International Data Sharing Efforts: Lessons from Canadian Open Genetics Repository (COGR)

Marina Wang¹, Shana White², Samantha Baxter², Michael Oates², Chet Graham², Matthew S Lebo^{2,3}, Jordan Lerner-Ellis¹, and the COGR Working Groups anadian Open Genetics Repository ¹ Mt Sinai Hospital, University of Toronto, Ontario Institute for Cancer Research ; ² Laboratory for Molecular Medicine, PPM; ³Brigham and Woman's Hospital, Harvard Medical School

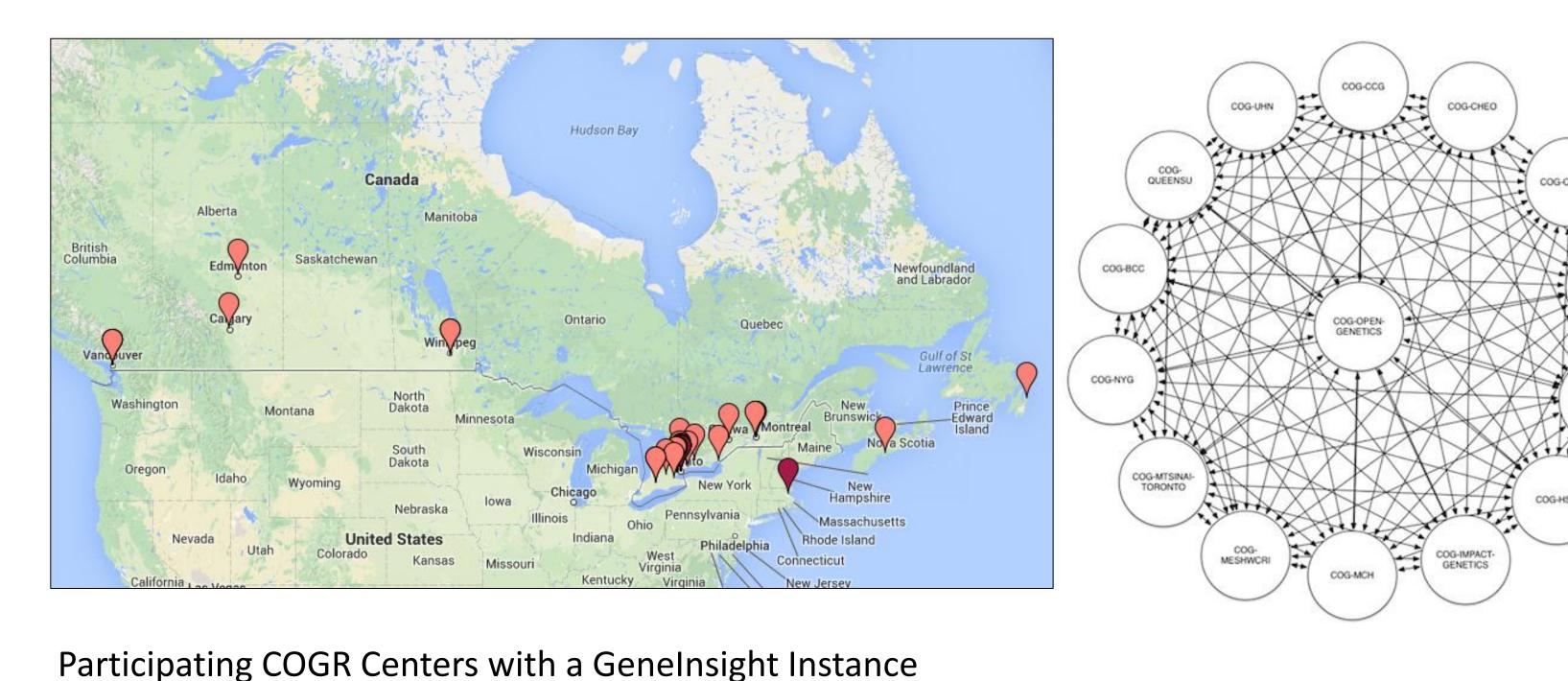
Background

knowledge and Individual laboratory 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 Utilizing laboratories Canada. across GeneInsight[®] as a common platform, labs variant collect, store and share information in real time.

