Could the bacteria in our gut help treat cancer?

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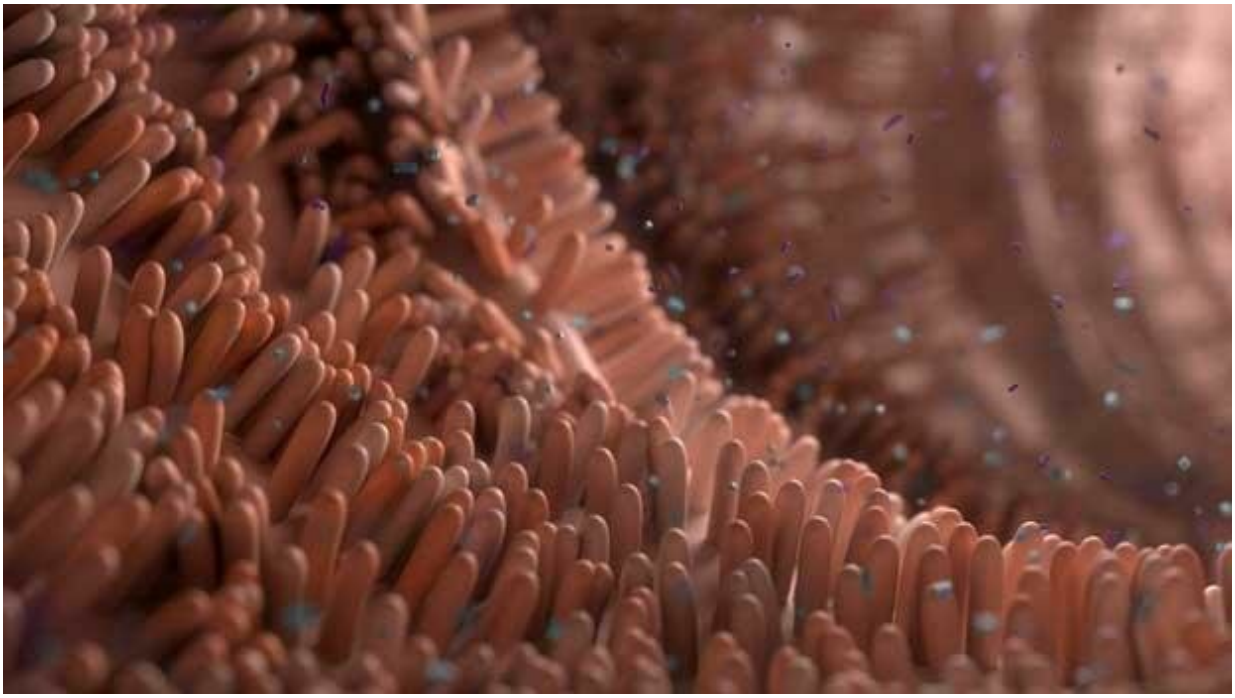

Our body is home to around 39 trillion bacteria, with the majority living in the gut. Credit: Cancer Research UK

"The microbiome is a huge part of who we are," says Dr. Marios Giannakis.

"We have more microbes in our bodies than human cells and yet we still don't fully understand the role they play in health and disease."

The microbiome is a collection of trillions of microorganisms, spanning bacteria, fungi and viruses, that call the human body home.

Giannakis, a doctor and researcher at the Dana Farber Cancer Institute in Boston in the US, is among those pondering how these microbes might be tied to bowel cancer.

This is because a large proportion of our microbiome is found in the gut, with research suggesting that these vibrant communities might be helping some cancers develop. That's why Giannakis, and a team of 12 other international experts, have been given up to £20 million from Cancer Research UK's Grand Challenge scheme to find out more.

Gut bacteria can protect us

Bacteria make up most of the gut microbiome and are the major focus of research linking it to cancer. Professor Emma Allen-Vercoe, a world-leading microbiologist from the University of Guelph in Canada, has spent her career studying these organisms, with her early work contributing to the first hints that bacteria might be involved in bowel diseases, including cancer.

"The immediate reaction people have when they're told that they have tiny microbes in their gut is that they cause disease and that they need to be got rid of," says Allen-Vercoe, now part of the Grand Challenge team. "But they're actually really protective."

The types of bacteria that protect us from harm and how they do this is, however, uncertain. "It isn't as simple as getting an infection and becoming sick," she says, adding that it's not necessarily just a case of having a balance of 'good' and 'bad' bacteria either.

"It's more about how the body and other microbes interact with and

control 'bad bacteria' to neutralise them."

If that isn't complicated enough, researchers are also working against a backdrop of everyone's microbiome being different.

"This makes it incredibly hard to find patterns, unless you look at enormous numbers or patients," says Allen-Vercoe.

Until now, there simply hasn't been the means to explore the microbiome and its relation to cancer in the epic detail it needs.

