

New boost for pancreatic cancer therapy

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Scientists at Fox Chase Cancer Center are developing a new way to treat pancreatic cancer by boosting the effects of gemcitabine (Gemzar)—the chemotherapy drug that is considered standard therapy for the disease. Although gemcitabine is the first line of defense against pancreatic cancer, many cells find ways to evade the treatment. The new research, which will be presented at the AACR Annual Meeting 2012 on Monday, April 2, found several compounds that appear to improve the cancer-killing effect of gemcitabine.

After a diagnosis of [pancreatic cancer](#), only 5 % of people live beyond five years—so any technique that boosts the effects of the current regimen could have a major impact on survival.

"Although gemcitabine can successfully kill many pancreatic cancer [cells](#), using it as a single agent hasn't really been effective because there are still a small percentage of cells that develop some kind resistance to the drug," says study author Neil Beeharry, Ph.D., a postdoctoral associate in the lab of Tim J. Yen, Ph.D., also first author on the paper, at Fox Chase Cancer Center in Philadelphia. "I think finding this 'X factor' is really going to enhance our ability to treat patients."

During the study, Beeharry, Yen and their co-authors Jeffrey R. Peterson, Ph. D. and Lauren Fink, Ph. D., searched for compounds that would boost the effects of gemcitabine by targeting those resistant cells. They started with kinase [inhibitors](#)—a class of drugs that target enzymes known as kinases—which play an important role in cancer and other cellular processes. As a result, kinase inhibitors are increasingly being

used to treat various types of cancer.

They first exposed a pancreatic cell line to gemcitabine, then to 160 kinase inhibitors. Most of the kinase inhibitors either didn't do anything or killed cells that hadn't been exposed to gemcitabine and therefore had no resistance to it, suggesting they might be harmful to normal cells. However, a small percentage—around 5%—did not kill cells that hadn't been treated by gemcitabine, but did appear to hurt the cancer cells that were treated with gemcitabine. This suggested these compounds were specifically targeting only those cells affected by gemcitabine.

The researchers then looked up these inhibitors in a first-of-its-kind database established last year by Fox Chase scientist, Jeffrey R. Peterson, Ph.D. (also co-author on the paper) and colleagues, which catalogued the effects of nearly 200 kinase inhibitors. By using this database, they learned the cellular pathways targeted by these specific inhibitors— information which may one day help doctors customize therapies even further, says Beeharry.

Ultimately, by boosting the effects of [gemcitabine](#), a complementary kinase inhibitor may enable doctors to administer a lower dose of chemotherapy, with fewer side effects.

Ideally, researchers will develop a similar approach to improve the effects of other chemotherapy drugs for particularly deadly cancers, such as platinum-based treatments for ovarian cancer, Yen explains. "The field is moving towards this rationally designed approach, using standard therapy and a booster," he says.

Provided by Fox Chase Cancer Center

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