

Scientists discover new pathway that prevents bowel cancer treatment from working

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Leading scientists at the University of Birmingham have discovered a previously unknown pathway that prevents specific drugs from working in patients with bowel cancer.

The research findings pave the way for increasing the number of [bowel cancer](#) patients who can be successfully treated, say the scientists.

Bowel cancer, also called [colorectal cancer](#), affects the large bowel, which is made up of the colon and rectum. It is the fourth most common cancer in the UK, with over 42,000 people diagnosed with bowel cancer every year in the UK. It is also the second biggest cancer killer, with 16,000 people with bowel cancer dying in the UK every year.

The University of Birmingham-led research involved the study of 184 tumor samples and medical records of bowel cancer patients participating in the [COIN trial](#), as well as research carried out in mice, [cell cultures](#), and a laboratory model for pre-malignant colorectal cancer.

Co-senior author Andrew Beggs, Professor of Cancer Genetics & Surgery at the University of Birmingham, explained: "About 60% of bowel cancers are sensitive to drugs called anti-EGFR inhibitors which work by blocking a key pathway in these cancers.

"However, despite this, in cancers that should be sensitive to them, these drugs only work in patients about 50% of the time."

Co-senior author Dr. Fedor Berditchevski, also of the University of Birmingham, added: "Scientists have previously found that if bowel cancer patients have a mutation in a gene called RAS, the anti-EGFR inhibitors will not work.

"However, our research has now discovered a new pathway involving a tetraspanin protein called TSPAN6 that is frequently inactive in bowel cancer patients and this makes these drugs less effective. Crucially, our research also shows that if this pathway is active in a patient's cancer then the [drug](#) will work, irrespective of whether they have a mutation in RAS or not."

First author Dr. Regina Andrijes, a Postdoctoral Fellow at the University of Birmingham, concludes: "This is the first time a tetraspanin protein has been shown to be directly involved with bowel [cancer](#). Our research findings show that this new pathway could act as a biomarker for treatment with anti-EGFR drugs in [bowel cancer](#), increasing a patient's chance of survival and the number of patients who could benefit from these drugs who previously would not have."

The researchers are now set to undertake a clinical trial of using this marker to better identify [patients](#) for anti-EGFR treatment.

The study, published today (September 13th) in the *Proceedings of the National Academy of Sciences (PNAS)*, was carried out in collaboration with University Hospitals Birmingham NHS Foundation Trust, Semmelweis University in Hungary, and Assiut University in Egypt.

More information: Tetraspanin 6 is a regulator of carcinogenesis in colorectal cancer, *Proceedings of the National Academy of Sciences* (2021). doi.org/10.1073/pnas.2011411118

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