Clinical genetics resources at NCBI: ClinVar and ISCA support evidence-based interpretation of human variation

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What is ClinVar?

- **Focus.** ClinVar is a database of relationships asserted between genetic variation and observed health status.
- **Supporting evidence**. Structured observations are recorded to facilitate aggregation, comparison, search, and re(evaluation). Includes: observations in affected and controls , peer reviewed publications, functional studies, and *in silico* predictions.
- **Attribution.** Sources are acknowledged, with gateways to publications and external databases.
- **Review status.** Confidence in any assertion is indicated as a range from a single source submission to practice guidelines.
- **Standards**. Terminology consistent with community standards (below)
- **Unrestricted Availability**. Data can be downloaded and integrated into external databases and local analysis pipelines.

Standards – a shared language for a shared need

Phenotype SNOMED CT®, HPO, MeSH	**Sequence Consequence** Sequence Ontology
Variation HGVS, RefSeqGene/LRG	**Clinical Interpretation** ACMG Guidelines
Review status Standardized scale: single submitter, expert panel, practice guideline	**Assay** - Standards from community for sequence validation, coverage/depth measures, quality scores

A community driven effort

ClinVar has been developed in close collaboration with the medical genetics community. Data fields, nomenclature, and evidence standards represent a synthesis of the current systems used by leading academic and commercial groups for the scoring of variant clinical significance.

ISCA: a demonstration of this model in practice

The International Standard Cytogenetic Array consortium includes over 50 labs. This effort combines the submission of observed variants and associated phenotypes to a central database at NCBI, where existing clinical interpretation can be evaluated using an evidence-based curation process to improve the standard of care in cytogenetic testing.

https://www.iscaconsortium.org/
http://www.ncbi.nlm.nih.gov/dbvar/studies/nstd37/
http://www.ncbi.nlm.nih.gov/gap

What datasets are loaded now?

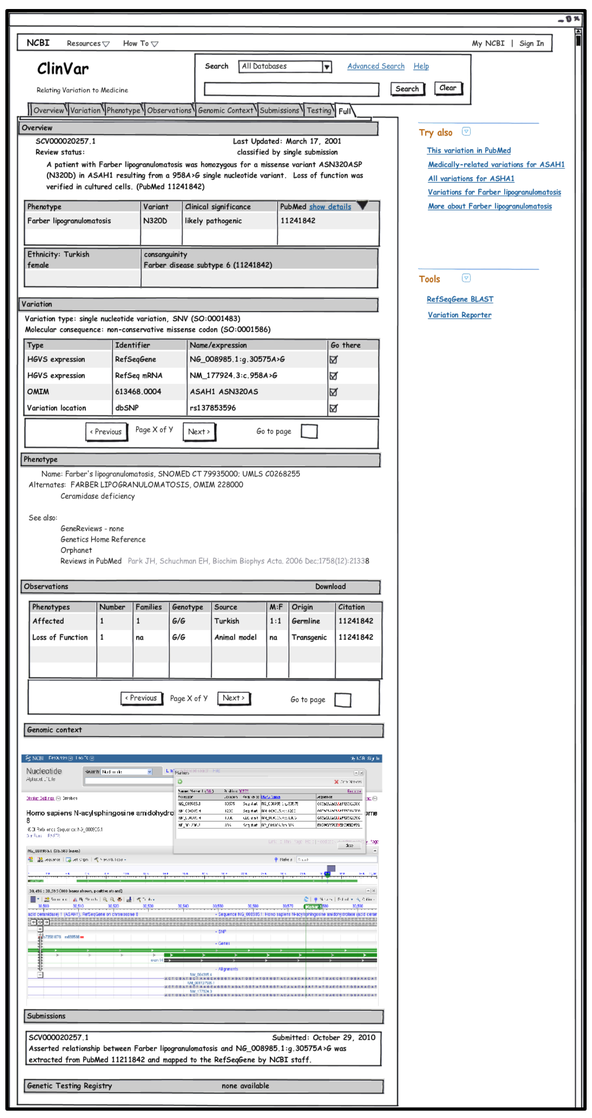
Currently about 20,000 variants have been loaded from multiple sources.

When will it be available?

ClinVar is in the final stages of being made completely public. Data managed in ClinVar are provided now via the Variation Reporter (www.ncbi.nlm.nih.gov/variation/tools/reporter) and Variation Viewer (http://www.ncbi.nlm.nih.gov/sites/varvu). Reports for ftp, an interactive web interface, and an api via e-utilities will be available early in 2012.

