The Canadian Open Genetics Repository- Updates and Discussion

CCMG Meeting Nov 2014

COGR
Canadian Open
Genetics Repository

Overview

- To create Canada's unified, open-access, clinical-grade genetic database using a commonly shared platform

- Designed to hold all types of information related to human gene variants and their relationship to rare and common diseases

- Also, create and disseminate variant assessment procedures to each laboratory to help standardize clinical classification

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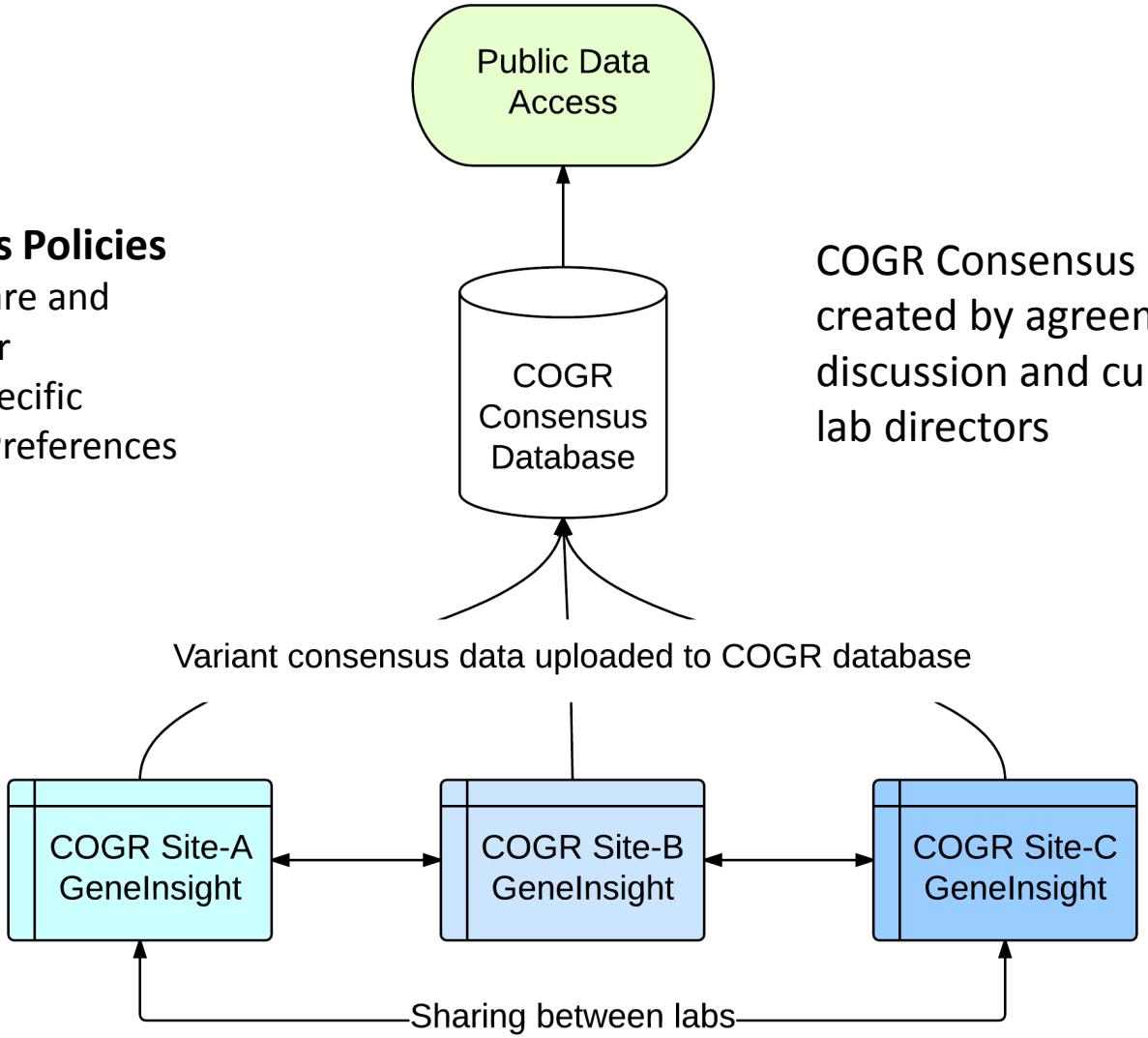
Overview

