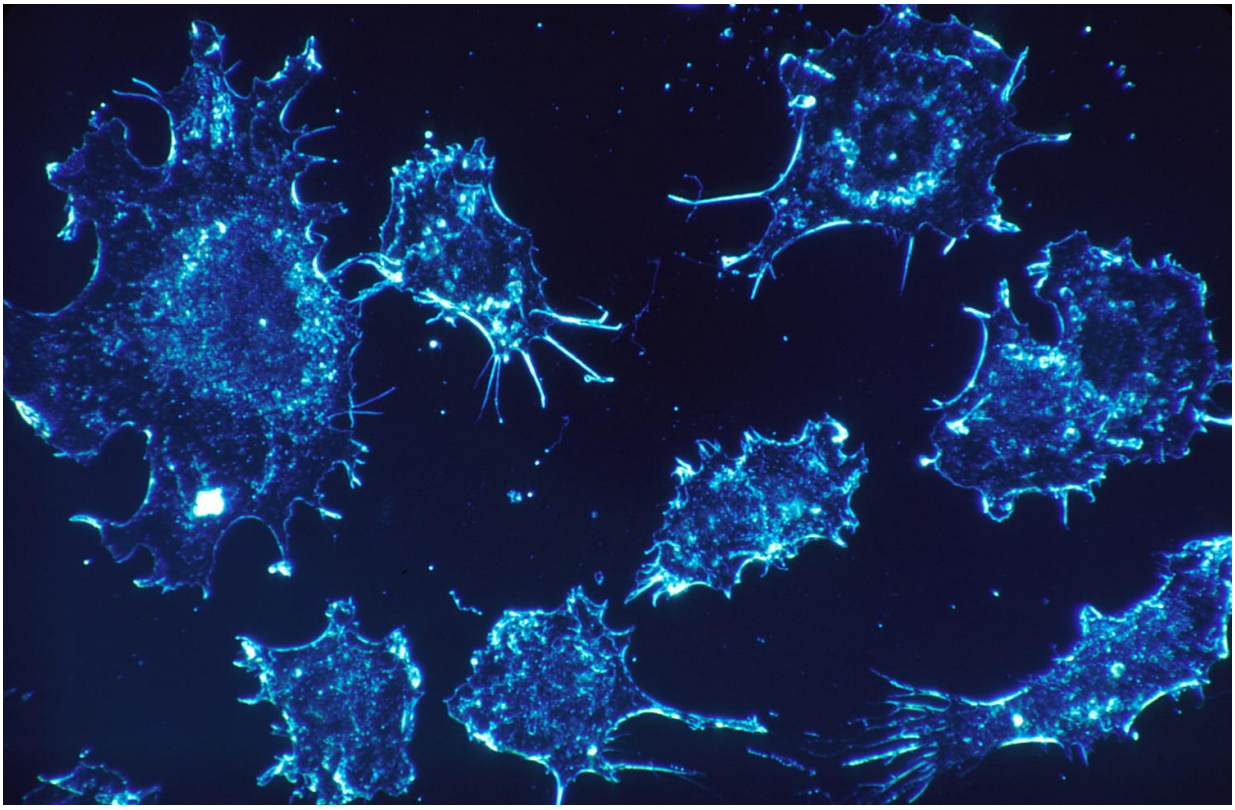
MedicalXpress

Promising new pancreatic cancer treatment moves forward

March 4 2019



Credit: CC0 Public Domain

Even among cancers, pancreatic cancer is an especially sinister form of disease. The one-year survival rate is extremely low, and treatment progress has lagged behind that of many other malignancies.

A study published today in the journal *Nature Medicine* led by researchers at Huntsman Cancer Institute (HCI) at the University of Utah (U of U) describes a new therapeutic approach with potential for patients with pancreatic cancer. These researchers discovered a combination drug therapy that may effectively combat the disease. HCI researchers first observed anti-cancer impacts in a laboratory setting and, subsequently, in its first use in a human patient.

The study has already progressed to a clinical trial that is now open at HCI and will soon be open at other sites in the United States. Details about the clinical trial, called THREAD, are available under National Clinical Trial Number 03825289. The combination therapy uses two drugs already approved for use by the Food and Drug Administration for other diseases, including cancer. The new drug combination is administered through pills taken orally.

Pancreatic tumors are characterized by mutations in a gene called KRAS. When KRAS is mutated in this way, it sends constant signals that promote abnormal cell division and growth in cancer cells. As a result, tumors grow out of control. At the same time, like all cells, pancreatic cancer cells must recycle their components to provide building blocks for new growth in an essential cell function known as autophagy. Previous studies to combat pancreatic cancer that were focused either on the role of KRAS or on impacting autophagy were not effective.

The new HCI study, using an approach that simultaneously targets both abnormal KRAS signaling and the autophagy process, shows a strong response in mouse models and may be a promising therapy for patients with pancreatic cancer. Conan Kinsey, MD, Ph.D., a physician-scientist at Huntsman Cancer Institute and the Department of Internal Medicine at the U of U and Martin McMahon, Ph.D., a cancer researcher at HCI and Professor of Dermatology at the U of U, led the study.

"We were able to observe that the combination of these two drugs—which, when used individually, don't have much of an impact on the disease—appears to have a very potent impact on the growth of pancreatic cancer," says McMahon. "We have observed this in the lab in petri dishes, then in mouse models, and now in a pancreatic cancer patient on a compassionate use basis. Indeed, we proceeded from a petri dish to a patient in less than two years—a timeline that is rarely seen in medical science."

The HCI-led research is bolstered by a separate study published in the same issue of the journal. This study outlines complementary findings regarding the effects of autophagy in pancreatic cancer in the laboratory setting and was led by Channing Der, Ph.D., Sarah Graham Kenan, Ph.D., and Kirsten Bryant, Ph.D., at the University of North Carolina (UNC) Lineberger Comprehensive Cancer Center. McMahon and Der learned about the parallel nature of their research programs at a scientific meeting one year ago. Given the critical need for advances in pancreatic cancer therapies and the promise of their collective findings, they worked together to push their studies forward on a companion basis.

"In our paper, we show the response of a pancreatic cancer patient who had received surgery and multiple lines of chemotherapy prior to this combination," said Kinsey, who was also the patient's physician. "This patient, who has since succumbed to the disease, nevertheless had a remarkable response to these drugs for several months. We need to carefully evaluate this new combination therapy in the context of clinical trials to better understand if good responses might be seen in multiple patients. We also need to identify the specific features of any patient who may benefit, before any recommendation can be made about use on a larger scale."

These preliminary findings are being rigorously scrutinized in clinical

trials to observe and understand whether the combination of these drugs is safe and effective for pancreatic cancer patients. The trial is underway at HCI and is underway or planned at the University of California, San Francisco, and Columbia University in New York.

More information: Protective autophagy elicited by RAF→MEK→ERK inhibition suggests a treatment strategy for RAS-driven cancers, *Nature Medicine* (2019). DOI: 10.1038/s41591-019-0367-9 , www.nature.com/articles/s41591-019-0367-9

Provided by Huntsman Cancer Institute