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Promising strategy for treatment of lung cancer

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A research team at the Sahlgrenska Academy at the University of Gothenburg, Sweden, has shown in a study that two closely related enzymes could be targets for the treatment of lung cancer. The discovery was made when the researchers blocked the production of the two enzymes in transgenic mice. This resulted in inhibition of cell growth, fewer tumours and greater survival among the mice.

The article is being published in the journal Proceedings of the National Academy of Sciences (*PNAS*). With many types of cancer, the growth and spread of tumours is stimulated by Ras and Rho proteins. For these proteins to function, they need to be modified by the closely related enzymes FT and GGT. A number of pharmaceutical companies have therefore developed substances that reduce the activity of these two enzymes with the aim of inhibiting the function of Ras and Rho proteins and so slowing the development of the disease.

However, treatment with various substances to block these two enzymes has often been non-specific, and their efficacy has varied widely. This has made it difficult for researchers to assess the true potential of these enzymes as targets for medicines.

"We therefore developed genetic strategies in mice, known as transgenic mice, to switch off the genes coding for FT and GGT, enabling us to investigate whether a complete blockade of FT or GGT can inhibit the development of lung cancer, and whether this has side-effects in the lungs," explains researcher Anna-Karin Sjögren, who led the study

together with Meng Liu, both from the Department of Clinical and Molecular Medicine.

In their study, the researchers used transgenic mice which produce a mutated Ras protein that causes lung cancer. First, production of FT or GGT in these mice's lungs was stopped by switching off the relevant genes.

"When we turned off the FT gene, the mice developed fewer lung tumours and lived longer," says Meng Liu. "At cellular level, the blockade of FT meant that the tumour cells were no longer able to divide. When we blocked the production of GGT, we saw the same effects: inhibition of cell growth, fewer lung tumours and improved survival."

In experiments where both genes were switched off at the same time, the number of lung tumours dropped sharply and the mice lived much longer. This means that the absence of these two enzymes does not have any obvious side-effects in the lungs, and that lung tumour cells seem to be more sensitive to the treatment than normal lung cells.

"Our findings show that FT and GGT are promising targets for the treatment of lung cancer," the researchers explain. "The next step in our research is to find out whether blocking these enzymes can have side-effects in other tissues."

More information: Meng Liu, et al., Targeting the protein prenyltransferases efficiently reduces tumor development in mice with K-RAS-induced lung cancer, *Proceedings of the National Academy of Sciences*.