Key Summary

BRCA Share: A Collection of Clinical BRCA Gene Variants

Article Publication

Background

- Hereditary breast cancer accounts for up to 10% of all breast cancer cases, and variants in *BRCA1* and *BRCA2* may explain 25% to 28% of the familial risk.[1,2]
- Assessment of the clinical significance of variants can be challenging, but a resource that contains clinical observations for each variant can facilitate the process. An international partnership of the French Unicancer Genetic Group and Quest Diagnostics was formed to develop such a resource.
- BRCA Share™ is a database to publicly share clinical, genetic, epidemiological, and biological data on *BRCA* variants, with a primary focus on variants of uncertain significance (VUS). The first commercial participant was Laboratory Corporation of America (LabCorp),
- **Objective:** This publication describes the methods used to create BRCA Share and the resulting contents of the database.

Methods

- The Universal Mutation Databases of the French Unicancer Genetic Group, UMD-BRCA1 and UMD-BRCA2, were augmented with *BRCA* testing results from Quest Diagnostics and LabCorp.
- The BRCA Share™ databases contain:
  - Patient information (eg, demographic information, disease status of patient and relatives)
  - Sample information (eg, de-identified subject and family identifiers)
  - Mutation information (eg, NGS screening type, variant names, mutation class)
  - Availability of cell line, tumor, or other physical materials
- The BRCA Share™ databases were first accessible to users in July of 2015: http://umd.be/BRCA1/ and http://umd.be/BRCA2/.
- Investigators compared BRCA Share databases to other collections.

Results

- At the time of the study, over 6,200 unique *BRCA* variants were contained within the databases, representing an almost 30% increase compared to that previously contained within the UMD-BRCA1/2 databases.
- Of the over 6,200 BRCA variants identified, 334 were newly identified pathogenic or likely pathogenic variants.
  - These new variants increased the total number of pathogenic or likely pathogenic BRCA variants by 20%, to a total of 1,826.
- Of the variants in both BRCA Share and ClinVar, the largest collection of BRCA variants, 74% were classified identically; none of the differences were clinically actionable (ie, a pathogenic variant categorized as benign).
- BRCA Share also allowed users of the database to resolve discordant classifications. For example, there were initially discrepancies in 148 (29%) of submitted classifications, which dropped to 37 (7%) after internal review.

Conclusions

- The public/private partnership that developed the BRCA Share databases demonstrates a data sharing model that provides rapid, free (to academic researchers) access to classification information for genetic variants.

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Webpage

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