Gut Microbes May Up PD-1 Inhibitor Response

A recent study shows for the first time that patients’ gut microbiome may affect whether they respond to checkpoint inhibitors (J Clin Oncol 35, 2017 [suppl 7S, abstract 2]). The results, presented in February at the ASCO-SITC Clinical Immuno-Oncology Symposium in Orlando, FL, reveal that microbial diversity and composition may help predict whether PD-1 inhibitors will shrink melanomas.

Animal studies have demonstrated that the presence of certain intestinal bacteria boost the potency of checkpoint inhibitors. One 2015 study, for instance, determined that a CTLA-4–blocking antibody was more effective against melanoma in mice whose intestinal microbiome included certain species of Bacteroides (Science 2015;350:1079–84). However, researchers haven’t established whether gut bacteria provide the same benefits in humans.

To test this possibility, a team led by Jennifer Wargo, MD, and graduate student Vancheswaran Gopalakrishnan, of The University of Texas MD Anderson Cancer Center in Houston, sampled bacteria from more than 200 patients with metastatic melanoma who were about to undergo treatment. The researchers checked for differences between responders and nonresponders in the 112 patients who received a PD-1 inhibitor—either nivolumab (Opdivo; Bristol-Myers Squibb) or pembrolizumab (Keytruda; Merck).

The oral microbiome didn’t differ between responders and nonresponders, but the gut microbiome did, the researchers reported. Overall, respondents had more diverse gut bacteria, with higher abundance of microbes in the Clostridiales group and lower abundance of species in the Bacteroidales group. The scientists also detected a correlation between the composition of the gut microbiome and the number of cancer-killing CD8+ T cells that infiltrated patients’ tumors. “There seems to be a clear role for the microbiome in modulating host and antitumor immunity, as well as responses to immunotherapy,” says Wargo.

“This is very important work,” says Jeffrey Weber, MD, PhD, of the New York University Langone Medical Center, who wasn’t connected to the study. He adds that the number of patients in the study, which is large for microbiome research, gives him confidence that “this effect is real.”

The Clostridiales contains a variety of microorganisms, some that are beneficial and some, such as Clostridium difficile, that are pathogenic, and researchers now need to narrow down which species are responsible for the effects, says Christian Jobin, PhD, of the University of Florida, Gainesville, who also wasn’t connected to the study. “What we need to know is, what is the role of the microbes at the species level and which of their activities are implicated in the beneficial effect?” he says.

Wargo and Gopalakrishnan now plan to test whether modifying gut bacteria improves the response to checkpoint inhibitors. They are working with other researchers to design clinical trials that will alter the microbiome in patients with melanoma and evaluate their response to immune checkpoint blockade. –Mitch Leslie

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NOTED

President Donald Trump released his proposed budget for fiscal year 2018. To pay for a significant increase in defense spending, he suggests cutting allocations to a number of agencies and programs, including the NIH, which would see its budget slashed by $5.8 billion, about 20% of its current funding.

Multiple challenges are slowing broad implementation of personalized medicine, according to a report from The Personalized Medicine Coalition (available at www.personalizedmedicinecoalition.org). It says that the lack of standardized review of laboratory-developed tests, questions about regulatory oversight of next-generation sequencing, reimbursement concerns, and a lack of awareness about the value of personalized medicine have stymied its adoption.

Researchers have found that deaths from childhood cancer may be nearly four times more common than previously thought. They point to a clinical trial involving children with acute myeloid leukemia in which 1.6% of patients died (J Clin Oncol 2017 March 6 [Epub ahead of print]). In contrast, records in the SEER database show that about 6.2% of young patients die of the disease, noting that these children often don’t live long enough to receive treatment or enroll in a clinical trial.

Regeneron Pharmaceuticals and GlaxoSmithKline will collaborate with UK Biobank to sequence samples collected from 500,000 volunteer participants over the past 10 years. The companies aim to sequence 50,000 samples by the end of the year; sequencing of all of the samples in the UK Biobank is expected to take 3 to 5 years.

The UK’s National Institute for Health and Care Excellence said that women should be offered anastrozole if they have a family history of breast cancer to reduce their risk of developing the disease. Based on recent data, researchers concluded that if 1,000 postmenopausal women at high or moderate risk of breast cancer took anastrozole for 5 years, 35 cases of breast cancer would be prevented, compared with 21 if they took tamoxifen.