MedicalXpress

Compound enhances cancer-killing properties of agent in trials

June 9 2010

Adding a second agent may make a new, experimental anti-cancer drug effective against a wide range of cancers, researchers at the University of Illinois at Chicago College of Medicine have found.

A man-made compound called ARC was shown by UIC researchers in 2006 to cause tumor cells to die while leaving normal cells unharmed. ARC, an acronym for its long chemical name, resembles one of the chemical building blocks of DNA. Andrei Gartel, associate professor of molecular genetics, and coworkers found it by screening more than 2,000 compounds for their ability to inhibit a key step in the cell cycle.

Now Gartel's laboratory has found that adding ARC may greatly broaden the activity of an anti-cancer agent from Abbott Laboratories that is currently in FDA trials, making it effective in killing a wide range of cancer types.

The results are published online in the journal *Molecular Cancer Therapeutics*.

In the earlier study, ARC was able to induce apoptosis, or cell suicide, in cancer cells, and only did so to a much lesser extent in normal cells, said Gartel, who is also principal author on the new study.

ARC works mainly by targeting MCL-1, a member of the Bcl-2 family of cellular molecules, which protect cancer cells from the apoptosis induced by anti-cancer drugs. Gartel and his colleagues were interested

in whether ARC might be able to improve the activity of Abbott's investigational drug ABT-737, which inhibits several other members of the Bcl-2 family, but not MCL-1.

ABT-737 alone is effective against some small-cell lung cancer cell lines and leukemia cells, but ineffective against other cancer cells, including renal and prostate cancer cell lines.

Gartel and his colleagues knew from other research that because MCL-1 has a protective effect, preventing apoptosis, ABT-737 was not effective in cancer cells with active MCL-1. They decided to see if ARC, which inactivates MCL-1, could work together with ABT-737 to kill a wider range of cancer cells.

"We found that we could use much smaller concentrations of both agents together and effectively target and kill a broad range of cancer cell lines," said Gartel. "This combination of agents shows tremendous synergy."

Reducing the dose can lessen side-effects of potential therapies, Gartel said.

The new study suggests that ARC may have potential as an anti-cancer agent in combination therapies with ABT-737, targeting an important cellular pathway, Gartel said.

Provided by University of Illinois at Chicago