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Two specific agents worse than one in treating endocrine resistant breast cancer cells

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A new class of agents known as c-Src inhibitors is being tested in a number of different ways to treat breast cancer, but researchers at Georgetown Lombardi Comprehensive Cancer Center caution that they should not be used in combination with estrogen to treat endocrine resistant breast cancer.

That's because their new study, being reported at the American Association for Cancer Research (AACR) Annual Meeting 2012, shows that using estrogen and a c-Src inhibitor, PP2, cancel each other out. The benefit once seen in using estrogen was gone once PP2, an inhibitor of the Src-family of kinases used for laboratory studies, was added.

Instead, the findings suggest that using a c-Src inhibitor alone may offer another treatment option to estrogen-receptor-positive breast cancer patients whose tumor no longer responds to tamoxifen or aromatase inhibitors, explains the study's lead researcher, Ping Fan, Ph.D. Her research is conducted in the lab of V. Craig Jordan, OBE, PhD, DSc, FMedSci, scientific director at Georgetown Lombardi.

Most c-Src inhibitors have been approved for use in blood cancers and some are now being tested in solid cancers including breast cancer. C-Src helps control signaling pathways associated with growth, survival and cell migration, and increased activity of this protein has been observed in multiple tumor types.

The study results came about because a Georgetown Lombardi research team, led by Jordan, was testing whether a combination of estrogen and PP2, an inhibitor of c-Src used in laboratory experiments, could work synergistically to destroy breast cancer cells that no longer responded to endocrine therapy.

Clinical studies have shown that, for reasons that have not been fully explained yet, about 30 percent of endocrine resistant breast tumors respond to low doses of estrogen. The Georgetown Lombardi study was designed to see if using PP2 with estrogen could produce a stronger therapeutic outcome.

What they found was unexpected -- there was less, not more, of a killing effect when the two drugs were used together in the lab. Further investigation concluded that c-Src, one of the family of Src kinases inhibited by PP2, "is one of the important molecules in estrogen-stimulated pathways, so using an inhibitor of c-Src eliminates the beneficial effect of estrogen," says Fan.

They also found evidence that estrogen induces expression of multiple genes that act en masse to kill breast cancer cells.

"Our data suggest these two drugs should not be used together in resistant cancers," Fan says.

Provided by Georgetown University Medical Center