

GUT INSTINCT:

Reshaping the Gut Microbiota to Improve Cancer Therapy

Novel clinical trials show fecal microbiota transplantation improves cancer patient response to immunotherapy

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Source: [The Guardian](#), Photograph by Jennifer Barrow/Alamy

What if the secret ingredient to improving cancer treatment came from something we usually flush away? Often considered waste, human stool is a rich snapshot of the microbes (such as bacteria, fungi, and viruses) that live inside our gut. People already consume beneficial microbes through probiotic foods and supplements, but these contain only a few types of microbes. In contrast, stool contains a more diverse community of beneficial microbes. Although it may sound unpleasant, researchers are investigating whether "poop pills" containing this diverse microbial community can help cancer patients better respond to immunotherapy.

Typically, treatments such as chemotherapy and radiation have been used to destroy cancer cells. However, these approaches can damage healthy cells, leading researchers to develop therapies that use the body's own defenses. The immune system is the body's natural defense system that can find and destroy cancer cells. However, cancer cells have developed ways to put the "brakes" on the immune system, slowing its ability to

attack and allowing cancer growth. Immunotherapy drugs release these brakes, restoring the immune system's ability to recognize and eliminate cancer cells. While immunotherapy has transformed cancer care, it does not work for everyone and can cause severe side effects from immune activation, such as inflammation of the colon (colitis) and skin rashes. Therefore, researchers are exploring ways to improve both its effectiveness and safety.

One promising approach involves the gut microbiota – the trillions of tiny microbes living in our digestive tract. Typically, microbes have a bad rep for causing illness but the microbes in our gut form a community that provides benefits such as producing vitamins and supporting metabolism. Like a community of people, different microbes perform different roles, communicate with one another, and help maintain balance. A healthy gut microbiota can produce substances that help immune cells fight cancer. Growing evidence suggests that the gut microbiota influences how well patients respond to immunotherapy. This connection motivated Dr. Saman Maleki and his colleagues at Victoria Hospital to explore *whether changing the gut microbiota could improve immunotherapy outcomes*.

One way the gut microbiota can be changed is through fecal microbiota transplantation (FMT). In this process, stool from healthy donors is processed in the lab to extract beneficial gut microbes while removing all the unappealing bits. The microbes are then packaged into a tasteless, odourless pill. After taking these pills, the healthy gut microbes from the donor can join the patient's existing gut microbiota. By introducing new members into the patient's microbial community, FMT can help restore gut balance and support immune function. These innovative pills, named LND101, were pioneered here in London, ON at the Lawson Research Institute.



The digestive tract contains a diverse gut microbiota. These microbes can be extracted from the stool and captured in 'poop pills'. Cancer patients take these pills to receive beneficial microbes for their gut that can help respond to immunotherapy. Image modified from Shobujsk / Shutterstock.com.

To determine whether FMT could improve responses to immunotherapy, Maleki and colleagues conducted two clinical studies. In this context, response means the tumour stops growing, shrinks or disappears after treatment. [The first study](#), called PERFORM, was a phase 1 trial that focused on the safety of the combination of FMT and immunotherapy in patients with advanced kidney cancer. [The second study](#), FMT-LUMINate, was a phase 2 trial that expanded into patients with lung cancer and skin cancer to test this combination treatment. Together, these studies examined the safety of the combination approach, changes in the gut microbiota, and responses to immunotherapy.

The PERFORM trial recruited 20 patients with advanced kidney cancer. The patients were given FMT pills prepared from healthy donors followed by immunotherapy drugs. In this trial, 67% of patients responded to the treatment. Although half of the patients experienced severe side effects, FMT itself did not cause serious toxicities. The researchers also found that adding FMT to immunotherapy did not increase the number or severity of side effects. Interestingly, patients who responded to the treatment experienced fewer side effects. They

observed that patients who successfully incorporated donor microbes into their own gut community were more likely to benefit from immunotherapy. Some of these donor microbes were associated with reducing inflammation, which may help the immune system function more effectively. Overall, patients with these beneficial microbes were more likely to experience tumour shrinkage and fewer severe side effects.

To explore whether FMT could improve immunotherapy response in other cancer types, the LUMINate trial recruited 20 patients with lung cancer and 20 patients with melanoma, a serious type of skin cancer. Similar to PERFORM, patients received FMT pills followed by immunotherapy drugs. FMT was considered safe in both groups, however some adverse effects were observed in melanoma patients which may be linked to specific donor microbes. Despite this, promising results were observed in both groups. In lung cancer, about 39–45% of patients typically respond to immunotherapy alone, but in this LUMINate trial, 80% of patients responded to the combination of FMT and immunotherapy. Likewise, 75% of melanoma patients responded to the combination treatment compared with the usual response rates of 50–58% seen with immunotherapy alone. Researchers found that patients who responded to the treatment showed lower levels of harmful gut bacteria. These results suggest that FMT may work in part by reducing harmful bacteria in the gut community that weaken the immune system and interfere with its ability to fight cancer. Altogether, this trial showed that modifying the gut microbiota may enhance responses to immunotherapy in lung and melanoma. It also emphasized the importance of selecting donors with beneficial microbes.

Although the idea of using ‘poop pills’ to improve cancer treatment sounds unusual, it has led to interesting evidence that the gut microbiota can influence how patients respond to immunotherapy. Together, the PERFORM and LUMINate trials show that *reshaping the microbial community in the gut through FMT can improve responses to immunotherapy across multiple cancer types*. These early findings are promising; however, they come from small clinical trials with limited participant diversity. Currently, larger trials are now underway to evaluate the efficacy of FMT with immunotherapy so it can move forward in the clinic. While this is an emerging approach, it highlights how something considered waste may one day play an important role in cancer therapy and improve outcomes for advanced cancer patients.

Original Articles: Duttagupta, S., Messaoudene, M., Hunter, S. *et al.* Fecal microbiota transplantation plus immunotherapy in non-small cell lung cancer and melanoma: the phase 2 FMT-LUMINate trial. *Nat Med* 32, 1337–1350 (2026). <https://doi.org/10.1038/s41591-025-04186-5>

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