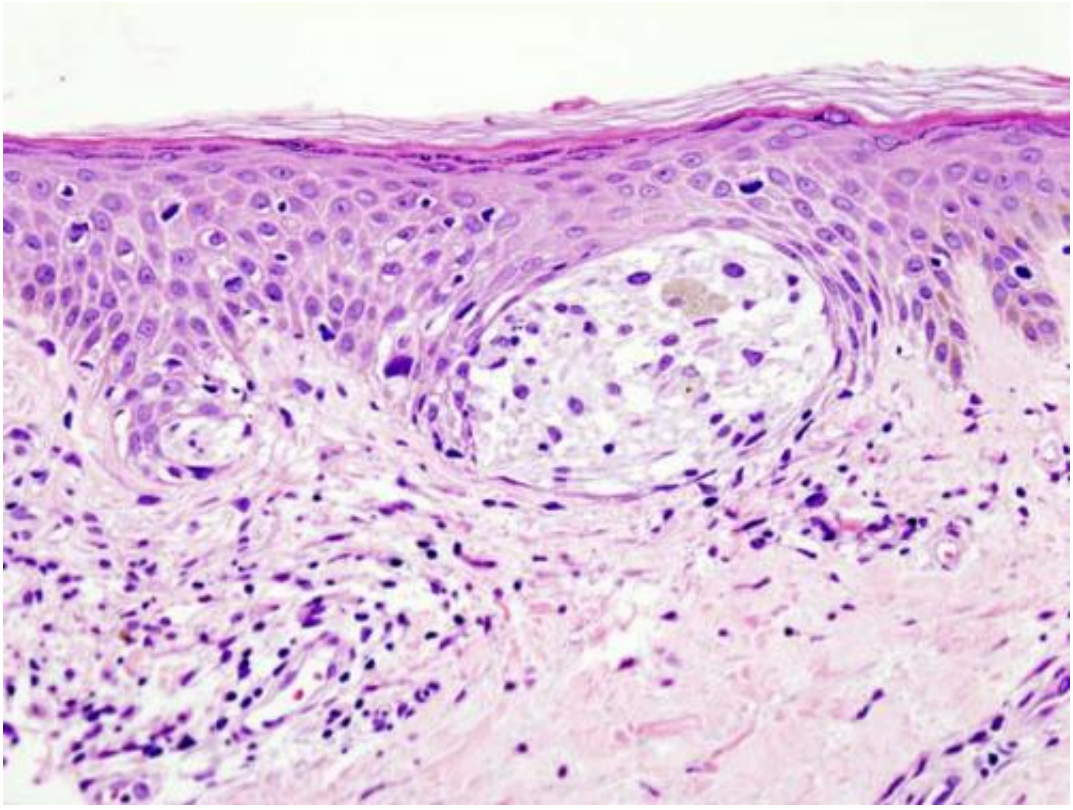
Gut bacteria associated with cancer immunotherapy response in melanoma

February 21 2017



Melanoma in skin biopsy with H&E stain—this case may represent superficial spreading melanoma. Credit: Wikipedia/CC BY-SA 3.0

Melanoma patients' response to a major form of immunotherapy is associated with the diversity and makeup of trillions of potential allies and enemies found in the digestive tract, researchers at The University of Texas MD Anderson Cancer Center report at the ASCO-Society for

Immunotherapy in Cancer meeting in Orlando.

Analysis of 113 fecal samples of patients with metastatic melanoma found that those who responded to a PD1 checkpoint inhibitor had a greater diversity of gut bacteria and larger volumes of a specific type of bacteria than those who did not respond.

This connection between a person's microbiome - trillions of bacteria harbored to varying degrees in the human body—and immune system could have major implications for cancer prognosis and treatment.

"Anti-PD1 immunotherapy is effective for many, but not all, melanoma patients and responses aren't always durable," said Jennifer Wargo, M.D., associate professor of Melanoma Medical Oncology.

"Our findings point to two potential impacts from additional research—analyzing the diversity and composition of the microbiome to predict response to immunotherapy and modulating the gut microbiome to enhance treatment," said Wargo, senior researcher on the project and co-leader of the Melanoma Moon Shot, part of MD Anderson's Moon Shots Program to reduce cancer deaths by accelerating development of therapies from scientific discoveries.

Designing clinical trials

PD1 is a protein on the surface of T cells, the immune system's specialized attack cells, that shuts down immune response. Anti-PD1 drugs use an antibody to block activation of PD1 by PD-L1, a ligand found on tumors and surrounding cells.

Wargo and colleagues are conducting preclinical research to better understand the mechanisms that connect bacteria and the immune system. They're also designing clinical trials to test the hypothesis that

modifying the gut microbiome might improve patients' responses to checkpoint inhibitors.

"Evidence from preclinical research had previously indicated a relationship between solid tumors, immune response, and the microbiome. Our study was the first of its type to look at the relationship between the microbiome and immunotherapy response in patients," said Vancheswaran Gopalakrishnan, first author and doctoral student at The University of Texas Health Science Center at Houston School of Public Health.

Gopalakrishnan, Wargo and colleagues examined oral and gut microbiome samples from 228 patients with metastatic melanoma. While no differences in response were found in connection with the oral samples, the 113 fecal samples told another story. Gopalakrishnan said the team conducted 16S rRNA sequencing, an analysis of the presence of 16S ribosomal RNA used to identify bacteria.

Among the 93 patients treated with anti-PD1 immune checkpoint blockade, the researchers had gut microbiome samples from 30 responders and 13 non-responders. They found:

- A greater diversity of types of bacteria in the responders' microbiomes.
- Increased abundance in responders of the Ruminococcaceae family of bacteria within the Clostridiales order.
- Increased abundance of Bacteriodales in non-responders and a much lower diversity of bacteria.

The researchers also conducted immune profiling before treatment for the presence of important immune system cells in the tumors. Responders had significantly increased immune infiltrates in their tumors, including the presence of CD8+ killer T cells, correlated to the

abundance of a specific bacterium.

Even as they conduct deeper research into the microbiome and the metabolites produced by bacteria to affect the immune response, the team is also studying ways to change the composition of the microbiome.

"The microbiome is highly targetable in a variety of ways," Gopalakrishnan said, including by diet, probiotics to boost the presence of helpful bacteria, antibiotics or by fecal transplants.

Provided by University of Texas M. D. Anderson Cancer Center