Scientists reprogram triple-negative breast cancer cells to respond to tamoxifen

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Using a small molecule decoy, investigators funded by the Samuel Waxman Cancer Research Foundation have managed to block protein interactions and induce epigenetic reprogramming in human and mouse breast cancer cells, essentially changing the gene expression of breast cancer cells to behave in a more normal manner. The research illustrates what may perhaps become an effective targeted epigenetic therapy in breast cancer. Interestingly, the targeted treatment showed exciting results in triple-negative breast cancer cells, reverting their function and appearance, and sensitizing them to tamoxifen and retinoids.

By introducing a small peptide, called the SID decoy, to interfere with protein binding in the Sin 3 PAH2 domain, scientists reduced the growth of triple-negative cancer cells by 80 percent. The decoy also blocked cancer cell invasion, which may shed light on preventing metastasis. The study was published in the June 29 print edition of the journal of the Proceedings of the National Academy of Sciences.

Triple-negative breast cancer is an aggressive form of breast cancer more commonly diagnosed in young women, African-American women and women with BRCA-1 mutated cancers, said medical oncologist Samuel Waxman, M.D., the study's senior author. Currently, the only treatment options that women with triple-negative breast cancer have are radiation therapy, surgery and chemotherapy. Women with triple-negative breast cancer do not respond to hormonal therapy or Herceptin and have a higher recurrence rate after chemotherapy.

"Hopefully, this breakthrough research means we can expand treatment options for women with triple-negative breast cancer and give them a chance at anti-estrogen hormonal therapy," said Dr. Waxman, a professor in the department of Hematology and Oncology at Mount Sinai Medical Center in New York City and the scientific director of the Samuel Waxman Cancer Research Foundation.

Arthur Zelent, Ph.D., a co-author of the study, said researchers plan to investigate small molecules that are predicted to have the same effect as the decoy peptide. "This could form the basis for a new class of targeted, epigenetic drugs in breast cancer," said Dr. Zelent, a team leader at The Institute of Cancer Research in the United Kingdom.

Elizabeth Woolfe, the executive director of the Triple Negative Breast Cancer Foundation, said though the study's results are too preliminary to make a clinical impact for cancer survivors today, she added, "The findings offer encouraging results that could lead to other promising research and the potential for new therapeutics for women facing triple-negative breast cancer."

Provided by Samuel Waxman Cancer Research Foundation