Clinical Working Group

Global Alliance for Genomics & Health

Charles Sawyers, Co-Chair (Memorial Sloan-Kettering Cancer Center, US); **Kathryn North, Co-Chair** (Murdoch Childrens Research Institute, AU); **Lena Dolman, Manager** (Ontario Institute for Cancer Research (OICR), CA)

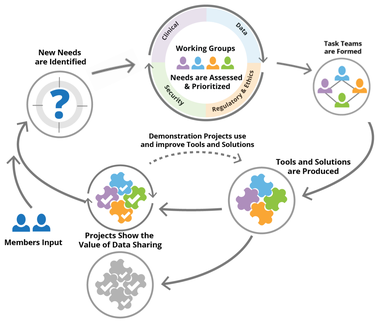
Overview

The **Clinical Working Group (CWG)** - one of the four working groups of the Global Alliance for Genomics and Health (GA4GH) - aims to enable compatible, readily accessible, and scalable approaches for sharing clinical and genomic data. Recognizing how much work is already ongoing in this area, the CWG seeks to add value to existing endeavors and incubate data-sharing demonstration projects. The CWG addresses both research and clinical use scenarios while remaining physician-oriented, researcher-focused, and patient-centred.

There are currently **>100 volunteers contributing** to the CWG.

How We Work

The CWG includes **Task Teams**, which focus on time-bound, actionable deliverables, and supports **Demonstration Projects**, which are multi-stage, cross-cutting projects utilizing GA4GH tools in real-world settings to illustrate the value of data sharing and knowledge exchange.



The CWG meets via teleconference on a bi-monthly basis, and hosts joint calls with the GA4GH Data Working Group on a bi-monthly basis, to facilitate the development of technical tools that can be readily applied to real-world clinical needs.

Get involved!

genomicsandhealth.org
theglobalalliance@genomicsandhealth.org
@GA4GH #GA4GH2016
www.facebook.com/GA4GH

Task Teams and Initiatives

Phenotype Ontologies

The **Phenotype Ontologies** Task Team strives to support international efforts to develop and promote a standard language and tools for recording clinical phenotypes, and exploring phenotypic data for diagnostics and translational research.

Recent Activities:
- Released layperson synonyms to make the Human Phenotype Ontology (HPO) more accessible
- Working to translate the HPO into multiple languages
- Integrating cancer phenotypes into the HPO, in collaboration with NCI Thesaurus
- Establishing a new Phenotype Exchange Format, “phenopackets”, which aims to standardize transfer of phenotype information among labs, databases, journals, etc

Co-Leads: Peter Robinson (Jackson Laboratory for Genomic Medicine, US), and **Peter Yu** (Palo Alto Medical Foundation, US)

eHealth

The **eHealth Task Team** aims to identify current efforts to collect and link genomic and phenotypic data, and then showcase these efforts to promote awareness and learning from best practices, harmonization efforts, and unified standards.

Recent Activities:
- Striving for standardization of ontologies into electronic health records (EHRs)
- Creation of a Family History Tools Inventory cataloguing both academic and commercial tools
- Release of a Statement of Best Practice for developers of clinically-oriented family history collection systems.

Co-Leads: John Mattison (Kaiser Permanente, US), and **Andrew Morris** (University of Edinburgh, UK)

Clinical Cancer Genome

The **Clinical Cancer Genome Task Team** works to harmonize clinical sequencing efforts in the global cancer community. It highlights existing efforts that are interoperable or moving towards sharing of data, and promotes outcomes by developing standards and best practices that support clinical decision-making.

Recent Activities:
- Perspective article on cancer data sharing published in *Nature Medicine* (May, 2016)
- Cancer data sharing survey results are currently under review for publication

Co-Leads: Mark Lawler (Queen’s University Belfast, UK), and **Charles Sawyers** (Memorial Sloan-Kettering Cancer Center, US)

Catalogues of Global Activities

As part of the GA4GH mission to act as a clearinghouse for global activities, the CWG has created catalogues of current world-wide activities related to data sharing in rare Mendelian diseases, and in electronic health data. CWG has additionally produced a catalogue of family history tools, and a catalogue of global genomic data initiatives (including precision medicine initiatives, databases & repositories, genomic research consortia, and other resources). These are accessible on the GA4GH website and open for public submissions.

