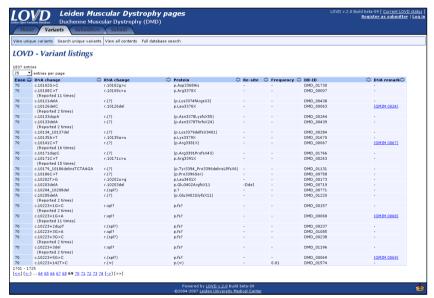
www.LOVD.nl







A flexible, free tool for collection, curation and display of individuals, phenotypes and DNA sequence variants



LSDB-in-a-Box

www.LOVD.nl

Leiden University Medical Center, Leiden, Netherlands Ing. Ivo F.A.C. Fokkema, Dr. Johan T. den Dunnen



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Main features

LOVD is an "LSDB-in-a-Box", i.e. all functionalities to establish, manage and display web-based gene specific DNA variant databases (LSDBs) are included.

LOVD allows users to link large numbers of DNA variants in one or more genes to an individual (multi-gene disorders or large scale next-generation sequencing). You can even use LOVD on your personal computer to browse through the variants in your own exome/genome.

The functional consequences of each variant can be set by the submitter and the curator separately, allowing easy separation of disease-associated from not associated variants. Detailed phenotype data can be stored on many different diseases, including longitudinal data. LOVD allows for many different ways to view and browse through the data, allowing users to take the path that they are most comfortable with.

LOVD includes powerful search functionalities on all data views. Searching of records can be performed per column and allows the use of boolean search terms (AND, OR and NOT). Curators can perform special "find and replace" actions on all data or copy or move data from one column to another in large sets of records at the same time.

LOVD has many possibilities to import new data through text files containing variant and individual data. Importing is independent of the order of the columns and optional columns can be left out. During import the data are checked for internal consistency. File formats supported include the VCF file and SeattleSeg annotation file formats.

Access levels

LOVD features six access levels, all with different rights.

The <u>Database Administrator</u> has full access to LOVD. There is only one account of this type and it is created during LOVD installation. The DB administrator has all rights.

An <u>LOVD Manager</u> has access to the LOVD Setup, with rights closely similar to the Database Administrator but a Manager cannot uninstall LOVD and is not allowed to create or edit other Manager accounts. The LOVD Manager creates gene databases (LSDBs), structures the data to be collected and displayed and manages the curators (per gene).

A <u>Curator</u> has access to specific genes, but no access to the LOVD Setup. The Curator has control over the variants, performs gene-specific configuration tasks (setting up gene custom columns), decides which data are public and curates incoming submissions.

A <u>Collaborator</u> receives full read-only access to specific genes. All non-public data will be visible to the Collaborator, but he has no rights to edit or remove this data.

Through registration, a <u>Submitter</u> creates an account which allows the submission of new variant and individual data. Depending on the LOVD system settings, submitters can edit and/or update previously submitted data. Other than this a Submitter has only access to the public part of the LOVD gene databases.

A website Visitor can view all the data that has been labeled to be public.

Flexibility

LOVD has many settings that can be configured by LOVD managers and curators, given ample possibilities to customize an LSDB as desired. The custom column feature includes functionality to, on a per gene basis, add new columns, specify their content and determine their collection (e.g. checkbox, drop-down menu, free text field). Custom columns are connected directly to the submission form and support explanation and examples to guide submitters. LOVD comes with a set of HGVS recommended preconfigured variant, variant screening, individual and phenotype columns, which can be added by curators and LOVD managers in a click.

Mutalyzer

LOVD integrates tightly with Mutalyzer allowing submitters and curators to check the correct description of variant data (according to HGVS standards) in relation to the reference sequence used and to predict the effect of the variant on RNA and protein level. Mutalyzer allows LOVD to map variants from genomic positions to positions on transcripts and vice-versa, allowing curators to easily store variants on multiple transcripts per gene.

Publish your work

By enabling the "Include in the global LOVD listing" setting, the database name and location will be shown on the central LOVD website, thereby getting immediate peer recognition. By being on this list, your database is included in the LOVD querying services allowing users to search LOVD installations world-wide for the presence of a certain variant. Your variants will be included in the LOVD track in the major genome browsers, significantly increasing visibility of your database.

LOVD can be used pre-publication to get into contact with colleagues that may have supporting or missing information. For this, both phenotype descriptions and/or gene variants can get a **VIP** status. **VIP-phenotypes** are those for which whole genome/exome studies were performed but for which insufficient evidence was gathered to prove causality with variants in a specific gene. **VIP-variants** are those remaining after stringent filtering that could not be linked to nor excluded as causative. Others studying VIP-phenotypes or identifying VIP-variants are invited to contact the submitter to collaborate.

Required software

LOVD is an "LSDB-in-a-Box" completely based on Open Source software. Besides LOVD all additional software required is common, freely available and usually already installed on the server of a hosting provider. Please note that some hosting providers may not always include a MySQL database, but obtaining all software for an LOVD installation on an own webserver is simple.

- Apache HTTP webserver (or other webserver, we encourage Apache 2.0 or up)
- PHP scripting language (version 5.3.0 and up)
- MySQL database (version 4.1.2 and up)

The software required to run LOVD works on Linux, Macintosh and Windows, amongst others.