Participating Centers and Data Sharing Model

Experiences



British Columbia Cancer Agency

North York General Hospital

200

50

0

Agree

Children's Hospital of Eastern Ontario

British Columbia Children's Hospital

Current Variant Sharing

Our progress thus far has highlighted the critical need for robust and sustainable IT infrastructure. Our goal is that continued use of a common variant assessment tool and real-time variant sharing will increase standardization and discussion.

Survey results from COGR laboratories

Use formal tracking system for variants in the literature	Yes: 46% No: 54%
Lab uses consistent set of terms for classification	Yes: 65% No: 35%
Lab has written rules for evidence- based classification of variants	Yes: 40% No: 60%
Variant data are linked to disease type	Yes: 61% No: 39%
Maintains database tracking families associated with particular variant	Yes: 55% No: 45%
Reassess variants every time seen in new patient	Yes: 65% No: 35%

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

Credit Valley Hospital-Trillium Health Partners Canada's Michael Smith Genome Sciences Centre Edmonton Molecular Diagnostics-University of Alberta Research Molecular Genetics Lab-Women's College Hospital Kingston General Hospital- Queen's University Hamilton Health Sciences-McMaster University

Aims & Platform

<u>Aim 1</u>. Design freely available and consistent variant assessment procedures.

• Individual variant data will be transformed unified format, eliminating into а discrepancies, omissions, and duplications.

Aim 2. Data extraction and transfer.

• The project team will devise and optimize procedures to support the extraction of disease, gene and variant data currently held within participating laboratories.

Aim 3. Data access and dissemination.

Methods will be developed such that accurate and readily accessible data will be

Participating laboratories are currently sharing:

• 7 Diseases: HBOC, HCM, Lynch syndrome, FAP, MUTYH-Associated Polyposis (MAP), Alpha-1 Antitrypsin Deficiency (A1AD), Somatic Cancer

McGill University Health

United Health Network

University of Manitoba

Alberta Children's Hospital

• 52 Genes

Mt Sinai Hospital

Impact Genetics

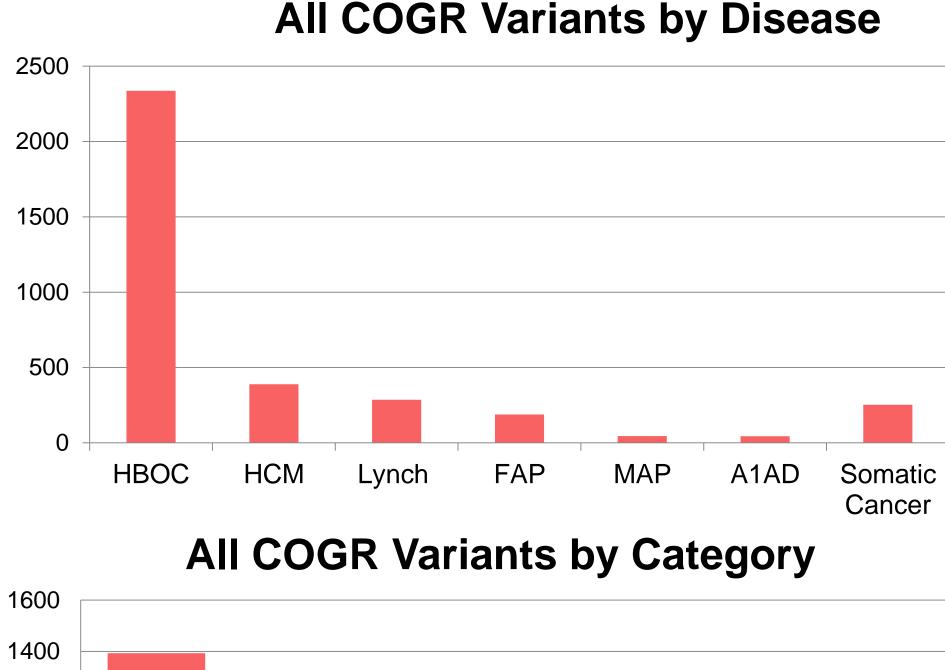
Memorial University

Sick Kids Hospital

Western University

• <u>>3,000 variants</u>

P- Pathogenic **LP-** Likely Pathogenic



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 everincreasing volumes of patient data being generated by clinical labs.

Future Directions

Continuing initiatives include:

- Establishing committees of disease area experts to create consensus interpretations for variants categorized by multiple laboratories.
- Make consensus variant interpretations

presented to different stakeholder groups in appropriate summary levels. Individual laboratories see their variants with specific detail while the diagnostic community views a more general summary that is mindful of privacy and confidentiality.

