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News

New finding may unlock secrets of BRCA mutations

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New research could help scientists better understand just how mutations in BRCA genes raise a person's risk of [breast](#), [ovarian](#), and other cancers.

The work could improve the accuracy of genetic tests for these mutations, and may even have implications for treatment in the future.

Repairing damaged DNA

Scientists have known for about a decade that the BRCA2 gene is involved in repairing a cell's damaged DNA. When mutations in the gene disrupt that repair process, DNA damage can accumulate, eventually leading to cancer.

A small percentage of breast and ovarian cancers are caused by [mutations in BRCA1 or BRCA2 genes](#). BRCA mutations are also linked to cancers of the pancreas, stomach, and prostate.

The new study, done by researchers at the University of California, Davis, shows exactly how the normally functioning BRCA2 gene helps repair DNA – which other proteins it interacts with and what they do. This level of detail was not known before.

The technique the researchers used to make this discovery is equally important; it opens the door to a better understanding of how different mutations in the gene may affect the DNA repair process and lead to cancer.

A window into mutations

Researchers Ryan B. Jensen, Aura Carreira, and Stephen Kowalczykowski were able to “purify” the protein coded by the BRCA2 gene in a test tube – essentially separating it from all other proteins found in cells. Isolating the protein in this way makes it much easier to see exactly how it behaves.

“Now that researchers can purify the protein, they can create a mutation in the lab and see what it does directly,” says William Phelps, PhD, director of preclinical and translational research at the American Cancer Society. The Society funded Kowalczykowski early in his career, and Jensen is currently an ACS Postdoctoral Fellow.

There are hundreds of different BRCA mutations, Phelps says. Some are known to raise cancer risk, while the significance of others is still not known. This new technique could help researchers figure out if those other mutations have consequences, and that could lead to better genetic testing down the line.

Potential for better treatment

The discovery could also help researchers develop more effective cancer treatments one day, Kowalczykowski says. Now that scientists understand how BRCA2 works, they can look for drugs that affect that mechanism and potentially make cancer cells more susceptible to treatment.

Researchers are already doing similar work with drugs called **PARP inhibitors**, which have shown some success against BRCA-related cancers (including some hard-to-treat triple-negative breast cancers) in early studies.

PARP inhibitors work on a second DNA repair path, different than the one used by the BRCA genes. In normal cells, both pathways can work to repair DNA damage. But in BRCA-related cancers, one repair pathway is already broken. PARP inhibitors block the remaining pathway, making it harder for the cancer cells to resist treatment with other drugs. Normal cells are less affected because both of their repair pathways are still intact.

The study appears in the journal *Nature*.

Reviewed by members of the **ACS Medical Content Staff**

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