COGR Access Policies
Based on “Share and Share Alike” or Permission Specific Collaborator Preferences



COGR Consensus database created by agreement, discussion and curation from lab directors

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19 GeneInsight Instances Created

Organization	Upload Status	Sharing Status
Alberta Children's Hospital, Calgary AB	Uploading	
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
Impact Genetics Inc., Bowmanville ON	Pending	
McGill University Health Complex, Montréal QC	Uploaded	Pending
McLaughlin Centre, SickKids Hospital, Toronto ON	Uploading	
McMaster University (Hamilton Health Sciences), Hamilton ON	Pending	
Memorial Health University Medical Center, St. John's NL	Pending	
Mount Sinai Hospital, Toronto ON	Uploaded	Sharing*
North York General Hospital, Toronto ON	Pending	
Queen's University, Kingston General Hospital, Kingston ON	Uploaded	Pending
Women's College Hospital, Toronto ON	Uploaded	Sharing
University of Alberta, Dept of Medical Genetics, Edmonton AB	Uploading	
University Health Network, Toronto, ON	Uploaded	Sharing
University of Manitoba, Regional Health Authority, Winnipeg MB	Pending	
University of Montreal, Sainte-Justine Hospital, Montréal QC	Uploading	
Western University, University Hospital, London, ON	Pending	

* Also sharing with VariantWire

VariantWire

- Data-sharing network for clinical genetic testing labs to share variant and gene interpretations in real time
- Consortium supported by GeneInsight

Participating Laboratories
Partners HealthCare Laboratory for Molecular Medicine
ARUP Laboratories
Mount Sinai School of Medicine Genetic Testing Laboratory
Mount Sinai Hospital in Toronto
Canadian Open Genetics Repository
Children's Hospital of Eastern Ontario

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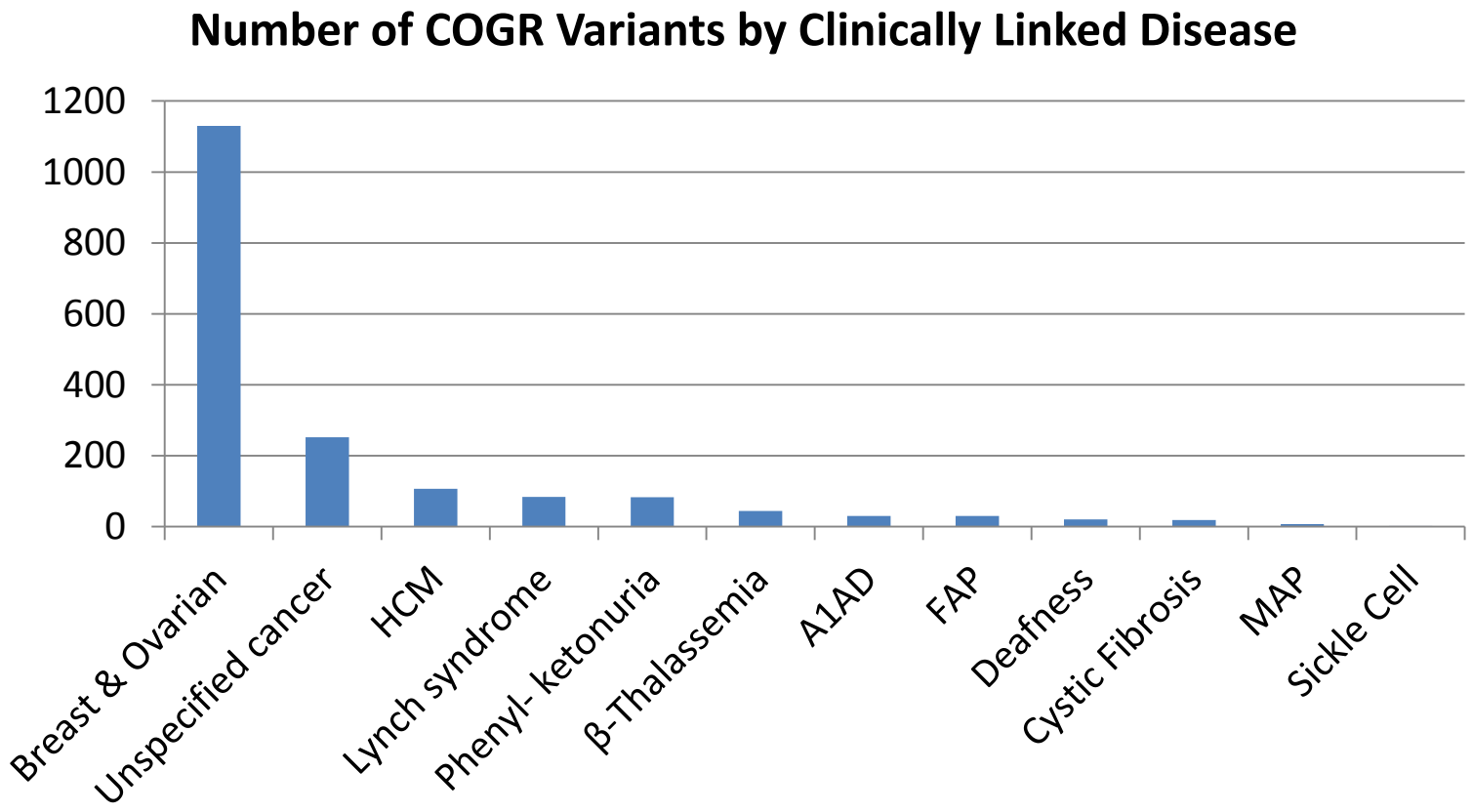
COGR Variant Numbers

