# New target for lung cancer identified

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Researchers have uncovered a key part of a chain reaction of signals that tell some lung cancers to grow. This new insight into a major cancer signalling pathway could prioritise new drug targets.

Using lung cancer cells from patients, researchers from The Institute of Cancer Research, London [5], and The Royal Marsden NHS Foundation Trust [6] analysed a network of signals called the PI3K signalling pathway. The pathway usually sends signals that regulate the natural cell cycle but it is often mutated and hijacked in a range of cancers, including lung cancer.

The study was published in *Oncology* [7] and received funding from Cancer Research UK [8], the Experimental Cancer Medicine Centre and the National Institute for Health Research Biomedical Research Centre [9].

Non-small cell lung cancer (NSCLC) makes up around 80% of all lung cancers and the PI3K signalling pathway is known to play a role in the development of some of these tumours. However, the exact genetic changes that corrupt the signal and drive these lung cancers are not known.

Researchers homed in on a specific segment of this signalling pathway by analysing key proteins along it, called AKT, S6K and GSK3?, to see if their activation spurred cancer into action.

## Link with shortened survival

Thirty eight patients with advanced NSCLC were enrolled into the study. Cancer cells from fluid that had built up around the lungs and needed to be drained were analysed. The researchers assessed the proteins that were activated in the mutated PI3K pathway and explored the relationship between specific genetic alterations and patient survival.

Researchers found that patients with higher levels of phosphorylated (active) S6K had shortened survival, making this protein a critically important target in NSCLC. There was a correlation between activated AKT and S6K, but not between activated AKT and GSK3?. This suggests that S6K signalling is dependent on AKT signalling, while GSK3? is not tightly

regulated by AKT.

Dr Udai Banerji [10], Reader in Molecular Cancer Pharmacology at the ICR, who led the study, said: ?Non-small cell lung cancer is difficult to treat. This link between the protein S6K and worse survival outcomes shows us that it could be an important target.

"We also revealed that activation of GSK3? can happen independently of the other proteins to drive cancer?s growth. We currently use drugs that inhibit the PI3K pathway and activation of the AKT protein to slow cancer?s progress. If cancer can overcome this by rerouting its signals through the GSK3? protein, it could be a possible path that enables resistance to drug treatment.?

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**Links**
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