New bowel cancer model uncovering how it avoids immunotherapy drug

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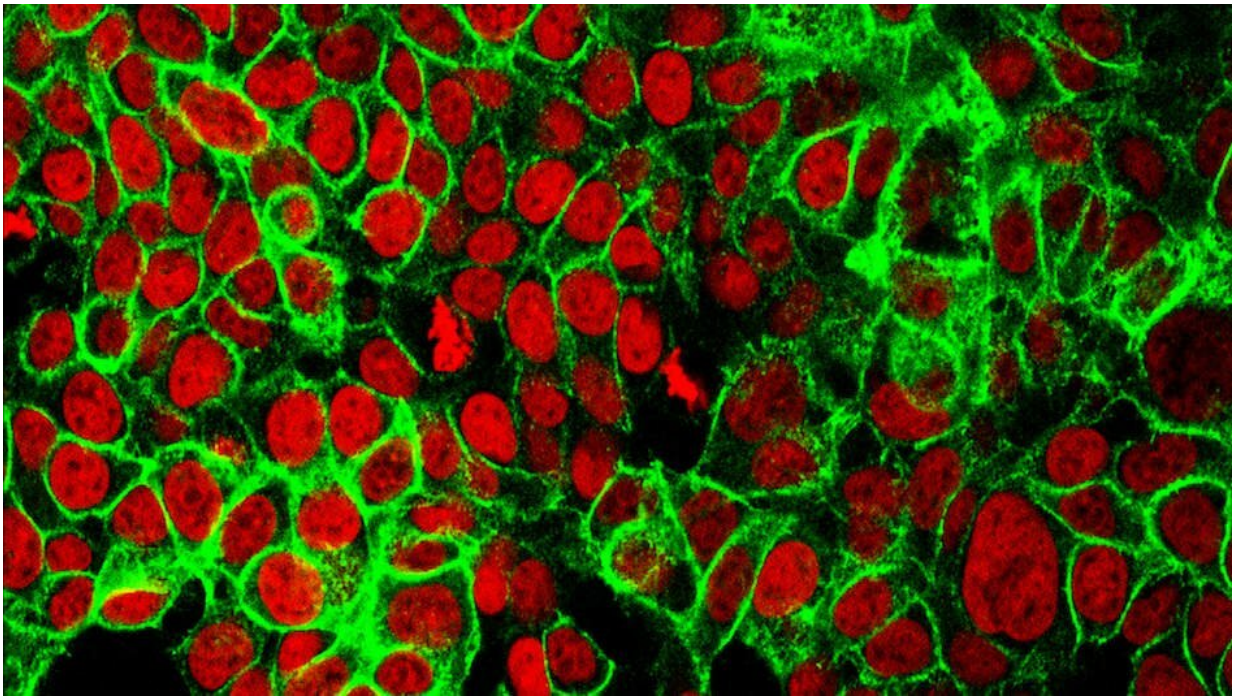

Credit: Institute of Cancer Research

Scientists at the Institute of Cancer Research, London, have developed a complex model system that mimics the most common form of bowel cancer and is showing how it 'hides' from immunotherapy.

Initial results of an ongoing study presented at the 2020 National Cancer Research Institute (NCRI) Virtual Showcase shed new light on how

bowel cancer develops resistance to cibisatamab, a new immunotherapy drug owned by pharmaceutical company Roche.

Bowel cancer is the third most common type of cancer worldwide, and while some patients with the disease are treated with immunotherapy drugs, the vast majority of cases don't respond to current immunotherapies.

These bowel cancers develop environments inside the body which suppress the immune system, resisting treatment.

Understanding how this occurs could help more patients respond to immunotherapy.

Bowel cancer model that mimics immune system responses

A team at the ICR developed a model for bowel cancer in the lab which mimics the disease and immune response environment found in patients, aiming to work out how bowel cancers develop resistance to cibisatamab.

Cibisatamab is an antibody-based drug that simultaneously binds to a protein called CD3 on white blood cells and a protein on tumor cells called CEA. It is undergoing clinical trials in bowel cancer showing promising activity, but some tumors can become resistant to it.

The new model uses bowel cancer cells taken from patients and built into three-dimensional structures—so-called patient-derived organoids (PDOs) – and combines them with white blood cells and individual micro-environmental factors or tumor microenvironment cells.

Cibisatamab

The researchers tested the effect of cibisatamab on this system and have already uncovered intriguing initial results. Ultimately, the results could help direct the use of cibisatamab, in combination with other treatments.

The results were presented at the NCRI conference by Maria Semiannikova, who is carrying out the research for her Ph.D. under Dr. Marco Gerlinger's supervision.

Maria Semiannikova, Ph.D. student at the ICR, said, "It was a pleasure to introduce my Ph.D. project, which is uncovering new clues about drug resistance to an immunotherapeutic antibody in collaboration with a major pharmaceutical company, at the NCRI Virtual Showcase. The NCRI conference is always a highlight in the calendar for cancer researchers across the UK."

Dr. Marco Gerlinger, Team Leader in Translational Oncogenomics at the ICR, and Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust, said: "Cibisatamab is a promising new immunotherapy drug, but not all patients with bowel cancer respond. Our new model—which mimics both real tumors and the micro-environment around them—is helping us to rapidly dissect in the laboratory how we might counter this resistance."

Provided by Institute of Cancer Research

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