COGR will provide an instance of the GeneInsight platform to all participating labs.

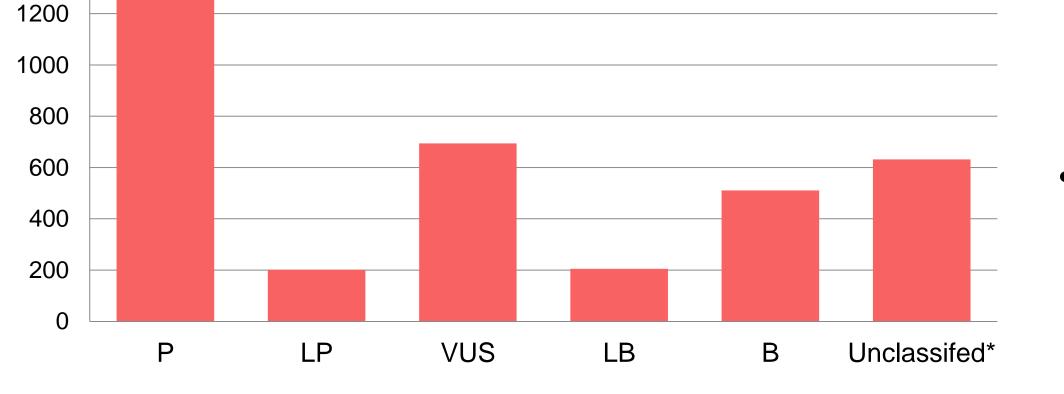
Gene lnsight	White, Shana 上 🔻								Q Diseases/Drugs	Disease	spondgs	
for better care	Dashboard F	Reports "Remote"	🗙 Va	riants "Any Source" '	'All 🗶 p.Al	a596Val (c.1787C>T) 🗙 🗙 🕂					
Diseases/Drugs	DSC2 c.17	87C>T (p	Ala596Val)									
Genes	Interpretation APPROVED	Unk Sig F	ound In 2 Repo	ts, 2 Families								
Variants Create							Sho	w in Alamu	t Expand All Collapse	All Networ	ked Labs	
aved Searches	LAB-DEMO-	C Informatio	Close									
rameters >	ALIASES		RE	PORT ALLELE NAM	IE, DNA CHANGE, /	ND AMINO ACID	CHANGE					
Save Reset Search	# REPORTS		# F. 4	AMILIES								
Vetworked Labs Interp. Mode	SPLICING IMP		SO	URCE								
Variant contains 🔻	Predicted Unlik	ely Impact										
+	Current Int	terpretation	Import									
Gene Name/Symbol contains V							CONTENT APP REVISION APP			.3 02:26 PM by G .3 02:26 PM by G		
Networked Labs equals V	REASON(S) New Evidence) FOR UPDATE										
Any Source 🔹 🕇	CATEGORY Likely Benigr			DISEA	SES/DRUGS			PHEN	NOTYPE			
Category equals All Unknown Significance \[]	EXCLUDE FROM REPORTS			INHERITANCE SCORE								
Tests & Panels	European An		mes from a broad popul						. Furthermore, it is pres NP rs148185335). In sun			
Reports	References	S										
References	Source	Author	(s)	Title				Year	Assoc. Comments	Actions		
	PUBMED 200		n AD, Tan BY, Zikusok	ISOK Comprehensive desmosome mutation analysis in north americans v			nericans with	2009	Paper excluded this	uded this View		
	Ext. Source	Transcript	DNA	AA	Region	DNA Type	AA Type	Interp		# Rpts	# Fams	
	LAB-DEMO-C	NM_024422.3	c.1787C>T	p.Ala596Val	Ex 12	Sub	Mis	Likely Be	nign (ARVC)	5	4	

VUS- Variant of Unknown Significance **LB-** Likely Benign

B- Benign

*Unclassified variants are under review, pending classification.

- Over 3,000 variants are being shared 250
 - 391 have been reported by 2 different labs
 - 50 have been seen by 3 different ¹⁵⁰ labs
- 100 The majority of variants categorized by multiple labs have concordant categories.



Concordance of Variant Categories Between Labs

P/B vs VUS

LP/LB vs VUS

Likelihood

(LP vs P or LB vs B)

- available stakeholder groups with to different but appropriate levels of summary.
- collaborate Continue to other with efforts international data-sharing 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 Email: cogr@opengenetics.ca Web: http://opengenetics.ca