Antibiotics May Affect Response to CAR-T Therapy for Lymphoma and Leukemia

Researchers explore the relationship between gut bacteria and the body's response to CAR-T therapy.

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CAR (chimeric antigen receptor) T cell therapy, in which a patient's own immune cells are genetically engineered to target and kill cancer cells, has revolutionized the treatment of certain blood cancers. However, up to 60% of patients receiving CAR T therapy still experience relapse and up to 80% of patients experience serious side effects, including neuroinflammation—both of which present an obstacle to CAR T therapy's widespread adoption.

In a collaboration between Memorial Sloan Kettering Cancer Center and the University of Pennsylvania, Damon Runyon Physician-Scientist Melody Smith, MD, and her colleagues are investigating how a patient's gut bacteria might play a role in their response to CAR T therapy, given the significant body of evidence linking the gut microbiome to T cell function. Studies have shown that introducing new gut bacteria through fecal transplant can improve response to immunotherapy, while exposure to antibiotics before cancer treatment can weaken response.

The team's findings, published in Nature Medicine, indicate a similar relationship between gut bacteria and CAR T therapy response. In a retrospective analysis of patients with B cell lymphoma and leukemia, the researchers found that patients who had taken antibiotics in the four weeks prior to treatment had worse survival rates and increased nervous system damage. They also analyzed stool samples from CAR T cell recipients and identified specific bacteria associated with better clinical outcomes. The presence of bacteria belonging to the Clostridia class, for example, was associated with no detectable cancer within 100 days of treatment.

With this study, Dr. Smith and her team have opened a new door for investigation of the gut microbiome's role in anti-cancer immunity. Their findings also indicate specific clinical interventions—whether adjusted antibiotic use or probiotic measures such as fecal transplant—that may improve response to CAR T therapy and decrease its harmful side effects. In short, CAR T cell recipients may one day prepare their gut bacteria to join forces with their immune system in the body's fight against cancer.

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