

Active hedgehog signalling in connective tissue cells protects against colon cancer

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Many types of cancer are caused by gene mutations in the signalling pathways that control cell growth, such as the hedgehog signalling pathway. A new study from the Karolinska Institutet, published in the journal *Nature Communications*, now surprisingly shows that in colon cancer hedgehog signalling has a protective function.

Mutations that lead to the activation of hedgehog signalling are the cause of almost all cases of basal cell carcinoma (a common form of skin cancer) and certain types of [brain tumours](#).

Previous studies have indicated that hedgehog signalling is also important in other types of cancer, such as colon cancer – one of the commonest types of cancer in Sweden.

The research team at the Department of Biosciences and Nutrition at Karolinska Institutet's campus in Huddinge, led by Marco Gerling and Rune Toftgård, has been working alongside researchers in Holland looking at the possibility of influencing cell growth in colon cancer by altering hedgehog signalling.

In view of the fact that tumours consist of different types of cells apart from the cancer cells themselves, the researchers used various databases to analyse gene expression in colon cancer. Although the team was not able to find any activation of the signalling pathway in the cancer cells, it was able to confirm earlier observations that it is only the hedgehog ligand, the protein needed to launch the signalling process that is produced by the cancer cells. In contrast, the hedgehog signalling pathway and expression of its target genes are specifically activated in the surrounding cells of the connective tissue.

To investigate the importance of the hedgehog signalling from [cancer cells](#) to [connective tissue cells](#), the researchers used a mouse model in

which the signalling pathway could be switched on specifically in the connective [tissue cells](#). When mice were treated with substances that induce [colon cancer](#), the mice with activated hedgehog signalling in the connective tissues developed significantly fewer tumours than those with a normal hedgehog function. When the team then did the opposite – inhibiting hedgehog signalling in different mouse models – the mice developed more tumours. The researchers were able to show that the [connective tissue](#) cells with activated hedgehog signalling change their gene expression and send a signal back to the tumour cells, inhibiting the development and growth of tumours.

"The results show that non-cancerous cells in tumours have a great capacity to influence how tumours develop," says Marco Gerling, one of the researchers. "In the long term we hope to be able to provide a detailed explanation of how the activation of hedgehog signalling in the cells surrounding the tumour can prevent the growth of tumours and to use this knowledge to develop new types of treatment that can restrain the development of cancer."

More information: Marco Gerling et al. Stromal Hedgehog signalling is downregulated in colon cancer and its restoration restrains tumour growth, *Nature Communications* (2016). [DOI: 10.1038/NCOMMS12321](#)

Provided by Karolinska Institutet

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