

## Study finds women with triple negative breast cancer and BRCA mutations have lower risk of recurrence

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Patients with triple negative breast cancer that also have mutations in the BRCA gene appear to have a lower risk of recurrence, compared to those with the same disease without the deleterious genetic mutation, according to researchers at The University of Texas MD Anderson Cancer Center.

The findings may offer a direction for study of personalized therapy in this select group of triple negative breast cancer patients, as well as highlight the unique need for genetic testing in a patient population. Ana M. Gonzalez-Angulo, M.D., associate professor in MD Anderson's Departments of Breast [Medical Oncology](#) and Systems Biology presented the findings in advance of the 2010 Breast Cancer Symposium.

"There is data on the number of breast cancer patients with BRCA mutations, as well as those that have triple negative disease. However, there is no understanding of the incidence of BRCA1 and 2 mutations in unselected patients with triple negative breast cancer," said Gonzalez-Angulo, the study's first and corresponding author. "Now, there are new drugs that appear to be more effective in treating triple negative breast cancer and BRCA status may be an important way of selecting patients that may respond to these therapies."

Triple negative disease - breast cancer that is estrogen, progesterone and

HER2-neu receptor negative - accounts for about 15 percent of all breast cancers. Currently, it's an area of much research focus in the breast cancer community because: it lacks effective targets effective for anti-cancer therapies; chemotherapy is only effective in about 40 percent of patients; and in those that do relapse, the disease is highly resistant and patients die quickly.

PARP inhibitors, a class of drugs of growing interest in cancer research, have shown promise in both patients with BRCA and triple negative disease. PARPs appear to be more effective in patients with BRCA mutations, as both PARP enzymes and proteins produced by the BRCA genes are involved in the repair of DNA. Therefore, the MD Anderson finding may provide an early idea of how to select those triple negative breast cancer patients that may respond best to therapy.

For this study, part of Gonzalez-Angulo's ongoing laboratory project, Molecular Characterization of Triple Negative Breast Cancer, the researchers sent both tumor and normal tissue of 77 women with triple negative disease to Myriad Genetics Inc. to identify germline (inherited) and somatic (in tumor only) BRCA mutations. Of those 77 patients, 15 (19.5 percent), were found to have mutations (14 germline, one somatic) -12 (15.6 percent) with BRCA1 and three (3.9 percent) with BRCA2.

The triple negative breast cancer patients were treated at MD Anderson between 1987 and 2006, and all but one received the same adjuvant chemotherapy regimen. The median follow-up was 43 months. The five-year relapse-free and five-year overall survival of the patients with either BRCA mutation, was 86.2 percent, and 73.3 percent, respectively, compared to 51.7 percent and 52.8 percent, respectively, in patients lacking mutations.

The researchers were surprised by the findings, however, Gonzalez-Angulo notes that prior studies conducted were case-controlled looking

at BRCA mutations carriers with all types of breast cancer. The MD Anderson study is the first to look exclusively at women with triple negative breast cancer, an unselected population.

Also surprising, the incidence of BRCA mutations in the triple negative breast cancer population was higher than expected, said Gonzalez-Angulo.

"It was interesting to find that a good portion of these women were not sent to genetic counseling - some didn't meet the criteria to be sent for testing, however they still had BRCA mutations," said Gonzalez-Angulo. "Perhaps we need to lower our threshold for patients with triple negative [breast cancer](#) for genetic counseling and to assess for mutation status - especially those under age 50 - despite not having the significant family history as others."

As a follow up, Gonzalez-Angulo plans to continue her ongoing laboratory research, with signaling pathways, RNA, DNA, and other mutations of the disease.

Provided by University of Texas M. D. Anderson Cancer Center

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