

## New drug blocks pancreatic cancer growth

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A newly developed drug can prevent the most common type of pancreatic cancer from growing and spreading in laboratory mice, according to a study led by Cedars-Sinai.

The study, published recently in the journal *Gastroenterology*, also demonstrated in mice that the drug, called Metavert, may prevent patients from developing a resistance to currently used pancreatic cancer chemotherapies.

"This is an exciting step toward improving survival rates in pancreatic cancer patients," said study lead author Mouad Edderkaoui, PhD, assistant professor of Medicine and Biomedical Sciences at the Samuel Oschin Comprehensive Cancer Institute at Cedars-Sinai.

"If the results are confirmed in humans, we could have a drug with the potential to significantly extend the lives of patients with pancreatic ductal adenocarcinoma (PDAC), which is very difficult to treat."

Ninety-five percent of pancreatic cancer patients are diagnosed with PDAC, which develops from cells lining small tubes in the pancreas. PDAC can be difficult to treat because the cancer cells prompt normal cells that reside in the pancreas--called stellate cells--to produce pancreatic scar tissue.

Scar tissue makes it difficult for chemotherapy agents and blood to enter the pancreas, said study senior author Stephen J. Pandol M.D., director of Basic and Translational Pancreas Research at Cedars-Sinai.

The cancer and stellate cell interaction also creates an environment that stimulates local tumor growth and cancer spread to distant sites in the body, said Pandol, a professor of Medicine at Cedars-Sinai. Additionally, the activity levels of certain enzymes rev up, fueling resistance to cancer treatments.

"I've seen patients who respond to therapy for a while, and then the disease takes off because the cancer becomes smart--it

blocks chemotherapy from working," Pandol said. "Metavert targets that action."

Over a four-year period, the investigators designed and synthesized new chemicals that inhibit cancer cell activity. They discovered that Metavert blocked drug resistance and also significantly boosted the positive effects of radiation and two chemotherapy agents commonly used in humans. In one of the mouse studies, Metavert increased the survival rate by about 50 percent.

The investigators currently are developing a version of the drug to test in humans, Pandol said.