Gut bacteria may help combat cancer

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The friendly bacteria in our gut may help fight cancer. Two new studies in mice show that some anti-cancer therapies work best when the microbes in our body are strong and healthy – which suggests that antibiotics and cancer might not always make a good combination.

We know that friendly, or commensal, bacteria can influence inflammation in the body, and that some forms of inflammation help cancers to grow – but it is unclear whether commensal bacteria have a direct influence on cancer development.

To find out, Laurence Zitvogel at the Gustave Roussy Institute in Villejuif, France, and her colleagues studied cyclophosphamide, a drug used to treat brain cancers and blood cancers including leukaemia. The drug works by encouraging the body to produce a certain type of immune T-cell that attack tumours.

Zitvogel's team gave the drug to mice with sarcomas – a rare cancer that develops in muscle, nerves and bones – and skin cancer. Within 48 hours, the cyclophosphamide had affected the lining of the small intestine, allowing some of the rodents' gut bacteria to escape and enter their lymph nodes and spleen.

Once there, it was these bacteria – not the drug itself – that encouraged immature immune cells in the lymph nodes to develop into the tumour-targeting T-cells.

For further evidence of the important role that the bacteria play, the researchers gave another group of mice antibiotics like vancomycin, which are known to disrupt gut bacteria, before they underwent the same cancer treatment. The cyclophosphamide was far less effective at combating cancer in these mice.

The results show that the links between bacteria and cancer needs much more careful study, says Cynthia Sears, who researches gut bacteria at Johns Hopkins University in Baltimore, Maryland. But it is far too early for people with cancer to throw out any antibiotics they are taking, she adds.

"Extending the results to humans requires deliberate study as antibiotics are can be life-saving in the setting of cancer and chemotherapy," she says. "One key source of life-threatening bloodstream infections in this setting can be the gut bacteria."

Meanwhile, a second study suggests bacteria may play an important role in the activity of other anti-cancer drugs. Giorgio Trinchieri and Romina Goldszmid at the National Cancer Institute in Frederick, Maryland, and their colleagues looked at oxaliplatin, a platinum-based drug used in human chemotherapy. The drug triggers the production of reactive oxygen species – molecules that destroy DNA and kill certain kinds of cells, including cancer cells.

The team gave the drug to 50 mice with various types of cancer cells injected underneath their skin. Half of the mice had previously received an antibiotic cocktail – three weeks later, about 80 per cent of these mice had died. By contrast, 80 per cent of the mice that were antibiotic-free were still alive after three weeks.

In response to the chemotherapy, inflammatory cells in the immune system normally ramp up

the production of reactive oxygen species. The inflammatory cells were less active in the mice treated with antibiotics – perhaps because the bacteria killed by the antibiotics usually help to prime the immune system to respond to the chemotherapy, say the team.

"When we started our studies, we suspected that platinum therapy may involve some immune pathway on which the gut microbiota could have a modulating effect," says Trinchieri. "But we were surprised by the extent to which inflammatory cell reactive oxygen species production was strictly dependent on the presence of gut microbiota."

"We must understand how to harness and control such microbial contributions to mammalian physiology," says Matthew Redinbo at the University of North Carolina at Chapel Hill. In 2010, Redinbo's team showed one way in which that kind of control is potentially possible. They realised that the toxic side-effects of some anti-cancer drugs relate to their effects on bacteria in the gut – and that the effects can be reduced by inhibiting an enzyme in the bacteria.

Crucially, Redinbo's approach targeted just one enzyme in the gut bacteria, rather than wiping out the entire gut flora, as many antibiotics can do. "The 'scorched earth' effects of antibiotics creates problems well beyond the impact it might have on cancer chemotherapy," he says.

Journal references: Zitvogel's study, *Science*, DOI: 10.1126/science.1240537; Trinchieri and Goldszmid's study, *Science* DOI: 10.1126/science.1240527