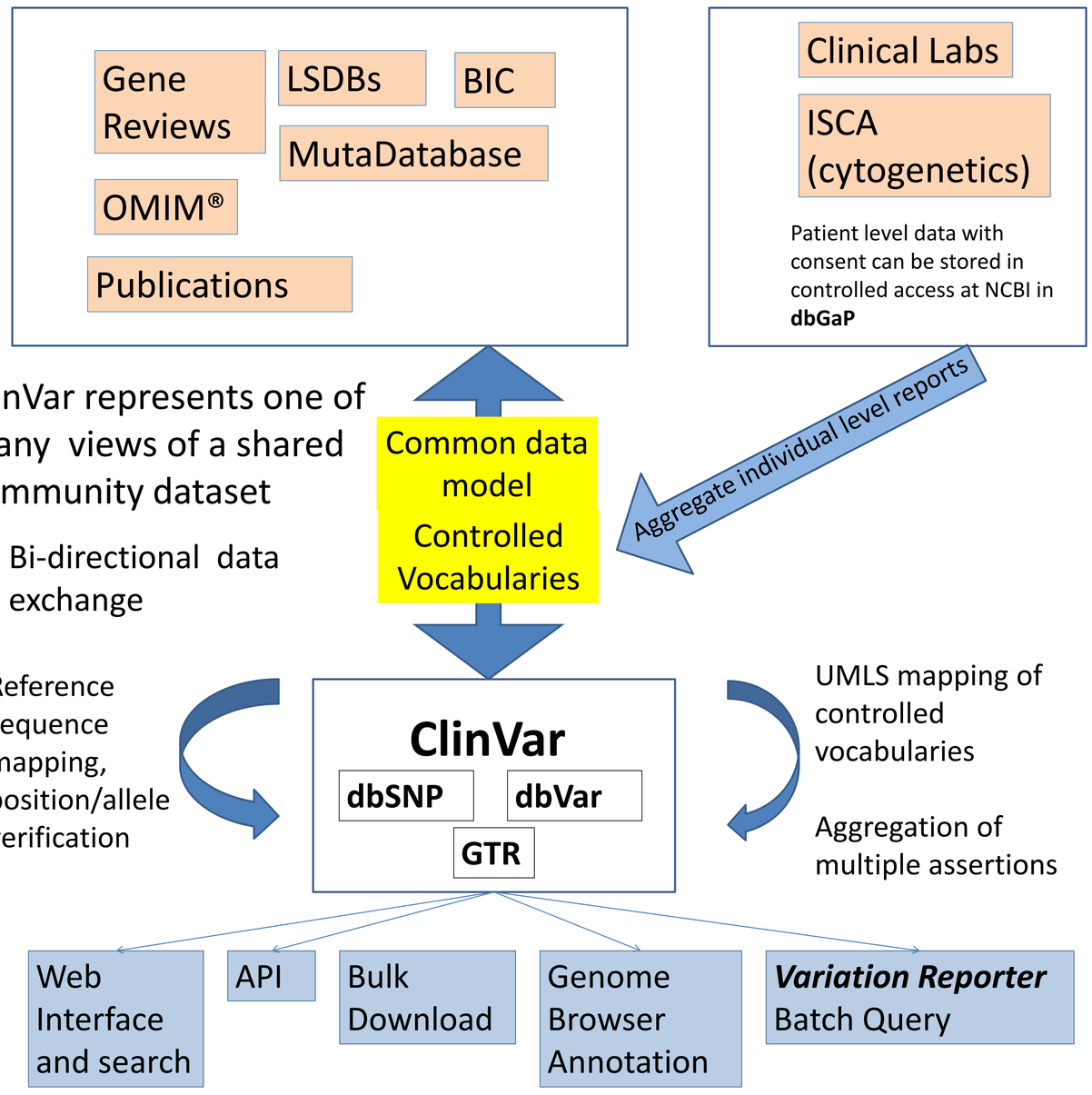
How do I learn more?

Detailed documentation including the data model, submission templates, and community discussion is available at: **http://www.ncbi.nlm.nih.gov/clinvar/**



Mockup of a full ClinVar record

The record is divided into sections:
Overview: description of the relationship between variation and phenotype
Variation: description of the variation, the consequence of the sequence change, identifiers including HGVS
Phenotype: description of the phenotype (in this case the diagnosis)
Observations: supporting evidence for the variation and the related phenotype
Genomic context: View of this variation on a RefSeqGene or the genome
Submissions: If this is a record for a signal submission (accession format SCV), then this section will list this submission and any reference submission (accession format RCV). If this is an RCV display, this section will list the SCV accessions on which it is based.
GTR: Any testing for this variation in the Genetic Testing Registry.



See Also:
Poster number: 1060T presenting a community view regarding the motivation and utility of this broad based community effort to integrate, curate, validate, and present a shared database of clinical variant data.

How do I join this effort?

We are currently working with academic and commercial clinical labs, curation groups, LSDBs, and other clinical variant databases.
Please contact the ClinVar team at the email address below.

Contact us: clinvar@ncbi.nlm.nih.gov

Home Page: http://www.ncbi.nlm.nih.gov/clinvar/

NCBI Booth **217**