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# Molecule's role in cancer suggests new combination therapy

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Researchers at the University of Illinois at Chicago College of Medicine have found that a molecule found at elevated levels in cancer cells seems to protect them from the "cell-suicide" that is usually triggered by chemotherapy or radiation.

The study, published online in the journal PLoS One on Feb. 29, suggests that two common cancer-fighting strategies may have "tremendous synergy" if used in combination, says Andrei Gartel, UIC associate professor of biochemistry and molecular genetics and medicine and principal investigator on the study.

Damage to a cell's DNA can set in motion a cascade of signals that triggers programmed cell death, or apoptosis. Radiation therapy and many chemotherapy agents target and damage DNA somewhat selectively in rapidly dividing cells, making them useful in fighting cancer. But many cancer cells develop resistance over the course of treatment and block the suicide pathway.

Based on the observation that a protein molecule in cancer cells called FOXM1 is elevated following DNA damage, Gartel and his co-author sought to investigate whether FOXM1 might have a role in protecting cancer cells from apoptosis.

Using human cancer cells that were exposed to either chemicals or radiation to damage DNA, the researchers used a variety of techniques to decrease the levels of FOXM1 in these cells.

"We found a significant increase in DNA-damage-induced apoptosis in cells with diminished levels of FOXM1," Gartel said. The results were the same no matter what caused the DNA damage, or what method the researchers used to reduce FOXM1.

The researchers were able to show that FOXM1 short-circuits apoptosis by suppressing the activity of another protein, JNK, which otherwise stimulates cell death, and by turning up an anti-apoptosis protein called Bcl-2.

Besides the radiation and chemotherapy drugs long used in cancer treatment, a newer class of chemotherapy agents called proteasome inhibitors has been showing promise. All known proteasome inhibitors reduce levels of FOXM1, Gartel said.

By combining standard chemotherapy drugs with proteasome inhibitors -- some of which are already FDA-approved for cancer treatment -- the drugs' effectiveness may be improved, he said.

Provided by University of Illinois at Chicago