New target for gastric cancer therapies

January 29 2019

Cardiff University researchers have uncovered new information about the underlying mechanisms for gastric cancer, providing hope of potential new therapies in the future.

The team, at the University's European Cancer Stem Cell Research Institute, found they could stop gastric cells dividing and growing by deleting a particular cell-surface receptor implicated in the function of stem cells.

Dr. Toby Phesse, Cardiff University, said: "The prognosis of gastric cancer is very poor, with very few treatment options available to patients, and thus we desperately need new clinical treatments for this disease.

"Some patients with gastric cancer have mutations in genes that are involved in the regulation of Wnt—a cell signalling pathway involved in cell division. It drives the development of cancer and the spread of cancers throughout the body.

"We also see an increase in some of the Fzd receptors, which transmit Wnt signalling, and this is linked to poor prognosis in gastric cancer.

"Despite this evidence, there is limited research investigating the potential of targeting Wnt receptors as a treatment for gastric cancers. We aimed to understand the implications of inhibiting Wnt by targeting Fzd receptors and whether this could be used as an effective treatment."

The scientists targeted a specific Fzd receptor called Fzd7, as this was identified the predominant Wnt receptor responsible for the function of stem cells in the stomach and intestine. They found that deletion of Fzd7 in gastric cells made these cells unable to respond to Wnt signals and they failed to divide and grow.

Dr. Phesse added: "This information gives us a potential new therapeutic route for gastric cancers, as we could target Fzd7 and consequently inhibit Wnt signalling and tumour growth. In fact, Vantictumab is a drug known to inhibit several Fzd receptors, including Fzd7, and is currently in clinical trials for the treatment of other cancers – like pancreatic, lung and breast.

"We have now shown in this work that Vantictumab has potent anti-tumour effects in gastric tumours with and without mutations to the Wnt pathway."

This research, in collaboration with the University of Melbourne, University Medical Center Utrecht, the Institute of Medical Biology Singapore, and Oncomed Pharmaceuticals, is published online in *Cancer Research*, a journal of the American Association for Cancer Research.

More information: Dustin Flanagan et al. Frizzled-7 is required for Wnt signaling in gastric tumors with and without Apc mutations., *Cancer Research* (2019). DOI: 10.1158/0008-5472.CAN-18-2095

Provided by Cardiff University