Discovery targets dormant bowel cancer cells before they form secondary tumours

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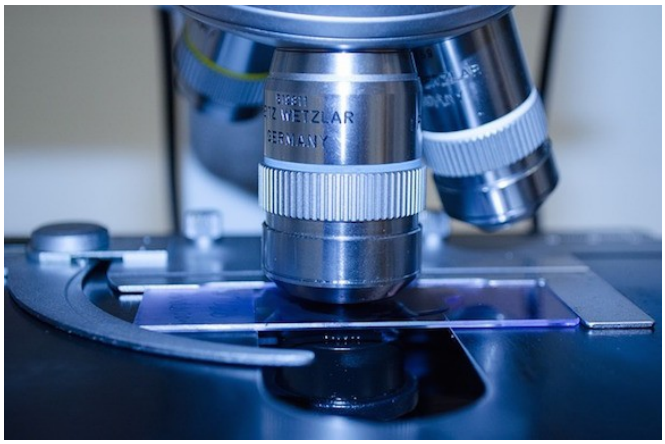

An international research team, led by the University of Melbourne, have discovered a way to control the stem cell behaviour responsible for the spread of bowel cancer.

The discovery will lead to treatments that target dormant cells, a major shift from conventional therapies that hit the growing cancer cells only.

A cell surface receptor – called Frizzled 7 - is the key to the stem cell activity that results cancer spreading. The majority of bowel cancer patients die from secondary cancers that spread throughout the body, not the primary cancer.

The findings have been published in *Stem Cell Reports* and herald an optimistic end to Bowel Cancer Awareness Month in June.

Lead researcher, Professor Elizabeth Vincan is the Head of the Cancer Biology Laboratory at the University of Melbourne and the Victorian Infectious Diseases Reference Laboratory at the Doherty Institute.

She says patients with bowel cancer often seek treatment once the cancer is advanced and has already spread to other parts of the body, most commonly the liver, where it can sit dormant for years before starting new cancer growth.

Her team has identified a molecule that is present in both actively growing and dormant cancer cells. The aim is to target the primary tumour in the bowel as well as the dormant cancer cells in secondary organs.

Bowel cancer is the second most common cancer in Australia and globally there were 1.4 million new cases and 694,000 deaths from bowel cancer in 2012 alone.

Conventional therapies and treatments have poor outcomes for bowel cancer patients because by the time they are detected, the cancer cells have spread to secondary organs, sitting dormant and undetected, until something triggers them to form a cancer again, and that then becomes the cause of death.

Previous research has shown a stem cell in the gut that is identified by a marker called Lgr5 plays a key role in initiating cancer growth.

This cell needs 'Wnt' proteins to regenerate the gut lining or epithelium (those tissues that line the surfaces of the gut) after it is damaged. And these Wnt proteins control cell function by binding to a cell surface receptor known as 'Frizzled'. There are 10 of these Frizzled receptors but the one involved in the Lgr5 stem cells was not known.

"It was like searching for a piece of the puzzle," Professor Vincan said. "We found that Frizzled7 was the one we were looking for. That is the one that is important in Lgr5+ stem cells and that is the one to target in cancer.

"If you knock out Frizzled7 while the cells are in a

dormant state they aren't able to make the tumour grow. The aim now is to try to get to those cells while they are dormant, before they start growing. It represents a shift in the targeted management of cancers.

"The next step is how to target Frizzled7 and develop anti-Frizzled7 antibody treatments that can be used in combination with other current therapies. We are collaborating with international scientists who are trialling imminent antibody treatments."

More information: "Frizzled7 Functions as a Wnt Receptor in Intestinal Epithelial Lgr5+" *Stem Cells* DOI: dx.doi.org/10.1016/j.stemcr.2015.03.003

Provided by University of Melbourne