

To starve pancreatic tumors, researchers seek to block 'self-eating,' other fuel sources

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To get the extra energy they need to fuel their uncontrolled growth, cancer cells break down some of their own parts for fuel - a process known as autophagy, or "self-eating." Researchers from the University of North Carolina Lineberger Comprehensive Cancer Center found a possible therapeutic strategy to block self-eating in one of the deadliest cancers, as well as to cut off the tumor's other energy sources.

The researchers are reporting preclinical <u>findings</u> for a potential two-treatment strategy to block multiple mechanisms of <u>cancer</u> cell metabolism in pancreatic cancer at the American Association for Cancer Research Annual Meeting in Chicago. The findings will be presented from 8 a.m. to noon on Wednesday.

"We know that <u>cancer cells</u> have a greater need for energy than normal <u>cells</u>," said UNC Lineberger's Channing Der, PhD, Sarah Graham Kenan Distinguished Professor in the UNC School of Medicine Department of Pharmacology.

"They get their energy by changing normal metabolic processes to allow them to generate more energy, and one of these processes is self-eating. Basically what a cancer cell does is it does this more efficiently than a normal cell."

In other studies, pancreatic cancer cells have been known to rely more heavily on autophagy, but UNC Lineberger scientists reported evidence that a type of treatment—an ERK inhibitor—actually increased their



reliance on this. The researchers believe the compound prevents the cell from relying on other energy sources, driving it toward autophagy.

"The cancer cell has many ways to achieve what it wants in terms of getting more energy," Der said. "We find that if you try to stop one, a cancer cell has the ability to compensate. I think the analogy many of us use is the 'whack-a-mole' concept where you knock one thing down, and something else pops up. We need more than one hammer basically."

To block multiple energy sources at once, the researchers used an ERK inhibitor to cut off these other <u>energy</u> sources, alongside with an investigational compound used to block <u>autophagy</u>, in the hopes of starving the cells completely. They reported at AACR that this cotreatment showed a synergistic effect.

"What if we could cripple more than one <u>energy sources</u> for the cell at once?" Der said.

Provided by UNC Lineberger Comprehensive Cancer Center

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