Data Sharing and Variant Classification Consensus Building in the Canadian Open Genetics Repository (COGR)

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Background

Individual laboratory knowledge and soiled data sets impede our knowledge of variants and prevents clinicians from receiving the most accurate interpretations for variants found in their patients. This in turn may prevent patients from receiving the most appropriate care.

The Canadian Open Genetics Repository is a collaborative effort to create a unified, open-access, clinical-grade database of variants reported by medical diagnostics laboratories across Canada. Utilizing GeneInsight® as a common platform, labs will collect, store and share variant information in real time.

As clinical laboratories adopt modern genomics technologies, the need for this type of collaborative framework is increasingly important.

Participating Centers with GeneInsight Instance

Organization	Upload Status	Sharing Status
Alberta Children's Hospital, Calgary AB	Uploaded	Sharing
Atlantic Cancer Research Institute	Pending	-
British Columbia Cancer Agency, Vancouver BC	Uploading	-
Children's & Women's Health Centre of BC, Vancouver BC	Pending	-
Children's Hospital of Eastern Ontario, Ottawa ON	Uploaded	Sharing*
Credit Valley Hospital, Trillium Health Centre, Mississauga ON	Uploaded	Sharing
Dept of Medical Genetics, University of Alberta, Edmonton AB	Pending	-
Hamilton Health Sciences, McMaster University, Hamilton ON	Uploading	-
Impact Genetics Inc., Bowmanville ON	Pending	-
Izaak Walton Killam Health Centre, Dalhousie University, Halifax NS	Pending	-
Kingston General Hospital, Queen's University, Kingston ON	Uploaded	Sharing
McGill University Health Complex, Montréal QC	Uploaded	-
Memorial Health University Medical Center, St. John's NL	Pending	-
Mount Sinai Hospital, University of Toronto, Toronto ON	Uploaded	Sharing*
North York General Hospital, Toronto ON	Uploading	-
Ontario Institute of Cancer Research (OICR), Toronto ON	Uploaded	Sharing
Regional Health Authority, University of Manitoba, Winnipeg MB	Uploading	-
Sainte-Justine Hospital, University of Montreal, Montréal QC	Uploading	-
SickKids Hospital and McLaughlin Centre, Toronto ON	Uploaded	Sharing
University Hospital, Western University, London ON	Pending	-
Women's College Hospital, University of Toronto, Toronto ON	Uploaded	Sharing

Aims & Platform

Aim 1. Design freely available and consistent variant assessment procedures.

- A free version of the Variant Assessment Tool has been made available on the COGR website.

Aim 2. Data extraction and transfer.

- The project team is currently supporting the extraction of variant data currently held within participating laboratories.

Aim 3. Data access and dissemination.

- Methods are being developed such that accurate and readily accessible data will be made public.

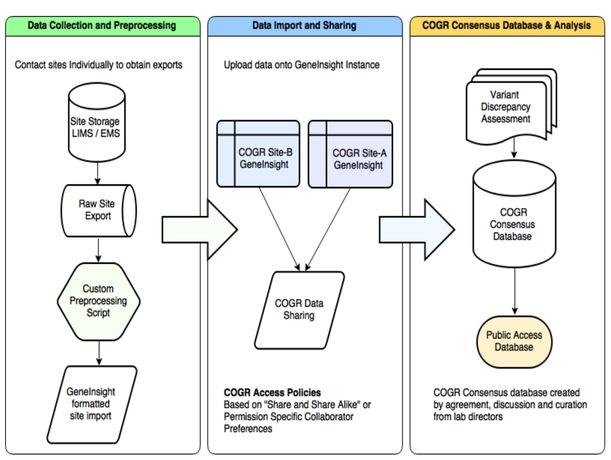
Data Sharing Model

COGR is providing an instance of the GeneInsight® platform as well as a custom Variant Assessment Tool to all participating labs.

GeneInsight provides a database that that captures all types of information related to human gene variants and their relationship to rare and common disease. Specifically this includes variant interpretations, reference sequence data and gene-disease associations.