Leads: Kathryn North, Mendelian (Murdoch Childrens Research Institute, AU), **Gil Alterovitz, eHealth** (Harvard University, US), **Meg Doerr, Family History Tools** (Sage Bionetworks, US), and **Lena Dolman, Genomic Data Initiatives** (OICR, CA)

Data-Sharing Demonstration Projects Supported by the Clinical Working Group

Matchmaker Exchange

Steering Committee: Michael Bamshad, Kym Boycott, Michael Brudno, Ada Hamosh, Matthew Hurles, Kathryn North, Anthony Philippakis, Heidi Rehm

Matchmaker Exchange (MME) is a collaborative effort to address the common challenge of exome and genome sequencing in both the research and clinical settings wherein the majority of cases lack a clear etiology after initial analysis. For such cases, finding a single additional case with a deleterious variant in the same gene and overlapping phenotype may provide sufficient evidence to identify the causal genetic basis. MME is a federated network of databases that facilitate the matching of similar genotypic and phenotypic profiles in order to identify the genetic causes of rare and undiagnosed diseases.

Recent Activities:
- 6 databases are now connected through the MME API: Australian Genomics Health Alliance (AGHA) Patient Archives, Broad seqr, DECIPHER, GeneMatcher, MyGene2, and PhenomeCentral
- 16 articles on MME were featured in a special issue of *Human Mutation* (Oct 2015)
- Recent mentions in the Toronto Star (May 2016) and in *Nature* (June 2016)

The Matchmaker Exchange is supported by the database participants involved as well as by: CanSHARE Network, IRDiRC, NIH Centers for Mendelian Genomics, Genome Canada, CIHR, Care4Rare, and RD-Connect.

Volunteer Contributors

49	56	15

BRCA Challenge

Co-Leads: Sir John Burn (Newcastle University, UK), and **Stephen Chanock** (National Institutes of Health, US)

The **BRCA Challenge** aims to advance the global understanding of the genetic basis of breast, ovarian, and other cancers by pooling BRCA genetic variants, and applying expert curation to variants to guide clinical decision-making. The **BRCA Exchange** web portal has pooled BRCA variants from several public repositories (ClinVar, LOVD, NHLBI EVS, 1000 Genomes, ExAC, ENIGMA, and others), and has enlisted the ENIGMA consortium to share consensus interpretations relating to these variants.

Recent Activities:
- The BRCA Exchange now displays ~20,000 unique variants in BRCA1/2 and ~3,300 expert classifications from ENIGMA
- An online forum connecting world-wide supporters of the BRCA Challenge was added to the web portal in September 2016
- The BRCA Exchange now allows users to visualize prior versions of the data releases

BRCA Challenge is supported by AstraZeneca, CanSHARE, and the NIH (including the BD2K initiative)

Cancer Gene Trust

Co-Leads: David Haussler, Charles Sawyers, Bin Tean Teh, Clare Turnbull, and **Emile Voest**

Now in development, the **Cancer Gene Trust (CGT)** aims to build an information network of aggregated, public somatic cancer sequencing data, as well as some clinical information, with the option to contact the centre holding the full clinical dataset to request more information on a case-by-case basis. Users will be able to build a research cohort or match a patient’s rare mutation with an effective therapy.

Recent Activities:
- Currently convening a cross section of clinicians, cancer researchers, and data holders (e.g., GENIE, ICGC, Cancer Core Europe, Genomic Data Commons)
- Demo of the CGT network being presented on Oct 17, 2016

Executive Committee of the Clinical Working Group

Charles Sawyers, Co-Chair (Memorial Sloan-Kettering Cancer Center, US)
Kathryn North, Co-Chair (Murdoch Childrens Research Institute, AU)
Gil Alterovitz (Harvard Medical School, US)
Kym Boycott (Children’s Hospital of Eastern Ontario Research Institute, CA)
Mark Lawler (Queen’s University Belfast, UK)
John Mattison (Kaiser Permanente, US)
Andrew Morris (University of Edinburgh, UK)
Anthony Philippakis (Broad Institute, US)
Heidi Rehm (Harvard Medical School, US)
Peter Robinson (Jackson Laboratory for Genomics Medicine, US)
Dan Roden (Vanderbilt University School of Medicine, US)
Lillian Siu (University Health Network, CA)
Bin Tean Teh (National Cancer Centre Singapore, SG)
Julia Wilson (Wellcome Trust Sanger Institute, UK)

For CWG questions, please contact Lena Dolman at lena.dolman@genomicsandhealth.org

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