Prenatal testing offers a window for finding a mother's cancer risk

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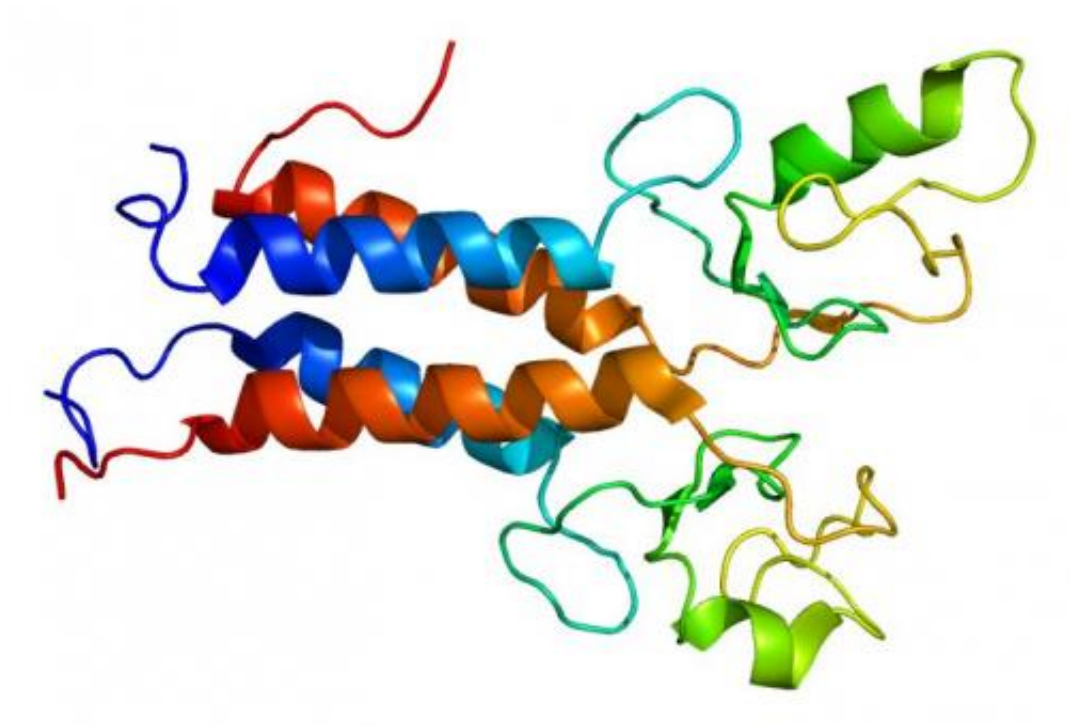

Complex Structure of the BRCA1 RING domain and BARD1 RING domain. Based on PyMOL rendering of PDB 1jm7. Credit: Emw/Wikipedia.

Harmful variants in the BRCA1 gene greatly increase a person's lifetime risk of developing breast, ovarian and pancreatic cancers, but most people are unaware they are carriers.

In a new study in the American Journal of Obstetrics and Gynecology,

researchers from Weill Cornell Medicine, Columbia University Irving Medical Center (CUIMC) and NewYork-Presbyterian explored the possibility of including BRCA1 testing at the time of obstetrical prenatal carrier screening. The researchers found that such an approach is not only cost-effective, it also can identify at-risk people at a time when cancer screening and other preventative strategies could save their lives.

An impactful point for maternal testing

Individuals who have inherited a BRCA1 gene variant have several options to reduce their cancer risk, such as enhanced screening and surgery. However, most patients only realize they are a BRCA1 carrier after they have already been diagnosed with cancer. Part of the challenge is finding when genetic testing would have the most impact. Pregnancy and obstetrical care may offer a unique window for screening and identifying patients before they develop cancer.

"Many patients will see their pediatrician as children, but once they become young adults, the next provider they see may very well be their OB/GYN when they're pregnant," said Dr. Shayan Dioun, member of the Herbert Irving Comprehensive Cancer Center (HICCC), assistant professor of obstetrics and gynecology at Columbia University Irving Medical Center (CUIMC) and first author on the paper.

"Obstetrical prenatal carrier screening is genetic testing that is primarily done to pick up mutations that affect the fetus or impact the pregnancy, but it offers an opportune time to test the mothers as well."

Simulated study demonstrates cost-effectiveness of BRCA1 testing during obstetrical care

The study simulated the clinical trajectory of a hypothetical cohort made

up of 1,429,074 pregnant patients that could have BRCA1 testing in the United States if it were added to prenatal carrier screening. That number of patients was selected based on previous research showing that 39 percent of pregnant patients undergo expanded carrier screening.

The model started with patients at age 33, based on the U.S. median age of prenatal carrier screening, and followed them until age 80, tracking the primary outcome of cost-effectiveness of BRCA1-testing at the time of obstetrical prenatal carrier screening as well as secondary outcome measures such as BRCA1 mutation positivity rates, cancer cases, cancer deaths, and direct medical costs.

The team found that adding a BRCA1 test resulted in the identification of an additional 3,716 BRCA1-positive patients, the prevention of 1,394 breast and ovarian cancer cases, and 1,084 fewer deaths. Compared to not testing for BRCA1, the addition of BRCA1 in prenatal carrier screening was cost-effective with an incremental cost-effectiveness ratio of $86,001 for every quality-adjusted life year.

"Often, individuals possess a fatalistic attitude towards cancer genetics, and believe that simply becoming aware of their genetic risk or predisposition for developing cancer is a sign that they will develop and succumb to the disease," said Dr. Melissa Frey, co-director of the Genetics and Personalized Cancer Prevention Program and an associate professor of obstetrics and gynecology at Weill Cornell Medicine.

"It is extremely important to recognize that using cancer genetics to understand one's lifetime risk for developing cancer does not increase that individual's risk profile—rather, it provides health care professionals with the tools we need to prevent cancer and save lives," said Dr. Frey, who is also senior author on the paper and a gynecologic oncologist at NewYork-Presbyterian/Weill Cornell Medical Center.

Expanding beyond BRCA1

While they only looked at BRCA1, the researchers believe that adding other hereditary cancer genes at the time of prenatal carrier screening—for example, BRCA2, RAD51C, RAD51D, BRIP1, and PALB2—could also be cost-effective. Dr. Dioun notes that typical panels given to patients at the gynecologic oncology clinics at Columbia look for mutations in over 70 genes.

"It is a minimal increase in cost for the genetic testing companies to add on more genes," said Dr. Dioun, who is also a gynecologic oncologist at NewYork-Presbyterian/Columbia University Irving Medical Center. "I would expect that there would be an even bigger benefit if all these genes were integrated. We would be picking up people with other mutations and potentially prevent them from developing other cancers."

Currently, no obstetrical prenatal carrier screening panel on the market includes BRCA1 or other hereditary breast and ovarian cancer genes. Drs. Dioun and Frey are in talks with genetic testing companies about integrating these genes into their products for women who are pregnant or planning to become pregnant.

The researchers hope to then initiate a prospective clinical trial to demonstrate feasibility and gather both patient and provider perspectives on the process.

More information: Shayan M. Dioun et al, Cost-effectiveness of BRCA1 testing at time of obstetrical prenatal carrier screening for cancer prevention, *American Journal of Obstetrics and Gynecology* (2024). DOI: 10.1016/j.ajog.2024.04.014

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