Researchers find breast cancer gene that's blocked by blood pressure drug

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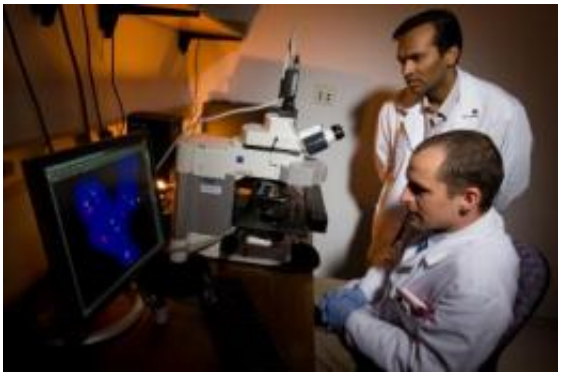

These are researchers Arul Chinnaiyan and Scott Tomlins. Credit: University of Michigan Health System

Researchers have identified a gene that is overexpressed in up to 20 percent of breast cancers and that could be blocked in the lab by a currently available blood pressure drug, according to a new study from the University of Michigan Comprehensive Cancer Center.

The gene, called AGTR1, caused normal breast cells to behave like cancer cells. This behavior was reversed by treatment with the blood pressure drug losartan. Tumors in mice that expressed AGTR1 shrunk by 30 percent eight weeks after treatment with losartan, a drug approved by the U.S. Food and Drug Administration to treat high blood pressure.

"We suspect our analysis has uncovered a new crop of potentially

important breast cancer genes. What's also exciting is this gene is blocked by a drug that's already available on the market," says study author Arul Chinnaiyan, M.D., Ph.D., director of the Michigan Center for Translational Pathology and S.P. Hicks Endowed Professor of Pathology at the U-M Medical School.

Results of the study appear online the week of June 1 in the Proceedings of the National Academy of Sciences.

The researchers looked at gene expression profiling data from nearly 3,200 microarrays available in the Oncomine database, a tool that allows rapid comparison of thousands of genes in human cancers. The researchers found genes that were dramatically overexpressed within subsets of tumors.

The gene that came up most often was ERBB2, which is better known as HER2, a gene that is overexpressed in 25 percent to 30 percent of all human breast cancers. HER2 is blocked by the targeted therapy Herceptin.

The next most commonly seen gene behind ERBB2 was AGTR1, which was seen in 10 percent to 20 percent of breast tumors. Specifically, AGTR1 was overexpressed only in tumors that were ERBB2-negative and that expressed the estrogen receptor, known as ER-positive. AGTR1 was found to be as much as 100-fold overexpressed in some tumors.

"AGTR1 is very analogous to HER2 or ERBB2. HER2 is a bona fide treatment target for patients with that type of breast cancer. This research defines a novel subtype of ER-positive breast cancer that we hope can be similarly targeted for treatment," says Chinnaiyan, a Howard Hughes Medical Institute investigator.

The researchers tested in cell cultures and in mice the effect of losartan

on AGTR1-positive tumors. When losartan was introduced, the AGTR1-positive tumors were reduced, while AGTR1-negative tumors were not affected. In the mice studies, losartan shrank AGTR1-positive tumors by 20 percent after two weeks and by 30 percent after eight weeks.

"Losartan may be a viable therapy for women with AGTR1 over-expressing breast tumors. This study lays the groundwork for a clinical trial to test losartan to treat breast cancers positive for AGTR1," Chinnaiyan says.

Researchers are discussing a possible clinical trial, but one is not currently designed or recruiting for participants.

Breast cancer statistics: 194,280 Americans will be diagnosed with breast cancer this year and 40,610 will die from the disease, according to the American Cancer Society.

Source: University of Michigan Health System (news : web)