New bowel cancer drug target discovered

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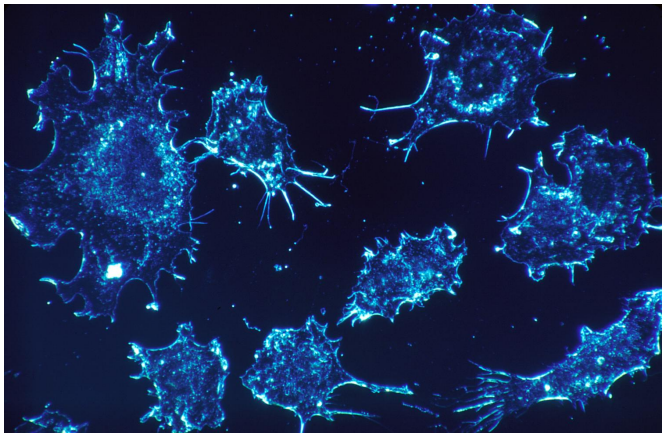

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Researchers at the Francis Crick Institute have discovered a new drug target for bowel cancer that is specific to tumour cells and therefore less toxic than conventional therapies.

"There has long been a need to find more effective and less toxic drugs to treat bowel cancer," says Laura Novellasdemunt, first author of the paper and researcher at the Francis Crick Institute. "We have found a novel drug target that could provide the basis for a better therapy in patients in the future."

Most bowel cancers are caused by a mutation in a gene called APC that in its healthy form acts to prevent cancer formation. Mutated APC genes cause excess activity of a cell signalling pathway called 'Wnt', which has been associated with bowel cancer for over 20 years.

Wnt signalling is vital for many organs, so drugs designed to block Wnt signalling in cancer cause very toxic side effects in other parts of the body. This has been a major hurdle in developing effective and safe bowel cancer therapies. The team at the Crick have found a way to exclusively target Wnt signalling in tumour cells, that reduces growth of tumours derived from colon cancer cells without the toxic effects on healthy cells. Their findings will be published in *Cell Reports*.

The team used the gene-editing tool CRISPR to cut the APC gene at various positions, and found a crucial part of the gene that causes dangerous levels of Wnt signalling and cancer formation.

Using a number of molecular techniques, they identified a protein involved in over activation of the Wnt pathway in cancer. Preventing the activity of this protein by genetic deletion or blocking it with drugs caused a reduction in Wnt signalling in cancer cells and slowed down tumour growth in mice. Importantly, the drug was found to act exclusively on the tumour cells, and have no effect on Wnt signalling in healthy cells.

"Current treatment for bowel cancer is mostly generic, while targeted therapy will help future development of personalised medicine," says Vivian Li, senior author of the paper and Group Leader at the Francis Crick Institute. "The protein that we've identified holds great promise as a therapeutic target for bowel cancer treatment."

The next step will be to see if deleting the gene that makes the protein in mice will prevent them from developing bowel cancer. This will provide further evidence that the protein is a viable anti-cancer drug target.

More information: 'USP7 is a tumor-specific WNT activator for APC-mutated colorectal cancer by mediating ?-catenin deubiquitination' *Cell Reports* (2017). DOI: 10.1016/j.celrep.2017.09.072 , www.cell.com/cell-reports/full … 2211-1247(17)31377-3

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