Cancer
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Reshaping the gut microbiome can boost chemotherapy delivery to tumors

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- Nanoparticle-based chemotherapy is widely used but liver clearance often limits its effectiveness
- The gut microbiome regulates how aggressively the liver clears these drugs from the bloodstream
- A common antibiotic reshaped gut bacteria in preclinical models, significantly reducing liver clearance and doubling how long chemotherapy remained in circulation to reach tumors
- The findings demonstrate that the microbiome itself drives the response, supporting the potential for microbiome-directed i nte r ve nt i ons

A new study led by researchers at The University of Texas MD Anderson Cancer Center has identified a way to reshape the gut microbiome that can enhance the delivery of certain chemotherapies to tumors, offering a potential strategy to make nanoparticle-based cancer drugs more effective.

The study, published in *Nature Materials* (https://www.nature.com/articles/s41563-026-02690-8), was led by Betty Kim, M.D., Ph.D. (http://faculty.mdanderson.org/profiles/yonsonbetty_kim.html), professor of Neurosurgery (https://www.mdanderson.org/research/departments-labs-institutes/departments-divisions/neurosurgery.html), ()Wen Jiang, M.D., Ph.D. (http://faculty.mdanderson.org/profiles/wen_jiang.html), associate professor of Radiation Oncology (https://www.mdanderson.org/research/departments-labs-institutes/departments-divisions/radiation-oncology-department.html), and Jennifer Wargo, M.D. (http://faculty.mdanderson.org/profiles/jennifer_wargo.html), professor of Surgical Oncology (https://www.mdanderson.org/research/departments-labs-institutes/departments-divisions/surgical-oncology.html) and Genomic Medicine (https://www.mdanderson.org/research/departments-labs-institutes/departments-divisions/genomic-medicine.html). Both Kim and Wargo are core members of the James P. Allison Institute (https://www.mdanderson.org/research/departments-labs-institutes/institutes/allison-institute.html)™, and this research was a collaborative project through the Platform for Innovative Microbiome and Translational Research (PRIME-TR) (https://www.mdanderson.org/research/departments-labs-institutes/programs-centers/prime-tr.html).

In preclinical models, reshaping gut bacteria with a short course of antibiotics roughly doubled how long nanoparticle-based chemotherapy remained in circulation, increased drug accumulation in tumors and improved survival across multiple cancer types.

Notably, the effect was driven by the microbiome itself rather than the immune system, suggesting that microbiome-directed approaches could one day be leveraged to enhance delivery for this class of chemotherapy.

“For decades, scientists have tried to address how aggressively the liver filters out nanomedicine by redesigning the drugs themselves. Our research shows that the host’s biology, specifically the gut microbiome, is just as important as the particle design,” Jiang said. “This is the first study to demonstrate that the gut microbiome can directly impact chemotherapy, opening up an entirely new strategy for boosting cancer treatment.”

How do gut bacteria impact chemotherapy delivery to tumors?

Nanoparticle-based chemotherapy – drugs packaged inside microscopic carriers like liposomes or albumin particles – is used to treat a range of cancers, including breast, ovarian and pancreatic. However, most of the therapy never reaches the tumor because immune cells in the liver, called Kupffer cells, aggressively clear the drug particles from the body.

Gut bacteria send chemical signals to those liver cells through molecules called bile acids, which are natural chemicals produced when gut bacteria process bile. When a commonly used antibiotic called metronidazole was administered to selectively reduce certain gut bacteria, bile acid levels dropped, causing the Kupffer cells to shift into a “quiet” state.

As a result, the Kupffer cells cleared fewer of the nanomedicine particles, allowing for extended circulation and increased accumulation in the tumor. This translated to significantly slowed tumor growth and prolonged survival in preclinical models of colon, breast, melanoma and pancreatic cancers.

How did researchers confirm the microbiome drives this effect?

To determine whether the microbiome itself was responsible, rather than residual antibiotic, researchers performed fecal microbiota transplantation (FMT), in which they transferred gut microbial communities from antibiotic-treated donors into germ-free recipient models. Testing confirmed the transferred material carried no detectable antibiotic, yet these recipients still exhibited the same improved tumor delivery seen in the original antibiotic-treated group.

Earlier research from the Wargo Laboratory (https://www.mdanderson.org/research/departments-labs-institutes/labs/wargo-laboratory.html) and PRIME-TR has shown that the gut microbiome can boost the effectiveness of immunotherapy by reinvigorating the immune system to attack cancer cells.

These results confirm that the beneficial effect is encoded within the microbiome and transferable between hosts. This study is the first to show that the gut microbiome can directly improve chemotherapy by changing how drugs are physically distributed in the body, positioning microbiome-targeted strategies as potential future approaches for enhancing nanoparticle cancer therapy.

