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Breast cancer study finds new type of mutation

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Mayo Clinic researchers have discovered a new class of molecular mutation in various forms of breast cancer, a finding that may shed new light on development and growth of different types of breast tumors. Called fusion transcripts, the mutated forms of RNA may also provide a way to identify tumor subtypes and offer new strategies to treat them, investigators say.

Their study, published in the April 15 issue of Cancer Research, is the first to systematically search for fusion genes and fusion transcripts linked to different types of breast tumors.

Oncologists currently recognize three basic types of breast tumors — estrogen-receptor (ER)-positive, HER2-positive, and triple negative.

"But breast cancer is much more complex than indicated by these three subtypes, and one of the challenges of treating the disease is to identify gene markers that predict how a tumor will respond to a specific treatment," says senior investigator Edith Perez, M.D., deputy director of the Mayo Clinic Comprehensive Cancer Center in Florida and director of the Breast Cancer Translational Genomics Program, which involves researchers at all three Mayo Clinic campuses.

"The discovery of subtype-specific fusion transcripts in breast cancer represents a step in this direction," she says. "Our findings indicate that fusion transcripts are much more common in breast cancer than had been realized. They represent a new class of mutation whose role in

breast cancer is not understood at all."

"Fusion transcripts have the power to produce proteins that are relevant to tumor development, growth, and sensitivity to treatment, so we may have a brand new set of genomic changes that may help us understand, and treat, breast cancer in a new way," says E. Aubrey Thompson, Ph.D., professor of Biology at Mayo Clinic's Comprehensive Cancer Center, and co-director of the Breast Cancer Translational Genomics Program.

"This is a novel discovery that will now require additional investigation," he says. "We need to understand what these fusion transcripts and proteins are doing."

Fusion transcripts are created when chromosomes break apart and recombine, an event that commonly occurs in cancer cells. During this process, fusion genes are created when two halves of normal genes become linked. Fusion genes (DNA) create fusion transcripts (RNA), which then produce fusion proteins.

"Mistakes are made," Dr. Thompson says. "That is one of the salient properties of tumor cells, because they are defective in repairing damage to their genes."

"These mutated proteins may have an entirely new, cancer-promoting function, or they may interfere with normal cellular functions."

Fusion transcripts are common in blood cancers, such as leukemia and lymphoma. Before this discovery, however, few were found in solid cancers such as breast tumors.

Because fusion genes, transcript, and protein are generally found only in tumors, they make ideal biomarkers to identify tumor cells, Dr. Perez says.

Also, proteins produced by fusion transcripts may be relevant to tumor growth, as has been seen in blood cancers and in lung cancer, she says.

"These transcripts may mark regions of localized chromosomal instability that are linked to growth of breast cancer. If we can develop drugs against these transcripts, they will be ideal therapeutic targets," Dr. Perez says. "We have a lot of exciting work to do in the next few years."

Provided by Mayo Clinic