New class of cancer drugs could work in colon cancers with genetic mutation, study finds

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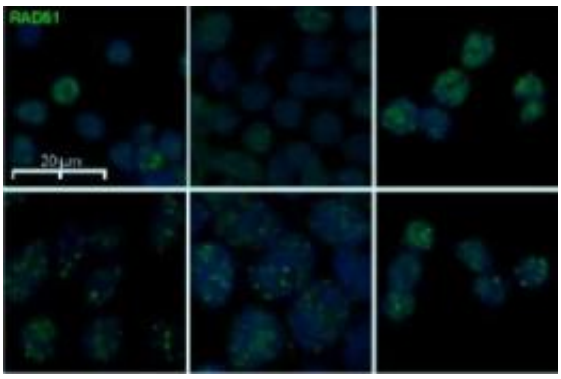

Cells with mutations in the MRE11 gene do not detect DNA damage induced after radiation. The left image represents the normal gene, the middle image represents one copy of the mutated gene, and right image represents two copies of the mutated gene. Credit: University of Michigan Health System

A class of drugs that shows promise in breast and ovarian cancers with BRCA gene mutations could potentially benefit colorectal cancer patients with a different genetic mutation, a new study from the University of Michigan Comprehensive Cancer Center finds.

Working in cell lines from colorectal cancer patients, researchers found that a new class of drugs called PARP inhibitors worked against tumors with mutations in the MRE11 gene.

About 15 percent of all colorectal cancers have what's called microsatellite instability, a type of error in the DNA. About 82 percent of those tumors have the MRE11 gene mutation.

"This is a potential broader application for PARP inhibitors, beyond breast and ovarian cancer. This is a class of drug that's already shown safety in early clinical trials and now might benefit some colorectal cancer patients as well," says lead study author Eduardo Vilar-Sanchez, M.D., Ph.D., a hematology/oncology fellow at the U-M Medical School.

The study, which was published in *Cancer Research*, also found that PARP inhibitors are even more effective when both copies of MRE11 were mutated. Each person carries two copies of each gene, which means mutations can occur in either one or both copies. The researchers suggest that PARP inhibitors could be targeted specifically to colorectal cancer patients who have two copies of the mutated gene.

Researchers are planning a phase I clinical trial to look at using PARP inhibitors in colorectal cancer patients with two mutated copies of MRE11. Future trials are being considered using PARP inhibitors to prevent colorectal cancer and other cancers in people with Lynch syndrome whose tumors have this mutation.

Microsatellite instability is also seen in prostate cancer and endometrial cancer, suggesting potential for PARP inhibitors to play a role in additional types of cancer as well, Vilar-Sanchez says, adding that more research is needed in these areas.

More information: *Cancer Research*, Vol. 71, No. 7, April 1, 2011

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