What's next for this approach?

In this study, FMT served to demonstrate that the microbiome drives the effect and can carry it between hosts – not as a proposed cancer therapy itself. The findings nonetheless present several promising avenues for clinical translation. The antibiotic metronidazole already is approved by the Food and Drug Administration and has a well-established safety profile, making short-course administration alongside nanoparticle-based chemotherapy a tractable near-term strategy for clinical investigation.

Rather than relying on prolonged antibiotic exposure that broadly depletes the gut microbial community, future research could explore how to selectively engineer a beneficial microbiome state through short-course antibiotic modulation, defined microbial consortia or bile acid-directed therapies that reproduce the effect.

The study also suggests that gut microbiome profiles and bile acid signatures could one day serve as biomarkers to predict which patients will respond best to nanomedicine and which might benefit from microbiome-modulating co-treatment beforehand.

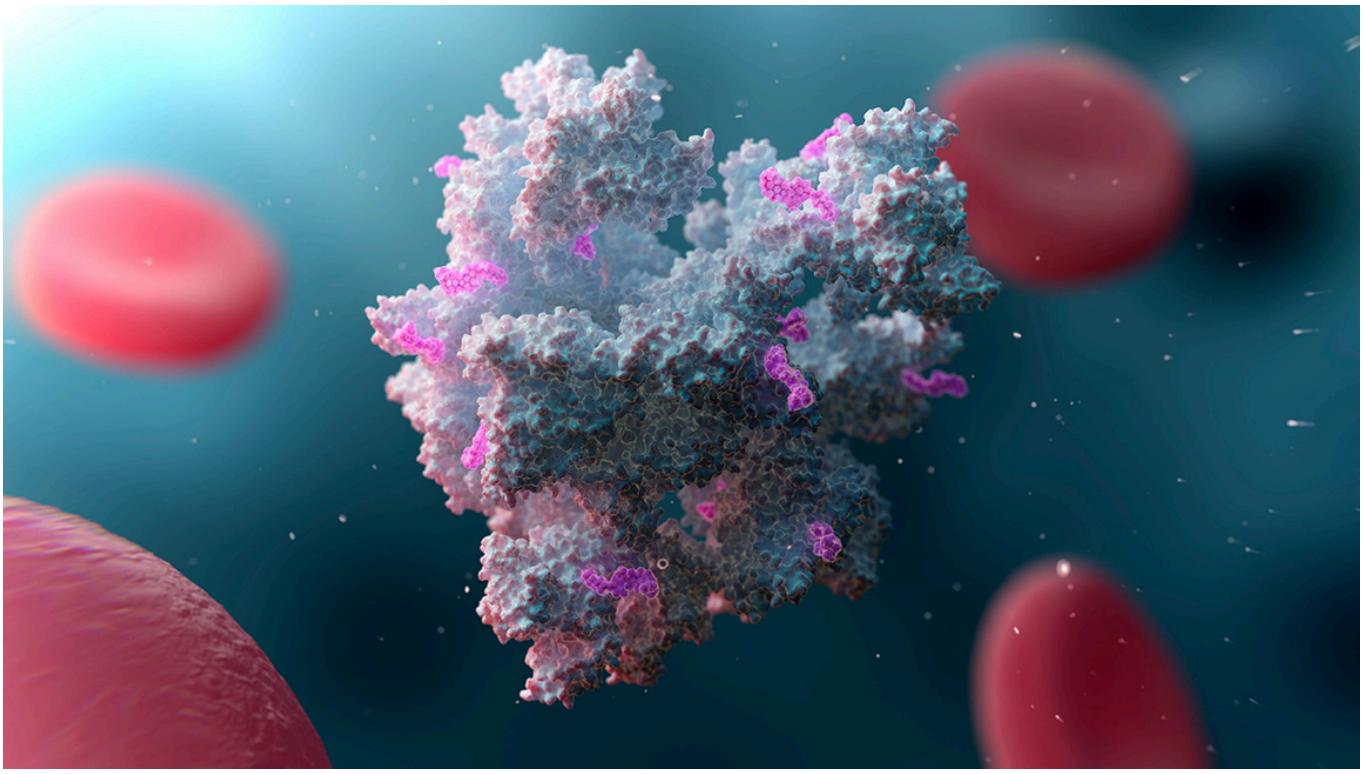
“Hepatic clearance is not a fixed physiological constraint but a dynamic state that can be modulated through the microbiome,” Wargo said. “By understanding how the microbiome shapes drug delivery, we can begin thinking about chemotherapy not just as a drug-tumor interaction, but as a drug-microbiome-host interaction, which changes how we might design treatment plans for patients in the future.”

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