

Researchers discover BRCA1 gene is key for blood forming stem cells

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Lead co-author Dr. Victoria E. Mgbemena at work in her lab studying the BRCA1 gene in the Hematology-Oncology Division of Internal Medicine at UT Southwestern. Credit: UT Southwestern Medical Center

Researchers at from the Harold C. Simmons Comprehensive Cancer Center have found that the *BRCA1* gene is required for the survival of blood forming stem cells, which could explain why patients with *BRCA1* mutations do not have an elevated risk for leukemia. The stem cells die before they have an opportunity to transform into a blood cancer.

"One of the great mysteries in cancer research is why inherited mutations, such as those in *BRCA1*, cause cancer only in specific tissues such as the breast and ovaries, rather than in all tissues. Our data suggest a 'die or transform' hypothesis, which could explain this tissue specificity," said Dr. Theodora Ross, Professor of Internal Medicine and Director of the Cancer Genetics Program at UT Southwestern.

Additional data from this study suggest these patients may have a tougher time with the side

effects of chemotherapy.

"Patients with certain *BRCA1* mutations may be at a higher than expected risk for serious complications during chemotherapy treatment," said Dr. Ross, who holds the Jeanne Ann Plitt Professorship in Breast Cancer Research and the H. Ben and Isabelle T. Decherd Chair in Internal Medicine in Honor of Henry M. Winans, Sr., M.D. "If we confirm these clinical findings in upcoming studies, giving patients preventative antibiotics or growth factors may be necessary to lower this increased risk of treatment side effects."

The study is published in *Cell Reports*.

According to the National Cancer Institute, more than 246,660 women will be diagnosed with breast cancer and 22,280 women will be diagnosed with [ovarian cancer](#) this year. Of these, about 10-15 percent are estimated to be affected by *BRCA1* and *BRCA2* genetic mutations, Dr. Ross said.

"Our data also illustrate why rare variations in the *BRCA1* gene are not always mutations that put women and men at high risk for specific cancers. We and others have learned that most rare 'spellings' of the *BRCA1* gene, spellings we call variations of undetermined significance, are not harmful," said Dr. Ross, a member of the Simmons Cancer Center.

Dr. Ross' laboratory investigates how cells transform from normal cells to cancer cells, and how some cancer cells are able to withstand specifically targeted cancer drugs. Among her main avenues of research is the *BRCA1* gene, which - when abnormal - predisposes women to breast and ovarian cancer.

What is BRCA?

BRCA1 and *BRCA2* are human genes that produce tumor suppressor proteins which help repair

damaged DNA. When either of these genes is mutated, or altered, DNA damage may not be repaired properly. BRCA gene mutations can raise the risk for several cancers, including breast, ovarian, prostate, and pancreatic cancer.

Provided by UT Southwestern Medical Center

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