ClinGen
Clinical Genome Resource

September 2, 2014

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Position Statement on Licensed Databases and plans for the Global Sharing of *BRCA1* and *BRCA2* Data

Genetic testing from single gene to genome scale sequence analysis is more frequently being offered in the clinical setting. However, the *same* variants are sometimes interpreted *differently* across laboratories. In addition, the majority of variants have insufficient evidence for a definitive classification and the proportion of those unclassified variants varies over populations. As a result, there is a significant risk that patients could be harmed by medical decisions made based upon unsubstantiated variant classifications or insufficient data on identified variants. Given the rarity of most variants of clinical relevance, it is imperative that all data on variants is fully shared to improve our understanding of genomic variation and the resulting patient care activities that are reliant on this information. The genomics community has already recognized and embraced global data sharing as a critical component of knowledge generation to support both knowledge discovery and translation of findings that maximize the utility of genomic testing for clinical use in different populations.

ClinGen investigators do not endorse the licensing and monetization of variant databases, which should be considered pre-competitive, and instead support the broadest sharing of data to ensure patient safety. The following are specific concerns about licensing and commercializing variant databases:

- Separating data into commercialized and non-commercialized databases will limit the full aggregation of data and reduce the ability to learn most effectively from the data and efficient comparative analyses. Allowing any variant data to be "sold" will broadly inhibit data sharing as many data sources may not share data in hopes of profiting from their data
- Ability to access commercialized databases will vary according to the financial capabilities of groups, creating disparity in the medical community and other consumers of the data
- Restricting data sharing is contrary to best practices of medical care and is unethical according to multiple resolutions adopted by the American Medical Association

In regards to the specific sharing of *BRCA1* and *BRCA2* variant data, public databases such as the NHGRI hosted Breast Cancer Information Core (BIC) database has been open access for nearly twenty years. In addition, the following are examples of projects known to ClinGen investigators that are consistent with the principles of open sharing:

ClinVar: ClinVar currently contains the largest publicly available dataset of *BRCA1* and *BRCA2* variants, including all variants from BIC, OMIM, the Sharing Clinical Reports Project, the Free-The-Data Campaign and individual laboratory submissions, and is being widely adopted as a source of variant interpretations and a mechanism for

groups to share their data across all genes. All ClinVar data is publically accessible and can be shared with, and downloaded into, other databases.

LOVD: LOVD has long-standing locus-specific databases for *BRCA1* and *BRCA2* that are in the public domain including: the BReast CAncer 1/2 literature unclassified variants database, the Zhejiang University Center for Genetic and Genomic Medicine *BRCA1/2* database, the LOVD 3.0 Shared database, and the LOVD – Proteomics database.

Universal Mutation Database (UMD): The UMD-*BRCA1/BRCA2* databases have been set up by a network of 16 laboratories in France. These databases currently contain published and unpublished information about the BRCA1/BRCA2 mutations reported in French diagnostic laboratories.

Global *BRCA* Challenge: A major effort organized by the Global Alliance for Genomics and Health (GA4GH) is underway to bring together the international community around studying the genetic basis of breast cancer. The *BRCA* Challenge aims to catalyze and support groups with data on *BRCA* variants and phenotypes, bringing together variant interpretations, as well as de-identified genotypic and phenotypic data. An international steering committee has been formed and enthusiasm for global data sharing has already been expressed by the major groups that have data on the *BRCA1* and *BRCA2* genes. This includes representatives from BIC, Canadian Open Genetics Repository (COGR), ClinVar, Consortium of Investigators of Modifiers of *BRCA1/2* (CIMBA), Evidence-based Network for the Interpretation of Germline Mutant Alleles (ENIGMA), Leiden Open Variation Database (LOVD), and Universal Mutation Database (UMD), as well as others.

In summary, we support proposals that encourage the sharing and aggregation of data. It is our intent to work with all sources of *BRCA1* and *BRCA2* data to bring the data together in one or multiple locations to support the most accurate interpretations of variants. Any activities that reduce the aggregation of data or limit access to such data are discouraged.

Thank you for consideration of our comments. Please do not hesitate to contact us with questions.

Sincerely,

ClinGen Principal Investigators