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HOXB7 gene promotes tamoxifen resistance

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Many postmenopausal women with early-stage breast cancers who initially respond well to tamoxifen become resistant to the drug over time and develop recurrent tumors. Johns Hopkins Kimmel Cancer Center researchers have found that a gene called HOXB7 may be the culprit in tamoxifen resistance.

Taken by mouth, tamoxifen is used at every stage of breast cancer to treat existing tumors and prevent new ones from developing. The drug works only in women whose tumor cells have a protein, called the estrogen receptor, which binds to the estrogen hormone. Tamoxifen binds to this estrogen receptor and blocks estrogen's effect on fueling cancer cells.

In experiments on cancer cells, the scientists found that when the HOXB7 gene is overexpressed, as occurs in many breast cancers, tumors cells became resistant to tamoxifen. Overexpression of HOXB7 results in proteins that interact with a series of other estrogen-activated genes and proteins, including the HER2 gene, known to make breast cancers aggressive. When the scientists knocked out the HOXB7 gene in one group of breast cancer cells, HER2 activation decreased and the cells became more responsive to tamoxifen. The scientists then showed how the HOXB7-HER2 interaction works.

"HOXB7 appears crucial in orchestrating estrogen receptors, HER2 and other receptors that promote aggressive tumor growth in breast cancer cells," says senior author Saraswati Sukumar, PhD, professor of oncology and co-director of the Breast Cancer Program at Johns

Hopkins. "Dialing down expression of the HOXB7 gene could stave off tamoxifen resistance."

Though it's not yet evident how to shut down HOXB7, Sukumar says that oncologists could potentially use the drug Herceptin to kill tumors in patients whose HER2 expression increases.

Provided by Johns Hopkins Medical Institutions

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