

'Hedgehog' pathway may hold key to anti-cancer therapy

August 26 2009

Scientists in Switzerland have discovered a way to block the growth of human colon cancer cells, preventing the disease from reaching advanced stages and the development of liver metastases. The research, published today in *EMBO Molecular Medicine*, shows that blocking the so-called Hedgehog-GLI pathway can prevent the growth of tumours, metastatic lesions and cancer stem cells, the cells thought to lie at the root of cancer growth.

Colon cancer often begins in a treatable form when it is confined to the bowel wall, but in frequent cases it can develop to an incurable metastatic stage. A Geneva-based research team has discovered the essential role played by HH-GLI in the progression of [colon cancer](#) to these late and incurable stages. HH-GLI is a signalling pathway used by cells to communicate with each other, often used to determine position, growth and survival.

"Previous works hinted at the possible role of HH-GLI in colon cancer, but this was denied by other studies, so its involvement was never entirely clear," said lead researcher Professor Ariel Ruiz i Altaba of Geneva University. "In this study we have proven that HH-GLI is essential for the development and growth of colon cancers. The research demonstrates the active presence of HH-GLI signalling in epithelial cells of colon cancers. Moreover, we find that metastatic tumours rely on this pathway for sustained growth. This identifies HH-GLI as a target for novel anti-cancer therapies against so far incurable forms of colon cancer in distant organs, such as the liver."

This research opens the possibility of new anti-cancer therapies, specifically the use of [RNA interference](#) and of Cyclopamine, a plant product known to block Hedgehog pathway activity. This and other similar molecules can now be considered for future research as a treatment for terminal patients with metastatic disease and to fight resurgent forms of the disease.

"Recurrence is a major problem in cancer treatment. Even after a patient has displayed an apparent complete recovery from a primary tumour, recurrence at nearby or distal locations has a poor prognosis," said Ruiz i Altaba. "While monitoring recovering mice we noted that tumours began to recur in all cases except for those treated with Cyclopamine for a short period of time after tumour disappearance. The treated mice were kept for up to one year after the treatment and remained healthy and tumour free."

Using these genetic or pharmacologic methods to block HH-GLI activity also prevents cancer stem cell self-renewal. Using a new in vivo assay to test the participation of cancer stem cells in a growing tumour, the research team demonstrated the essential role of this pathway for the maintenance and survival of cancer stem cells.

"This work firmly establishes the critical action of HH-GLI in human colon cancer cells, providing the platform for preclinical and future clinical work." concluded Ruiz i Altaba. "The finding that a blockade of HH-GLI for a relatively short period was sufficient to eliminate the tumour and prevent recurrence, without negatively affecting the health of the mice, opens the possibility for the use of a therapeutic window to eradicate the tumour without major side effects."

Source: Wiley ([news](#) : [web](#))

Citation: 'Hedgehog' pathway may hold key to anti-cancer therapy (2009, August 26) retrieved 2 May 2024 from <https://medicalxpress.com/news/2009-08-hedgehog-pathway-key-anti-cancer-therapy.html>

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