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Researchers pinpoint genetic pathways involved in breast cancer

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Using recent advances in genomics, researchers have uncovered a genetic pathway that affects the development of breast cancer, work that could help predict which patients are at risk of relapse for the disease.

By studying which genes are expressed - or "turned on" - in breast cancer , research led by Michigan State University's Eran Andrechek uncovered a role for several members of the E2F family of genes, which control cell division and growth.

Specifically, Andrechek's team found the activation of the specific gene E2F2 was associated with a higher probability of breast cancer relapse in humans. The research team, using rodent models, also found that removing the E2F2 gene significantly decreased the likelihood of a tumor.

The findings, to be published in the journal *Cancer Research*, are available online now.

"Genomic signatures - how genes interact and via what pathways - are a rapidly growing and a powerful method to analyze specific genes in the development, recurrence and spread of breast cancer," said Andrechek, an assistant professor in the MSU Department of Physiology and lead author of the paper.

After identifying which genes are being activated, physicians can tailor treatments for breast cancer and other diseases to individuals with

certain genetic makeups. For example, breast cancer patients with over-expression of a gene called HER2 are currently treated with the antibody Herceptin, which specifically targets the cells over-expressing HER2.

"With personalized medicine, we can use predictions of how genes will interact, and based on that we can make better use of existing treatments that will have more of an impact," Andrechek said.

As part of the research, Andrechek and his team focused on tumors initiated by Myc, a gene that is amplified in 15 percent of all human breast cancer cases. The team then analyzed the tumors to test which pathways were critical to tumor growth, first in computer models and then in rodent models.

In addition to the discovery of E2F2's role in tumor incidence and relapse, the research also revealed the gene was critical for the development of a type of basal tumor. These tumors are similar to the so-called "triple negative tumors" in human breast cancer that are more prevalent among blacks and are much more difficult to treat.

The article can be viewed online at http://cancerres.aacrjournals.org/content/early/2011/01/18/0008-5472.CAN-10-2386.abstract. Other contributing authors included Kenichiro Fujiwara, Inez Yuwanita, and Daniel Hollern.

An extension of Andrechek's work has recently been funded by the Elsa U. Pardee Foundation - a Michigan organization that has given more than $113 million in grants for cancer research - to explore therapy options based on genomic profiles.

"We want to examine how we can design therapies for specific tumor types by combining genomics and current medicines," he said. "We feel this holds great promise for personalized cancer therapy."