"We've all been working on this problem in our individual labs and hospitals," says Giannakis. "We've been studying the behaviour of bacteria and looking at the microbiomes in people who have cancer. It's thanks to the British public funding these efforts that we can bring all these individual pieces together under an umbrella of collaboration."

A worldwide partnership

The newly funded team, led by Professors Matthew Meyerson and Wendy Garrett, is as impressive as the challenge they're embarking on. They'll be working on lots of different projects, from reading the DNA of gut bacteria from thousands of people to running a clinical trial. And they'll be doing this across borders, with scientists, doctors, and patients from the United States, Canada and Europe sharing ideas, samples and most importantly, results.

Take Allen-Vercoe's lab, just an hour and a half drive from Niagara Falls. Her team will study microbes such as those found in colorectal cancerpatients, treated in Boston, and grow them in an artificial bowel they've dubbed the 'robo gut'.

"It turns out you can't grow microbes from the gut very easily in the lab,

so we needed another way to study them," says Allen-Vercoe.

The robo gut mimics nature using a special tank called a bioreactor. "We've created a bunch of bioreactor vessels that allows the whole microbiome from a person's gut to be grown in the lab."

But bacteria also interact closely with healthy bowel cells and the immune system, so to replicate human conditions these components are needed too. Professor Hans Clevers, from the Hubrecht Institute in the Netherlands and another Grand Challenge team member, is a world-leader in growing miniaturised human organs in the lab. These 'organoids' are essentially balls of gut cells that adopt the shape and form you'd expect to see in the human bowel but grown in the lab.

Thanks to Grand Challenge, Clevers' organoids will be flown from the Netherlands over to Canada.

What do we already know about the microbiome and cancer?

Allen-Vercoe says they're venturing into "an unknown frontier". But over the past couple of decades, clues from both the lab and the clinic suggest the microbiome is important to study. And one particular bacterium is thought to play a prominent role.

"Fusobacterium is found in and around one third of bowel cancers," says Allen-Vercoe. This link is too strong to be coincidence. And research points to lifestyle as potentially playing a role, with large studies showing that Fusobacteriaare more likely to be found in those who eat certain foods.

"People who consume inflammatory diets have a higher risk of Fusobacterium-associated bowel cancer," says Giannakis.

"This bacterium is also more frequently present in cancers of the right side of the colon and patients with Fusobacterium-positive tumours often have a worse outcome."

This suggests bacteria in the gut could help cancer develop and progress, but what can we do about it? Well, there's also evidence to suggest that tinkering with the microbiome in people is possible.

"In a different study, we gave people with a C. difficile infection an ecosystem of 'good' bacteria in a capsule," says Allen-Vercoe, who's spin-off company designs therapies that change the composition of bacteria in a person's gut.

Coincidently, two patients in this study had lots of Fusobacteriumin their microbiome, which dropped after treatment. "This has given us hope that applying a microbiome drug could remove some of the 'bad' bacteria in people with bowel cancer," she says.

It's time to understand these organisms' lives

"This Challenge is trying to answer a really big question that we've been trying to answer for nearly 10 years," says Allen-Vercoe. "We've been struggling to do that mainly because these are such difficult microbes to grow and manage."

But now technology has offered a solution. "Thanks to advances in the robo guts and organoids we can explore the microbiome in ways we couldn't possibly do before."

Scientists at Dana Faber are also working on developing new drugs that might be able to destroy individual 'bad' bacteria. And the library of clinical samples has been steadily growing.

"We are planning to collect thousands of specimens as part of a large study." says Giannakis. This could provide enough tumour and microbiome samples to hunt for patterns.

A final, intriguing complication in understanding the gut microbiome is that it varies between nations. Luckily, a previous Grand Challenge project has collected tumour samples from around the world, offering precious insight into the different microbiomes.

"Collaborating with Sir Mike Stratton's team and studying their samples means we can and look at tumours across the globe and really grasp how the microbiome changes with lifestyles and geographic location," says Giannakis.

How long until patients benefit?

The team don't expect to find all the answers in the next couple of years. This is big science, they know they're in for the long haul.

"Clearly certain parts of the proposal will have more immediate impact on patients than others," says Giannakis. He suspects some of the first people to benefit might be his patients taking the living ecosystems made by Allen-Vercoe.

"Patients who have recently had surgery to remove their colon cancers will get an ecosystem with about 40 different bacterial species in them," Allen-Vercoe says. The hope is these 'good' microbes will settle and displace the 'bad guys', and stop the cancer coming back.

"It's obviously an ambitious proposal," says Giannakis. "We have to be prepared for our findings taking us in unexpected directions."

But both are eager to get going.

"I've been studying these bacteria for years. Now we have the right team together to really get some answers," says Allen-Vercoe.

Provided by Cancer Research UK