

Common plant fiber gel doubled rate of tumor eradication

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Many people don't realize that the trillions of bacteria, viruses, and fungi residing within the gastrointestinal tract—collectively called the gut microbiome—are connected to overall health, and specifically to cancer.

Manipulating the gut microbiome to produce 'beneficial' commensal microbes, which protect the host from pathogens and can boost immune responses, among other things, could potentially help patients respond better to cancer drugs called [immune checkpoint inhibitors](#), a type of immunotherapy.

To that end, researchers at the University of Michigan have developed a new dietary fiber formulation that improves the potency of immunotherapies against cancer by modulating the gut microbiome. In the future, [cancer patients](#) treated with immune [checkpoint](#) blockers may benefit from consuming this inulin gel dietary fiber, said James Moon, the John G. Searle Associate Professor of Pharmaceutical Sciences in the College of Pharmacy. The findings appear in the June 24 issue *Nature Biomedical Engineering*.

Inulin, a dietary fiber found in chicory root, Jerusalem artichoke and other plants, is a prebiotic that helps produce colon-residing commensal bacteria. By formulating inulin into a more colon-targeted inulin gel formulation, the team was able to provide a rich source of nutrients to allow beneficial gut microbes to expand more in the gastrointestinal tract.

The inulin gel improved immune checkpoint inhibitor therapy in rodents with colon carcinoma as well as melanoma. For instance, when inulin gel was combined with an immune checkpoint inhibitor in a colon carcinoma rodent model, the rate of tumor eradication doubled (100% improvement), compared with the immune checkpoint inhibitor therapy alone.

"Consumption of the inulin gel expanded and increased the number of beneficial microbes in tumor-bearing mice," said Kai Han, postdoctoral fellow and first author of the study. "These are beneficial commensal microbes that are found in cancer patients who respond well to immune

checkpoint inhibitors."

"The current approaches to restoring a healthy gut microbiome include oral ingestion of defined probiotics or fecal microbiota transplantation," Han said. "However, it would be very challenging to develop these as pharmaceutical products due to scale-up manufacturing and quality control."

The human microbiome has recently emerged as the next frontier in drug development. Intense research interest in the microbiome is driven by evidence linking the potential health benefits of modulating gut microbiota to treating various diseases, including cancer, diabetes, obesity and neurodegenerative diseases. In particular, a series of recent studies showed that the gut microbiome plays a crucial role in cancer patients' response rate to immune checkpoint inhibitors, Moon said.

"We and others have shown that the gut microbiome has a crucial role in our immune responses," Han said. "Close to 70% of lymph nodes in our bodies are located in the gastrointestinal tract and therefore, microbes residing in the gastrointestinal tract closely interact with our immune cells. Maintaining a healthy gut [microbiome](#) nurtures our immune system so that our immune cells can effectively fight against cancer."

The group chose inulin because it wanted something that could be readily translated to the clinic. Inulin is a [dietary fiber](#) that is widely consumed by the public and is present in many plants. It's used as a sugar substitute and in candies and butter. By making inulin into inulin gel, researchers found that inulin gel coats the gastrointestinal tract much better, leaving more nutrients to the commensal microbes.

The inulin gel also works with anti-PD-1 plus anti-CTLA-4 combination therapy, (widely used immune checkpoint inhibitors) that treat many types of cancer, Han said.

Roughly 10-30% of cancer patients respond to immune checkpoint inhibitors, depending on the types of [cancer](#), and there is risk of serious immune-related complications and side-effects, Moon said. For instance, inflammation in the [gastrointestinal tract](#) and skin are common. Previous studies have shown that inulin consumption may alleviate gastrointestinal inflammation, such as colitis and IBD.

"So, inulin gel may alleviate gastrointestinal inflammation induced by immune checkpoint inhibitors and we are testing this idea now," Moon said.

"Generation of systemic anti-tumor immunity via the in situ modulation of the [gut microbiome](#) by an orally administered inulin gel"

More information: Han, K et al, Generation of systemic antitumour immunity via the in situ modulation of the gut microbiome by an orally administered inulin gel, *Nat Biomed Eng* (2021). [DOI: 10.1038/s41551-021-00749-2](#)

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