

Drug combination domino effect destroys pancreatic cancer cells

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(Medical Xpress) -- Cancer Research UK scientists have revealed how a combination of two very different drugs – currently being tested in clinical trials – amplifies the destruction of pancreatic cancer cells, according to research published in the [Journal of Experimental Medicine](#), today.

The team at Cancer Research UK's Cambridge Research Institute showed in mice that combining a chemotherapy [drug](#) called gemcitabine with an experimental drug called MRK003 sets off a chain of events that ultimately kills cancer cells – multiplying the effect of each drug on its own.

This drug combination is being tested in a clinical trial managed by Cancer Research UK's Drug Development Office in partnership with Cambridge University Hospitals Foundation Trust.

The research showed that MRK003, a gamma secretase inhibitor, blocks an important cell signalling pathway called Notch in both [pancreatic cancer](#) cells and the endothelial cells that line the blood vessels supplying tumors with essential nutrients.

The addition of MRK003 to gemcitabine – a drug used commonly in patients with pancreatic cancer – increased the ability of gemcitabine to destroy tumors.

Study author, Professor David Tuveson, group leader at Cancer Research

UK's Cambridge Research Institute, said: "This research is a real example of how research taking place in the lab directly influences decisions made in the clinic to improve treatment for patients.

"We've discovered why these two drugs together set off a domino effect of molecular activity to switch off cell survival processes and destroy pancreatic [cancer cells](#)."

The Cancer Research UK clinical trial is led by Duncan Jodrell, Professor of Cancer Therapeutics at the University of Cambridge.

Professor Jodrell, said: "We're delighted that the results of this important research are now being evaluated in a clinical trial, to test whether this might be a new treatment approach for patients with pancreatic cancer, although it will be some time before we're able to say how successful this will be in patients."

Father-of-two Richard Griffiths, 41, from Coventry, has been on the trial since being diagnosed with pancreatic cancer in May 2011. "Being told that I had cancer was devastating and it immediately made me worry about the future," he said.

"I have a close group of family and friends and I have had great support from this network, and my work have been very supportive too.

"After I was diagnosed, I was told about the trial and came to Cambridge to meet the team. I was given a lot of information and agreed to take part in this trial. It was mentioned that it was funded by Cancer Research UK and, as I go through the treatment, I have really come to appreciate how important that money is.

"After six cycles of treatment, a scan showed the tumors had reduced and so I have continued with the treatment. The trial gives you hope – I

really feel I can do this with the science behind me.”

Around 8,000 people in the UK are diagnosed with pancreatic cancer each year and the disease is the fifth most common cause of cancer death in the UK. Although the one-year survival rate for pancreatic cancer has more than doubled since the 1970s, the rate is still low with fewer than one in five patients surviving their disease for more than a year after diagnosis.

Dr. Julie Sharp, senior science information manager at Cancer Research UK, said: “This discovery shows how investigating the cell pathways involved in cancer can reveal new approaches to tackle the disease.

“There’s an urgent need for new drugs for pancreatic cancer. The disease is often not diagnosed until it has spread, making it very difficult to treat.

“Cancer Research UK previously funded the largest ever trial for people with operable pancreatic cancer, which led to a worldwide change in the way the disease is treated, helping to improve survival. But there is much more to be done.

“We’re prioritising research into pancreatic cancer, and other cancers where survival still remains low, aiming to save more lives in the future.”

More information: *Journal of Experimental Medicine*. Gamma Secretase inhibition promotes hypoxic necrosis in murine pancreatic ductal adenocarcinoma. Cook et al.

Provided by Cancer Research UK

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