The COGR data sharing model allows real-time variant sharing between labs. Ultimately a database of variant interpretations will be created for public access.

Below is a schematic of the COGR project workflow. and data sharing model.

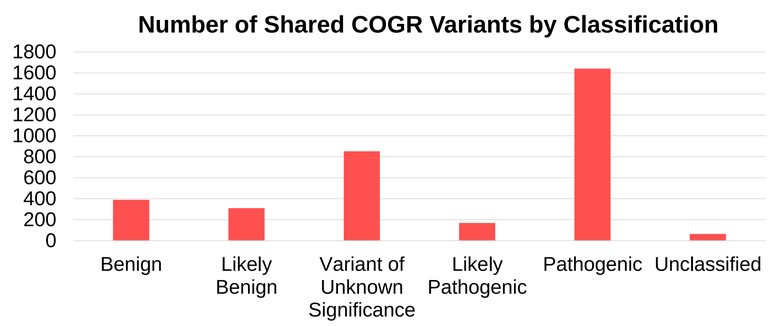


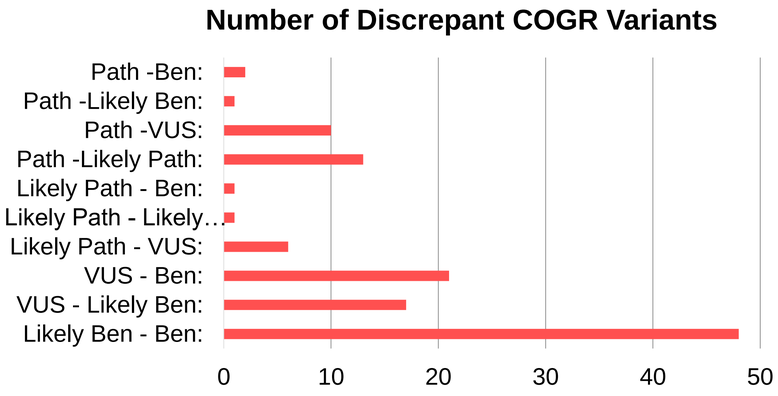
Current Variant Sharing

Currently Shared:

Total Shared Variants:
7914
Total Unique Variants:
2911
Total Genes:
90
Total Number of Diseases:
60

Disease	# of Variants
Hereditary Breast and Ovarian Cancer	1953
Lynch Syndrome	235
Hypertrophic Cardiomyopathy	151
Cystic fibrosis	91
Infantile myofibromatosis 2	83
21-hydroxylase deficiency	82
Familial adenomatous polyposis	68
Phaeochromocytoma	54
Charcot-Marie-Tooth disease	47
Alpha-thalassemia	43
Beta thalassemia	43
Achondroplasia	34
Beare-Stevenson cutis gyrata syndrome	32
Rett syndrome	30
Familial isolated hyperparathyroidism	21
Other (< 20 per disease)	208





# of Variants Seen By:

Only 1 Lab	2490
2 Labs	273
3 Labs	73
4 Labs	29
5 Labs	3

Total Agreements:
268

Total Disagreements:
102

Future Directions

The COGR project is positioned to help remove some of the chief obstacles to advancements in personalized healthcare including the lack of standardized resources and protocols for interpreting the ever-increasing volumes of patient data being generated by clinical labs.

Continuing initiatives include:

- Automation or semi-automation of the variant upload process for sites to facilitate the maintenance of updated variant information for all sites
- Make consensus variant interpretations available to stakeholder groups with different but appropriate levels of summary.
- Continue to collaborate with other international data-sharing efforts including ClinVar.

In summary, the COGR serves as a focal point for the collaboration of Canadian laboratories with themselves and other countries in the development of tools and methods that take full advantage of laboratory data in diagnosing, managing and treating genetic diseases. Furthermore, as more laboratories share data, knowledge will improve and ultimately lead to better patient care.

Canadian Open Genetics Repository
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