Drug duo turns on cancer-fighting gene in kidney, breast cancers

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A potentially powerful new approach to treating two lethal metastatic cancers — triple negative breast cancer and clear cell renal cell carcinoma, the most common form of kidney cancer — has been discovered by researchers at Mayo Clinic in Florida. In the online issue of Molecular Cancer Therapeutics, they report that two drugs, romidepsin and decitabine, work cooperatively to activate a potent tumor suppressor gene that is silenced in these cancers. Once the gene, secreted frizzled related protein one or sFRP1, went to work after the drugs were used, the laboratory tumor cells stopped growing and died.

Both drugs are approved by the Food and Drug Administration to treat blood cancer and are being tested individually in numerous solid cancers in which sFRP1 is disabled. This study was the first to test the use of both in these metastatic cancers linked to sFRP1, and the results are very encouraging, says senior investigator John Copland, Ph.D., a Mayo Clinic molecular biologist.

"We now have the basis for a clinical trial aimed at providing effective therapy for two drug-resistant cancers and perhaps many more tumor types in the future," Dr. Copland says. In addition to breast and kidney cancer, sFRP1 is disabled in colon, ovarian, lung, liver and other tumor types.

Dr. Copland and his colleagues earlier discovered that sFRP1 was silenced in certain cancers. This new work demonstrates that its expression can be restored by romidepsin, which is a histone deacetylase

inhibitor, and decitabine, a methyltranferase inhibitor. Both are epigenetic drugs, modifying genes in a way that affects whether they are turned on or off.

"Individually, each drug did not induce any form of cell death but, together, they killed all of the different cell lines of kidney and triple negative breast cancer that we tested in the laboratory," says lead investigator Simon Cooper, Ph.D., a Mayo Clinic molecular biologist who specializes in renal cancer.

The two cancers affect up to 80,000 Americans each year and therapies to treat both, especially when they are advanced, have been very limited, says co-author Edith Perez, M.D., deputy director of Mayo Clinic Cancer Center.

"But now, not only do we have a very promising lead on future therapy, but if this combination treatment works as we hope it does, we will have a biomarker to be able to test which patients might benefit the most," she says. "In other words, a biopsy test could identify patients whose tumors had lost sFRP1 function."

The approach to finding this potential new treatment strategy is novel, adds oncologist Michael Menefee, M.D., who is also a study co-author.

"This type of interdisciplinary preclinical research effort is important, not only because of the value of the science, but also because the drugs are already in the clinic and that will facilitate translational efforts and hopefully confirm the preclinical findings in patients with advanced malignancies," he said.

Provided by Mayo Clinic