Total Number of Variants: 3802

Total Number of Genes: 56

Total Number of Diseases: 13



HCM: Hereditary Cardiomyopathy
FAP: Familial adenomatous polyposis
MAP: MUTYH-associated polyposis

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COGR and VariantWire Data as of Sept 2014

	VariantWire	COGR
Variant Classification	#	#
Pathogenic	1,946	1,393
Likely Pathogenic	1,137	201
Uncertain Significance	4,536	694
Likely Benign	12,053	205
Benign	4,657	411
Resistant or Responsive*	57	-
Unclassified	-	632
Total Variants	24,386	3,536
Consistent Interpretations	#	#
Agree	302	200
Pathogenic vs. Likely Pathogenic	34	2
Benign vs. Likely Benign	51	23
Total Consistent Interpretations	387	225
Different Interpretations	#	#2
(Likely) Pathogenic vs. VUS	23	6
(Likely) Benign vs. VUS	60	16
(Likely) Pathogenic vs. (Likely) Benign	1	0
Total Different Interpretations	84	22

**Somatic Cancer Variants*

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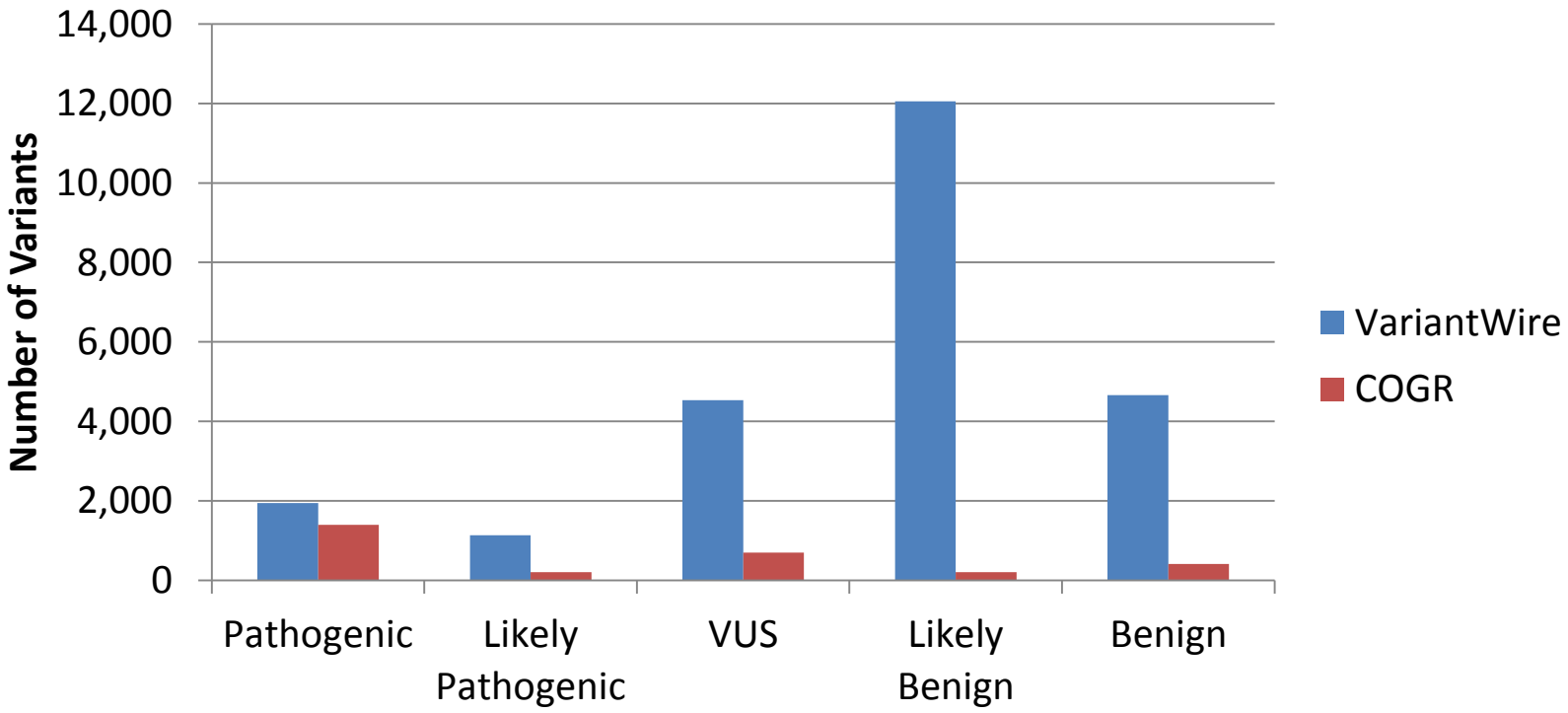
Current Variants Being Shared in COGR and VariantWire Databases



