# Canadian Open Genetics Repository (COGR): A Unified Clinical Genome Database as a Community Resource for Standardizing and Sharing Genetic Interpretations

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## Background

- COGR - a collaborative effort for the collection, storage, sharing and robust analysis of variants reported by medical diagnostics laboratories across Canada.
- COGR has three important qualities:
  - Its collaborative structure promotes real-time sharing between geographically distant laboratories and enhances the exchange of information about novel variants within the expert community.
  - COGR will present data to different stakeholder groups in appropriately understandable formats and levels of summary.
  - COGR provides a common Variant Assessment Tool to facilitate standardization across the Canadian clinical laboratories in the assessment process.

## Aims

Activity 1. Design of variant assessment procedures.

•The overall effort is to facilitate the process of transforming data-variant holdings into a unified format, while eliminating discrepancies, omissions and duplication of effort. Having the multiple stakeholders assess variant significance in a systematic, comprehensive, and consistent manner will foster knowledge aggregation from different individuals, institutions, and areas of expertise.

Activity 2. Data extraction and transfer.

•The project team will devise methods and operating procedures to support the extraction of the variant data currently held within participating laboratories in Canada. Our bioinformatics team will be responsible for working with each laboratory to ensure that their data are transmitted safely and efficiently to a central repository.

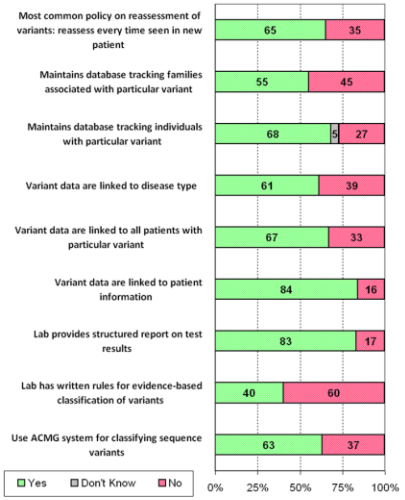
Activity 3. Data access and dissemination.

• Methods will be developed to make the data holdings both extremely accurate and readily accessible by all interested parties, including participating labs, clinicians, geneticists and scientists engaged in basic research. Our project team will put plans in place to encourage adoption of a unified platform, as well as to train and educate stakeholders as necessary.

## The State of Clinical Genetics in Canada: Results of an Online Survey

- Surveyed 60 clinical diagnostic stakeholders across Canada
  - 32 initiated survey, with 27 completions
  - 61% Lab Directors, 24% Clinicians, and 24% Genetic Counselors
- 80% of respondents have direct role in collecting variants
  - 90% have a direct role in interpreting variants
- 100% of respondents willing to share data holdings with team
  - Primary concern: Removal of patient data
  - ~50% wanted attribution for variants submitted
- Primary utility of COGR:
  - >90% would use it to determine if there is a consensus variant classification for a particular disease
  - 80% would use it to gather information from other participating laboratories
  - 60% would use it to identify genes associated to disease

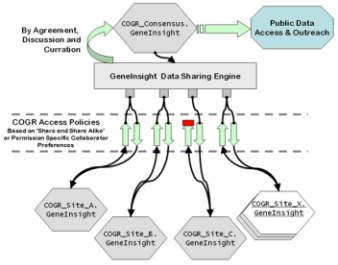
## Survey Results on Working Methods for Variant Collection and Classification



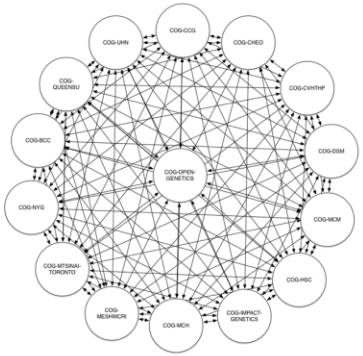

## Structure of Sharing

Common infrastructure for variant sharing using GeneInsight™ Knowledge Manager

- •Each lab interprets their own variation
- •Can interpret variants in context of multiple diseases
- •Variants are validated genomic and transcript reference sequences from NCBI
  - •Allows for accurate sharing across labs
- •Individual lab variants are shared with Central instance where consensus interpretation occurs




## Participating Centers

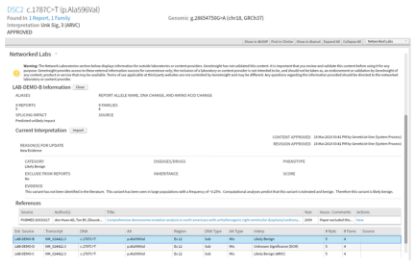




## Current Variant Sharing on Network

| Genes | Diseases | Pathogenic | Likely Pathogenic |
|---|---|---|---|
| 56 | 8 | 1265 | 89 |

| Uncertain Significance | Likely Benign | Benign |
|---|---|---|
| 632 | 138 | 216 |

Example of networked variant sharing using GeneInsight™



## Conclusions

Our initial results point to a need in the community for a shift to resources that will foster improved collaboration among Canada's clinical geneticists, clinicians, counselors and others dedicated to genetic research and healthcare. The COGR also serves as a focal point for the collaboration of Canadian laboratories with other countries in the development of tools and methods that take full advantage of laboratory data in diagnosing, managing and treating genetic diseases.

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