

Combination Therapy For Pancreatic Cancer

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BACKGROUND

Pancreatic cancer is an aggressive disease with limited treatment options and a high mortality rate. Pancreatic cancer is the 3rd leading cause of cancer death in the United States; despite some recent advances in systemic therapy, survival remains dismal in large part due to its profound drug resistance and its propensity for early metastasis. Typically, diagnosis of pancreatic cancer occurs only with advanced stages of the disease since there are currently no early markers for detection. Individuals with pancreatic cancer have a poor prognosis due to the late diagnosis, the extent of metastasis, and ineffective treatments. Survival rates are dismal and pancreatic cancer is not typically responsive to radiation and chemotherapy. An alternative approach for the treatment of pancreatic cancer as well as the design of a new class of therapeutics that can be used to treat this devastating disease is an immediate unmet medical need.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego identified unique combinations of drugs that together lead to very effective killing of pancreatic cancer cells and elicit rapid and nearly complete tumor regression in preclinical models.

APPLICATIONS

Early attempts to starve cancer cells to death as a therapeutic strategy had focused on the use of various autophagy inhibitors. However, we found that treatment of pancreatic cancer cells with autophagy inhibitors result in rapid development of acquired drug resistance due to activation of an alternative nutrient procurement pathway. We identified the mechanism responsible for activation of this novel survival pathway and have shown that its inhibition using clinically approved compounds, that can be subjected to further refinement, in combination with inhibition of autophagy results in rapid and near complete regression of human pancreatic cancer grown in mice

ADVANTAGES

Several potent inhibitors of autophagy have been developed but none of them is very efficacious *in vivo* due to rapid development of drug resistance. Inhibitors of the alternative nutrient procurement pathway we identified overcome this resistance mechanism. While drugs that inhibit the alternative nutrient procurement or block its induction in autophagy-inhibited cells have already been used individually in cancer no one has attempted to combine them with autophagy inhibitors and nobody has tested whether such combinations elicit efficacious tumor regression *in vivo*.

STATE OF DEVELOPMENT

The invention has been reduced to practice in preclinical models and cell cultures of human pancreatic cancer.

INTELLECTUAL PROPERTY INFO

The invention is patent-pending and is available for licensing and collaborations.

PATENT STATUS

Patent Pending

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OTHER INFORMATION

KEYWORDS

Pancreatic cancer, autophagy

inhibitors, cancer nutrient

procurement, tumor regression,

animal models of cancer, cancer

metabolism

CATEGORIZED AS

- **Medical**
- Disease: Cancer
- Therapeutics

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