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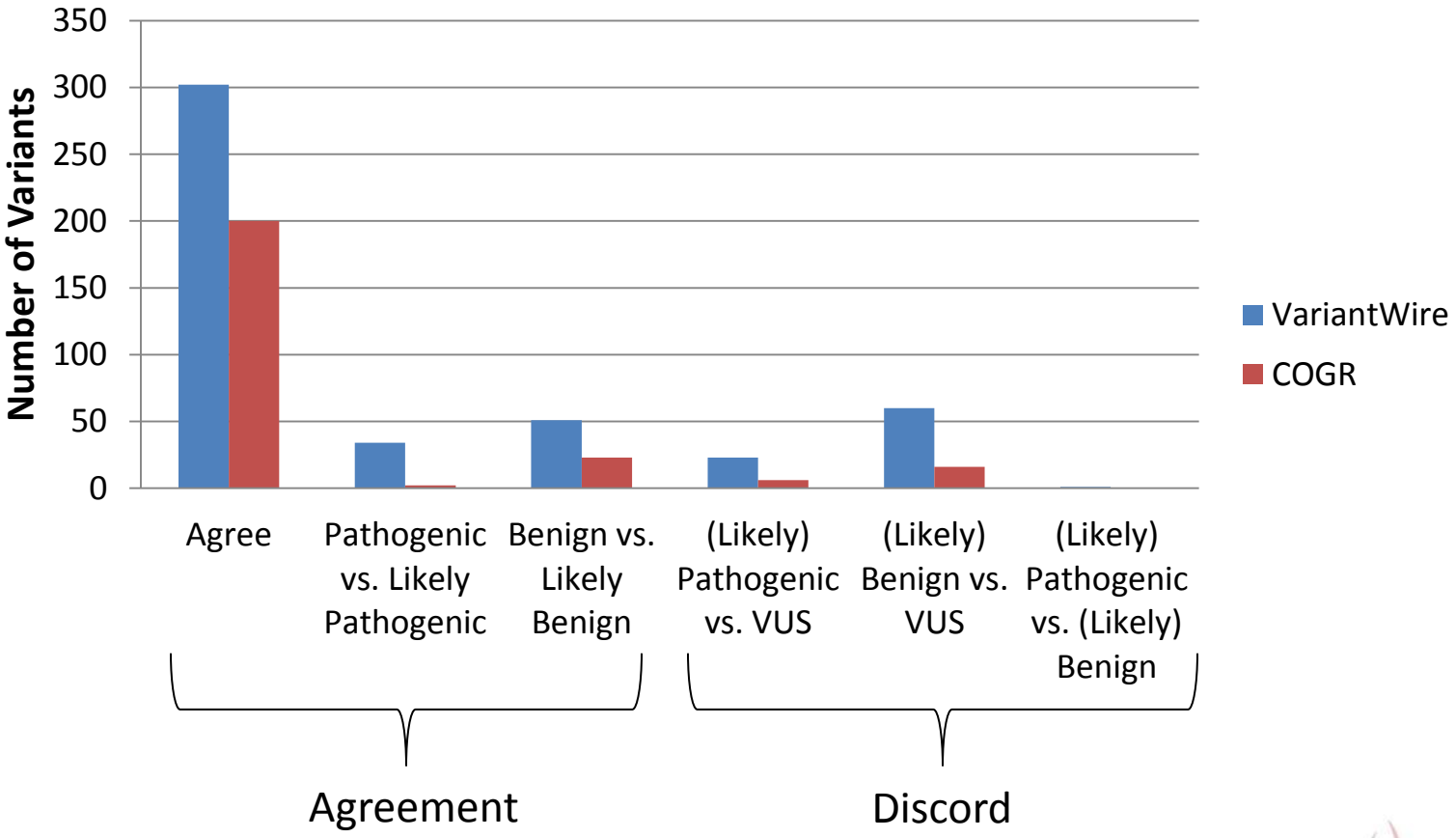
Agreement and Disagreement of Variant Interpretations



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Concerns- Funding

Concern: How will funding of GeneInsight instances work after the 3-year grant expires?

- *Discussions with OGI about applying funding towards nationwide license*
- *Affordable license fees for individual sites*
- *Jordan & Matt applying for additional funding*
- *Funding for years 4 and 5*

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Concerns- Continued Variant Upload

Concern: Will there be a quicker and easier way to upload variant data on a continued basis?

- *GeneInsight is capable of supporting APIs, however we currently lack the resources*
- *Create a system, individualized for each lab, to do a routine upload*
  - *We have resources within the 3 years to help automate or semi-automate uploads*

