New 'chemotherapy booster' could treat lung and pancreatic cancer

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A new drug that blocks cancer's escape route from chemotherapy could be used to treat deadly lung and pancreatic cancers, research has revealed.

Scientists at Newcastle University have been part of a study that has shown in human cancer cells and in mice that the drug, discovered at The Institute of Cancer Research, London, boosts the effectiveness of conventional chemotherapy.

The drug, known as CCT245737, is scheduled to begin first-in-human clinical trials in patients with lung and pancreatic cancers - two cancers with low survival rates that continue to resist currently available treatments.

The new study is published today in the journal *Oncotarget*, and was funded by Cancer Research UK and Sareum Limited.

The research, conducted at The Institute of Cancer Research in collaboration with colleagues at Newcastle University and the drug discovery company Sareum Ltd, shows the effectiveness of a new class of drugs called CHK1 inhibitors that can be delivered orally to patients.

Most chemotherapies work by damaging the DNA of rapidly dividing cells. But in response, cancer cells activate a molecule called CHK1 which delays cell division and gives cancer cells time to repair their damaged DNA.

Scientists hoped that blocking CHK1 could stop cancer cells from repairing DNA damage and prevent them from becoming resistant to the cell-killing effects of chemotherapy.

Researchers developed techniques to assess the method of action of CCT245737 in human cancer cell lines, and demonstrated that it potently blocked the molecule CHK1.

They also assessed CCT245737 in combination with chemotherapy in mice with tumours grown from human cancer cell lines, and found it achieved much greater anti-cancer activity than chemotherapy alone. Importantly, the mice did not experience any additional toxicity of the combined drugs and remained at a constant weight throughout the treatment.

Understanding cancer development

Professor Neil Perkins, who works at Newcastle University's Institute for Cell and Molecular Biosciences, said: "Research in my laboratory is aimed at understanding the basic mechanisms underlying cancer development and the response to therapy. I have been very happy to collaborate with researchers at The Institute of Cancer Research in the preclinical development of the Chk1 kinase inhibitor CCT245737.

"This is an exciting new drug with potential to make a difference in the treatment of many types of cancer. We hope that our research will help its use in the clinic."

Researchers also found that the CHK1 inhibitor could be used alone, without additional chemotherapy, to treat a type of blood cancer called lymphoma because this cancer type sustains heavy DNA damage during its formation.

Dr Jill Hunter, from Newcastle University's Institute for Cell and Molecular Biosciences, has been part of the research group.

She said: "It has been very exciting to be involved in this project. My work showed that CCT245737 might have uses for the future treatment of some types of B-cell lymphoma.

"I am currently looking at the mechanisms through which cancer cells respond to drugs of this type and I hope that my research will continue to help in the application of new types of anti-cancer

therapies."

It is possible that CHK1 inhibitors such as CCT245737 – which was designed and synthesised at the ICR with funding from Cancer Research UK – could be used on their own to treat other types of cancer with similar levels of DNA damage.

It is hoped that clinical trials of the new drug will show it to be an effective chemotherapy booster in lung and pancreatic cancers, which readily become resistant to current treatments.

Ian Collins, Professor of Medicinal Chemistry at The Institute of Cancer Research, London, said: "We're excited that our new CHK1 inhibitor, which was discovered at the ICR in collaboration with Sareum Limited, is progressing towards first-in-human clinical trials."

More information: "The clinical development candidate CCT245737 is an orally active CHK1 inhibitor with preclinical activity in RAS mutant NSCLC and Eμ-MYC driven B-cell lymphoma." www.impactjournals.com/oncotar … cle&op=download&path %5B%5D=4919&path%5B%5D=11234

Provided by Newcastle University