BRCA Exchange aggregates data on thousands of BRCA variants to understand cancer risk

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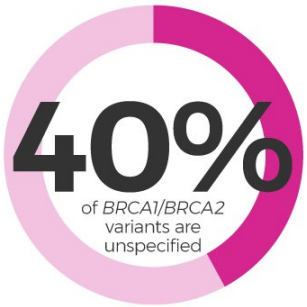
What is the BRCA Exchange?

A long-term demonstration project initiated by the Global Alliance for Genomics and Health (GA4GH) to enhance sharing of *BRCA1/BRCA2* data

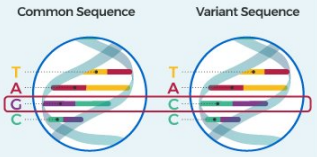
Problem: Clinical implications of 40% of *BRCA1/BRCA2* variants are unknown

Some *BRCA* genetic variants can increase risk of breast and ovarian cancer; others are completely benign. Scientists can only tell the difference once they understand how each variant affects the gene's function.



What is a gene variant?

An alteration in the most common sequence of DNA. The effect of variants on human health may be neutral, harmful, or unknown.



Solution: BRCA Exchange

BRCA Exchange aggregates "big data" on *BRCA* variants from research and health care databases around the globe. The **Evidence-based Network for the Interpretation of Germline Mutant Alleles (ENIGMA)*** contributes expert classifications for each variant.

Patients, clinicians, and others can review these details to inform their decisions on cancer prevention, screening, and intervention.

Making data available to:

Researchers

High-quality information on *BRCA1/BRCA2* variants.

Health care providers

Evidence-based decision-making for high-risk patients.

Patients & their advocates

Independent, expert information for *BRCA1/BRCA2* mutation carriers and advocates.

> "IF WE SOLVE THIS PROBLEM NOW, WE DON'T HAVE TO SOLVE IT AGAIN FOR OTHER GENES."

Robert Cook-Deegan,
Arizona State University

Available on the App Store and Google Play.

Major contributors of data to BRCA Exchange include: Breast Cancer Information Core, ClinVar, Leiden Open Variation Database, ExAC, 1000 Genomes, and NHLBI Exome Sequencing Project (ESP).

*Spurdle AB et al. Hu Mutat. 2012 | reference/link to PLOS Genetics/PubMed

cancer.gov

Credit: National Cancer Institute

A global resource that includes data on thousands of inherited variants in the BRCA1 and BRCA2 genes is available to the public. The BRCA Exchange was created through the BRCA Challenge, a long-term demonstration project initiated by the Global Alliance for Genomics and Health (GA4GH) to enhance sharing of BRCA1 and BRCA2 data. The resource, available through a website and a new smartphone app, allows clinicians to review expert classifications of variants in these major cancer predisposition genes as part of their individual assessment of complex questions related to cancer prevention, screening, and intervention for high-risk patients.

The five-year BRCA Challenge project was funded in part by the National Cancer Institute (NCI), part of the National Institutes of Health, and through the Cancer Moonshot?. A paper detailing the development of the BRCA Exchange was published January 8, 2019, in *PLOS Genetics*.

"This project has yielded a meta-analysis of BRCA1 and BRCA2 variants collected from multiple sources to understand how experts annotate specific mutations in the two genes," said Stephen J. Chanock, M.D., director of NCI's Division of Cancer Epidemiology and Genetics and lead author of the paper. "There's an urgent need for sharing data in cancer predisposition research. The BRCA Exchange is proof of principle that large-scale collaboration and data sharing can be achieved and can provide the latest and best quality information to enable clinicians and individuals to improve care."

Certain inherited variants in these genes can increase the risk of breast, ovarian, and other cancers by varying degrees, whereas others are not associated with disease. Clinicians and patients need to know whether a given variant is likely to be disease-associated (pathogenic) and how likely a pathogenic variant is to cause cancer (penetrance). Until now, the available data on the inherited variants in these genes were not aggregated in a comprehensive way.

The BRCA Exchange dataset is composed of information from existing clinical databases—the Breast Cancer Information Core, ClinVar, and the Leiden Open Variation Database—as well as population databases and data from clinicians, clinical laboratories, and researchers worldwide. It currently includes more than 20,000 unique BRCA1 and BRCA2 variants. More than 6,100 variants in the database have been classified by an expert panel, the Evidence-based Network for the Interpretation of Germline Mutant Alleles, and approximately 3,700 of these variants are known to cause disease. The BRCA Exchange pools variants from data resources worldwide, which should lead to inclusion of rare variants that are very occasionally observed.

With a single-point-of-access website, the BRCA Exchange provides information on these gene variants to clinicians, researchers, data scientists, patients, and patient advocates. It also serves as a demonstration project showing that this kind of comprehensive data sharing—requiring collaboration across hundreds of organizations, the establishment of an infrastructure to house the information, and the development of data-sharing protocols—is possible for other cancer predisposition genes and, indeed, for genes associated with other diseases.

Next steps for the project include collaboration with additional global data generators and data holders, continued technical development, and increased engagement with patients and patient advocates around the

world.

More information: Melissa S. Cline et al, BRCA Challenge: BRCA Exchange as a global resource for variants in BRCA1 and BRCA2, *PLOS Genetics* (2018). DOI: 10.1371/journal.pgen.1007752

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