Medical Xpress

Blocking cancer cell's energy generator could lead to new targeted treatments

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Cancer Research UK scientists have found that blocking the pathway used by some kidney cancer cells to generate energy can kill the cancer cells, sparing the healthy ones. The research is published in *Nature* yesterday.

Cells need energy to grow and divide. This energy is generated through a process called the TCA cycle (also known as the Krebs cycle), which is supported by a range of cellular catalysts called enzymes. Without these enzymes the cycle grinds to a halt, causing the cells to die.

But, in the rare genetic condition 'hereditary leiomyomatosis and renal cell cancer' (HLRCC), which can lead to a very aggressive form of kidney cancer, one of these enzymes, Fumarate Hydratase (FH), is missing and yet the kidney cancer cells are able to survive.

The researchers found that these cells were able to get around the loss of the TCA cycle by switching to a pathway that builds and breaks down a molecule called haem, an important by-product of the TCA cycle. By blocking the action of a key enzyme called Haem Oxygenase, the researchers were able to specifically target the Fumarate Hydratase-deficient cancer cells while leaving normal kidney cells unaffected.

Professor Eyal Gottlieb, lead researcher at Cancer Research UK's Beatson Institute in Glasgow, said: "By using the latest chemistry and computer technologies we were able to look at every energy generating reaction taking place in the cell and predict the effect of blocking these

pathways. Armed with this knowledge we now need to confirm our findings in HLRCC patients and ultimately develop targeted drugs that selectively kill kidney cancer cells.

“We also want to use our approach to find other pathways and expose weaknesses in cancer cells that could be exploited, suggesting a whole new range of drugs to kill cancer cells.”

Dr. Julie Sharp, senior science information manager at Cancer Research UK, said: “Ten years ago, Cancer Research UK scientists found that faults in the gene for Fumarate Hydratase lead to the condition HLRCC. These latest results show us that the adaptation that the cancer cells use to survive could also be exploited as a weakness, and potentially lead to the design of new treatments.

“Recent research has found that levels of Fumarate Hydratase are also reduced in other types of kidney cancer, suggesting that if they are using the same pathway to generate energy then a drug to block this process could be used to treat a wider range of people with kidney cancer.”

More information: Frezza, C. et al (2011). Haem oxygenase is synthetically lethal with the tumour suppressor fumarate hydratase *Nature* DOI: 10.1038/nature10363

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