Fecal Transplants Boost Immunotherapy

Altering gut bacteria may help overcome resistance to checkpoint inhibitors in people with melanoma and other cancers.

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Using stool transplants to alter the gut microbiome may turn cancer patients who do not respond to checkpoint inhibitor immunotherapy into responders.

A growing body of evidence shows that the gut microbiome—the ecosystem of bacteria and other microorganisms in the intestines—plays a key role in health and disease, including immune response. Researchers previously showed that melanoma patients with more diverse gut bacteria had more active T cells in their tumors and responded better to PD-1 checkpoint inhibitors, such as Keytruda (pembrolizumab) or Opdivo (nivolumab). Mice that received fecal transplants from cancer patients with good treatment response had greater T-cell activity and slower cancer growth, setting the stage for testing this approach in humans.

Researchers at the University of Pittsburgh and the National Cancer Institute gave advanced melanoma patients who initially did not respond to Keytruda or Opdivo a single stool transplant, administered via colonoscopy, from donors who responded well to immunotherapy.

Six of the 15 evaluable patients saw their tumors shrink or had stable disease after they restarted Keytruda. In these responders, gut bacteria composition rapidly shifted toward more favorable types associated with checkpoint inhibitor response, T-cell activation and reduced immune suppression. Fecal transplants “changed the gut microbiome and reprogrammed the tumor microenvironment to overcome resistance,” the researchers concluded.

The team is now working to identify specific types of bacteria linked to favorable immune response. They hope to develop oral capsules containing a cocktail of beneficial microbes that can be used instead of fecal transplants.