

Combination therapy may enhance gemcitabine activity

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Oncologists who treat patients with pancreatic cancer may be one step closer to understanding why gemcitabine, the only currently available treatment, works in some cases but not in others, according to a paper in *Cancer Discovery*, a journal of the American Association for Cancer Research.

David Tuveson, M.D., Ph.D., a professor of pancreatic cancer medicine at the University of Cambridge, utilized a laboratory model to test the combination of [gemcitabine](#) and nab-paclitaxel in pancreatic cancer.

"The combination has shown promise in an early clinical trial, and clinical results from a pivotal phase III trial will be reported in 2013," said Tuveson. "However, we know very little about the mechanism of action because tumor samples have been so small."

Using a laboratory model of metastatic pancreatic [ductal adenocarcinoma](#), the researchers showed that combination treatment increased intratumoral gemcitabine levels due to a marked decrease in the primary gemcitabine metabolizing enzyme, cytidine deaminase.

[Paclitaxel](#) appeared to reduce these levels through reactive oxygen species-mediated degradation, resulting in increased stabilization of gemcitabine. Tuveson said understanding these mechanisms of action are important and will lead to better administration of the therapeutic combination if the larger human trials prove positive.

"For example, we predict from this mechanistic study that nab-paclitaxel may be most effective if we administer it first, and delay administration of the gemcitabine. The next step is to test this prediction, since it could help a great deal with patient treatment," said Tuveson.

Provided by American Association for Cancer Research

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