

Blocking 'lock and key' site of lung cancer proteins could lead to new treatments

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A Cancer Research UK study reveals that stopping two essential lung cancer proteins from joining together at their 'lock and key' site could lead to new treatments for the disease. The research is published in the journal *Cancer Cell*.

Looking at [lung cancer](#) in mice who have faults in their RAS protein – a fault responsible for around 20 per cent of lung cancers – the scientists found they could put the disease to 'sleep' by blocking the 'lock and key' site at which another protein called PI3-kinase joins with RAS.

And the researchers, from Cancer Research UK's London Research Institute, were able to significantly shrink the lung tumours by combining their new molecular blocker with a drug called trametinib. This [drug](#) stops RAS activating another important pathway that it

controls in lung cancer.

Professor Julian Downward, [lead](#) researcher based at the Cancer Research UK London Research Institute, said: "Around 20 per cent of lung cancers are caused by faults in the KRAS gene which codes for RAS proteins. These faulty RAS proteins are predominantly caused by smoking and are at the heart of some lung cancers making cancer cells grow out of control.

"But no drugs have been developed that can target them leading to it being termed 'undruggable'. We hope that casting new light on how to stop RAS from joining with other proteins that are needed to keep lung cancers alive could one day lead to [new drugs](#) to treat the disease."

This study overcomes a major challenge in developing targeted drugs that hit RAS proteins and the mechanisms involved. Previous research has tried to stop them from working entirely by switching the whole [protein](#) off but this has failed as it also affects healthy cells, causing severe side-effects.

By specifically blocking the 'keyhole' site where the two proteins join the researchers hope that any new drugs would have fewer side-effects.

Professor Nic Jones, Cancer Research UK's chief scientist, said: "The complexity of lung cancer means that it remains a major challenge for researchers to develop new and effective drugs for the disease. Research like this is part of our commitment to support more research into lung cancer so that we understand more about the disease in the hope that it will lead to new treatments and save more lives."

More information: Castellano, E., et al. Requirement for interaction of PI3-Kinase p110 α with RAS in lung tumor maintenance. *Cancer Cell* (2013)

Provided by Cancer Research UK

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