Drug shrinks lung cancer tumors in mice

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Small cell lung cancer can be difficult to treat with standard chemotherapy.

(PhysOrg.com) -- A potential new drug for lung cancer has eliminated tumours in 50% of mice in a new study published today in the journal *Cancer Research*. In the animals, the drug also stopped lung cancer tumours from growing and becoming resistant to treatment. The authors of the research, from Imperial College London, are now planning to take the drug into clinical trials, to establish whether it could offer hope to patients with an inoperable form of lung cancer.

One in five people with lung cancer have small cell lung cancer and only three per cent of these people are expected to survive for five years. With this form of lung cancer, tumours spread quickly so it is rarely possible to remove the tumours surgically. Because of this, small cell lung cancer is treated with chemotherapy, with or without additional

radiotherapy. Initially, the treatment often appears to work, reducing the size of the tumours. However, the tumours usually grow back rapidly and then become resistant to further treatment.

The researchers behind today's study have identified a drug that, in some mice, was able to completely shrink tumours away. In the mouse models, it was also able to stop tumours from growing and it helped other forms of chemotherapy to work more effectively. If the drug proves successful in humans, the researchers hope that it could help patients with this kind of lung cancer to live longer.

In small cell lung cancer, tumours spread quickly because the tumour cells grow and divide faster than normal cells. Previous research carried out by the Imperial team showed that these tumour cells proliferate faster because they are fuelled by a growth hormone called FGF-2. This growth hormone also triggers a survival mechanism in the tumour cells that makes them become resistant to chemotherapy.

In today's study, the researchers looked at the effect of a drug called PD173074, which blocks the receptor that FGF-2 uses to attach to the tumour cells. The drug stopped cancer cells from proliferating and from becoming resistant to treatment in 'test-tube' laboratory models. In one animal model of small cell lung cancer, the drug eliminated tumours in 50% of mice and in a second, similar mouse model, the drug enhanced the effect of standard chemotherapy.

Professor Michael Seckl, corresponding author of the study who heads the Section of Molecular Oncology and Lung Cancer Research at Imperial College London, said: "Lung cancer is the most common cancer killer in the world and over 100 people in the UK are diagnosed with the disease every day. Around one in five of those people will have small cell lung cancer. Although it responds to chemotherapy initially, the tumours soon become resistant to treatment and sadly nearly all people

with the disease do not survive.

"We urgently need to develop new treatments for this disease. Our new research in mice suggests that it may be possible to develop the drug PD173074 into a new targeted therapy for small cell lung cancer. We hope to take this drug, or a similar drug that also stops FGF-2 from working, into clinical trials next year to see if it is a successful treatment for lung cancer in humans. An added bonus of this drug is that it could be taken orally, which would make it less invasive than some other forms of cancer therapy," added Professor Seckl.

The researchers first studied the effect of PD173074 in the lab, on cells taken from human tumours. The drug stopped cells from proliferating and prevented FGF-2 from triggering their survival mechanism, so the cells could be killed with standard chemotherapy agents. The effect of the drug was dose-dependent, so the more drug the researchers added to the cells, the less the cells proliferated.

The researchers then studied PD173074 in mice using two different types of human small cell lung cancer tumours. They tested the drug on its own and alongside the standard chemotherapy agent cisplatin, which is frequently used to treat patients with the disease. In the first mouse model, PD173074 given on its own killed off tumours in 50 per cent of the mice and these mice remained disease-free for at least one year. In the second mouse model, both PD173074 and cisplatin alone slowed down tumour growth. When the drugs were combined, they slowed down tumour growth significantly faster than either drug on its own.

The researchers also used PET scanning to show that the drug reduced DNA synthesis in the tumours, which indicates that the drug was preventing cell proliferation. The researchers also found that the rate of cell death, or apoptosis, in the tumours increased after the drug was given to the mice.

PD173074 was developed in 1998 to stop blood vessels from forming around tumours. Today's research is the first to show this drug has a therapeutic effect on tumours in mice.

Source: Imperial College London (news : web)