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Researchers find genetic rearrangements driving 5 to 7 percent of breast cancers

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Researchers at the University of Michigan Comprehensive Cancer Center have discovered two cancer-spurring gene rearrangements that may trigger 5 to 7 percent of all breast cancers.

These types of genetic recombinations have previously been linked to blood cancers and rare soft-tissue tumors, but are beginning to be discovered in common solid tumors, including a large subset of prostate cancers and some lung cancers.

Looking at the genetic sequencing of 89 breast cancer cell lines and tumors, researchers found two distinct types of genetic rearrangements that appear to be driving this subset of breast cancers. The recurrent patterns were seen in the MAST kinase and Notch family genes. The findings were published online in *Nature Medicine* ahead of print publication.

"What's exciting is that these gene fusions and rearrangements can give us targets for potential therapies," says Arul Chinnaiyan, M.D., Ph.D., director of the Michigan Center for Translational Pathology, Howard Hughes Medical Institute Investigator, and S.P. Hicks Professor of Pathology at the U-M Medical School. "This is a great example of why treating cancer is so challenging. There are so many different ways genes get recombined and so many molecular subtypes, that there's not one solution that will work for all of them."

"The research provides additional evidence that these types of genetic

rearrangements seem to be a significant cause of solid tumors," he adds.

The discoveries illuminate a promising path for future research, Chinnaiyan says. Gene sequencing offers opportunities to develop treatments for individuals whose tumors carry specific genetic combinations – a process commonly known as "personalized medicine."

The study demonstrated that the genetic rearrangements had profound effects on breast cancer cells in the lab, both in tissue culture and in mouse models.

"We cloned each of these rearrangements and introduced them into normal breast cell lines, where they appeared to have cancer-causing effects," Chinnaiyan says.

Previous U-M research showed that half of prostate cancers have a genomic rearrangement that causes the fusion of two genes called TMPRSS2 and ERG. This gene fusion, believed to be the triggering event for these prostate cancers, was initially discovered in 2005 by U-M researchers led by Chinnaiyan.

Provided by University of Michigan Health System