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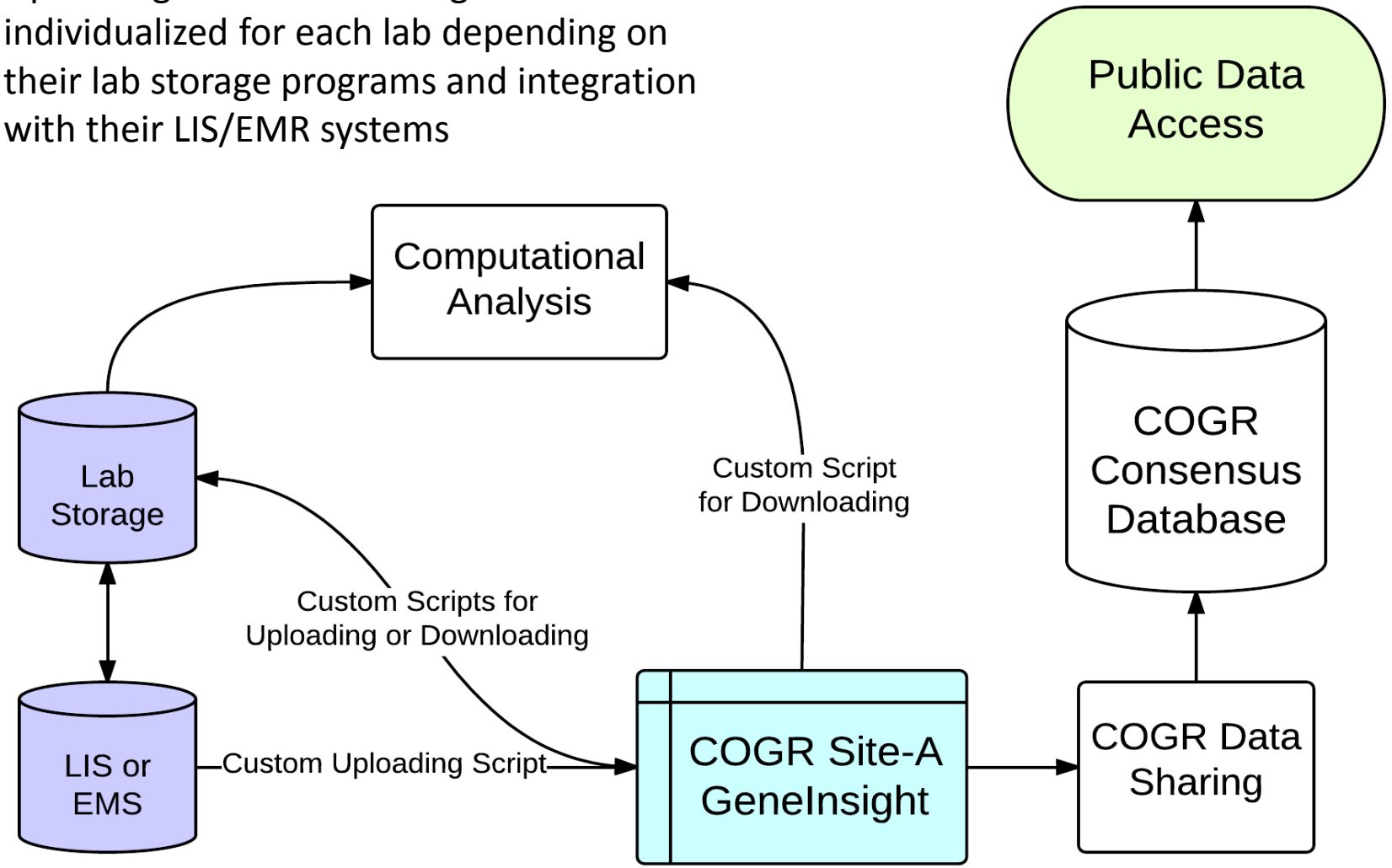
Automated Uploading Schematic

Uploading and Downloading are individualized for each lab depending on their lab storage programs and integration with their LIS/EMR systems



Sharing and Agreements

- Sharing permissions
  - Sharing with other labs and/or VariantWire is optional and requires strict permission based access
- ClinVar
  - Data is automatically pulled from ClinVar
  - We can assist with pushing of variant data into ClinVar

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Variant Assessment Tool (VAT)

- GeneInsight already has capacity to track literature for each variant
- Additional features to be integrated into GeneInsight
  - All variant information pulled from Alamut
  - Allele control frequency data (ESP, ClinVar, 1000 genomes)
  - Ability to search pubmed/google for literature

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Publications

- Plan on announcing the COGR through publication
  - Manuscript will be circulated
  - Permission to include each lab director as a "Working Group Member"
- Potential BRCA variant collaboration as proof of principle for the COGR

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DISCUSSION

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