There's an App for That: When the Meaning of a BRCA Mutation Isn't Clear-Cut

By Julie Grisham, **Monday, February 11, 2019**

A new database and mobile app called BRCA Exchange is making it easier for experts to share information about cancer-related gene mutations.

Summary

> Clinical genetics experts from MSK and other institutions have launched the BRCA Exchange. This online database shares information about individual BRCA mutations and how they might increase cancer risk.

Many people have heard that mutations in the genes *BRCA1* and *BRCA2* increase the risk of developing certain cancers, especially **breast cancer** and **ovarian cancer**. What they may not know is that the connection is not always clear-cut.

The reason is that there are many possible mutations in these genes, not just one. Not all of these changes, also known as variants, result in the same risk of developing cancer: For about 40% of BRCA mutations, the health effects are unclear. This can be confusing and stressful for the people who carry them.

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To address these unknowns, clinical genetics experts from Memorial Sloan Kettering and other institutions around the world have launched the **BRCA Exchange**. This online database shares data about BRCA mutations and what they actually mean for cancer risk. It is also available as a mobile app. People can search the database for information on *BRCA1* and *BRCA2* variants and how experts classify the risks of different mutations in real time. The creators hope that opening up the database to others in the field will lead to better classification of the variants that have an unknown risk.

“One of the nice features of the mobile app is that users can elect to receive notifications when classifications change in the future,” says **Kenneth Offit**, Chief of MSK’s **Clinical Genetics Service** and a member of BRCA Challenge, the international group that created the BRCA Exchange. The database is open sourced, but as Dr. Offit points out, it is intended primarily for those with genetic training who are interpreting results for people who have been tested.

Coping with the Unknown

When a gene contains a mutation, that means that its instructions for how to make a protein have been altered. But not all genetic mistakes lead to the same outcome.

Some may dramatically change the shape of the resulting protein, leading to a severe disruption in how the protein functions. Others may have little or no effect.

There are five categories of gene variants: benign, likely benign, uncertain, likely pathogenic, or pathogenic. Benign mutations are not cancer causing, and pathogenic ones are cancer causing. The problem is the many variants in the uncertain group. These are also called variants of unknown significance.

When a person learns they have a pathogenic BRCA mutation, doctors and genetic counselors usually recommend that they take measures to protect themselves. This often means undergoing **more frequent cancer screenings**. Many women with these mutations take medication to reduce their cancer risk. They may also choose to have surgery to remove their breasts, ovaries, or both.

But when a person learns they have a BRCA variant of unknown significance, the next steps are less clear. People are advised to turn to experts in cancer genetics for guidance. "Now, through the BRCA Exchange, experts as well as members of the informed public will have increased access to this important information," says **Mark Robson**, a clinical geneticist and Chief of MSK's Breast Cancer Medicine Service.

Concerns about how to classify variants go beyond the BRCA genes. Other genes linked to cancer are at issue as well. Last year, MSK clinical geneticist **Michael Walsh** led the development of **new guidelines** for using tumor genetic testing to classify the meaning of variants in hereditary cancer genes.

A Growing Popularity and a Growing Need for Research

The BRCA Exchange was established as a resource so doctors can review the classifications and help people understand their risk. A panel of experts in cancer genes developed the classifications. The database also provides information on gene variants to researchers, data scientists, patients, and patient advocacy groups. It already includes more than 20,000 *BRCA1* and *BRCA2* variants. As genetic testing becomes more widespread, that number will continue to grow.

Additionally, as more people get genetic testing, it is becoming increasingly important to make sure that people understand what the results mean for their own cancer risk, as well as understanding the limits of the tests themselves. To figure out the best way for people to receive this kind of health information, a team of clinical genetics experts **recently launched** the BRCA Founder Outreach (BFOR) study. The study is being spearheaded by MSK and three other cancer centers.

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Kenneth Offit
clinical geneticist

Dr. Offit is one of the leaders of BFOR. He says it’s important to get genetic testing done by healthcare providers who can help interpret the results rather than a direct-to-consumer test offered by companies like 23 and Me. In the BFOR study, individuals of Ashkenazi Jewish ancestry who are more likely to carry certain BRCA mutations are offered testing for those mutations at no cost. They access the study via a **website** and can choose to receive their results from their own doctor or another expert.

“Together, projects like the BRCA Exchange and the BFOR study are using the power and reach of the internet to empower both experts and healthcare providers to make more accurate and more accessible genetic information available,” Dr. Offit concludes.

The BRCA Exchange is partially funded by the Division of Cancer Epidemiology and Genetics at the National Cancer Institute and the Beau Biden Moonshot Act. Participants in the project have received funding from government and corporate grants in the United States and other countries. The BFOR study is funded by a number of philanthropic organizations.

Comments

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Feb 12, 2019 • 5:13 PM