Certain combinations of gut bacteria protect stem cell transplant patients from immune reactions, finds study

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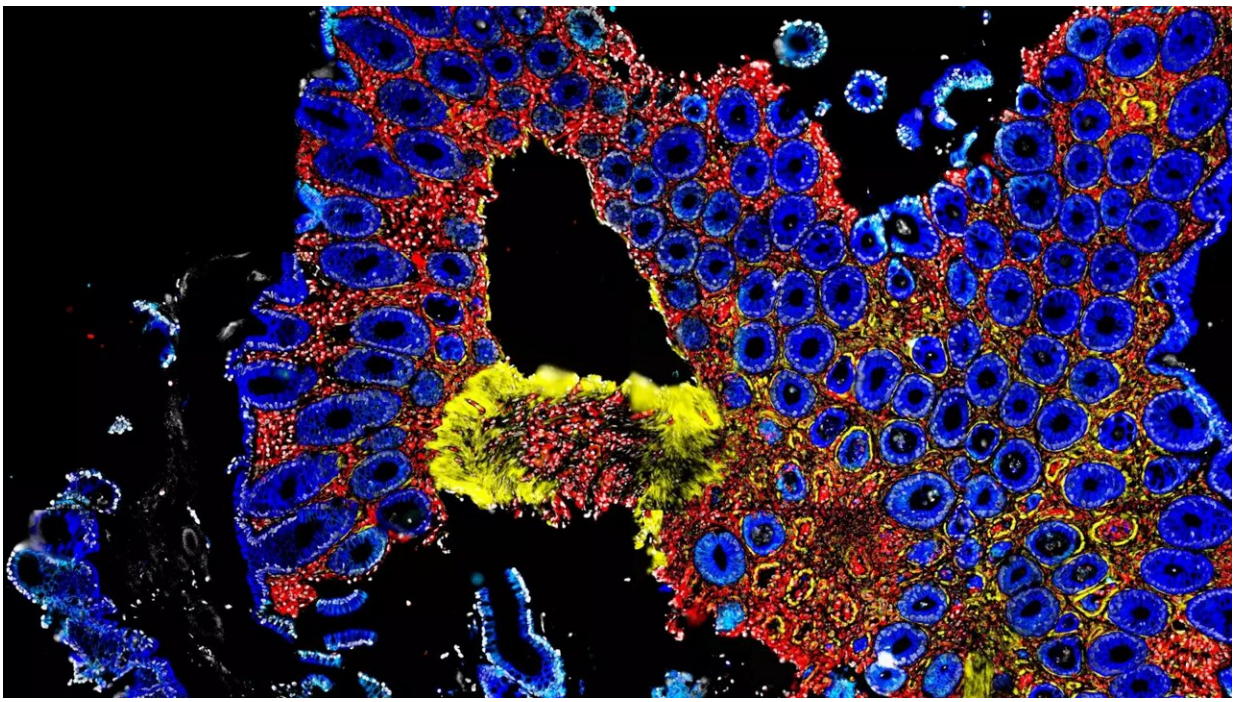

Intestinal tissue during a graft-versus-host reaction: Donor cells (red) attack the body of the patient. Credit: Sebastian Jarosch, Dirk Busch / TUM

After stem cell transplantation, the donated immune cells sometimes attack the patients' bodies. This is known as graft versus host disease or GvHD. Researchers at the Technical University of Munich (TUM) and

the Universitätsklinikum Regensburg (UKR) have shown that GvHD is much less common when certain microbes are present in the gut. In the future, it may be possible to deliberately bring about this protective composition of the microbiome.

Stem cell transplantation can save the lives of patients suffering from cancers such as leukemia. However, graft versus host reactions occur following around half of these procedures. In a sense, they are the reverse of the rejection response seen after organ donations, in which the body attacks the donated organ. Here, the donated cells attack the patient's body, for instance, in the digestive tract.

It has been known for some time that microbes in the gut play a role in determining whether GvHD occurs. A team working with Dr. Erik Thiele Orberg, who heads a research group at the Clinic and Polyclinic for Internal Medicine III of TUM's Klinikum rechts der Isar, Ernst Holler, Senior Professor of Allogenic Stem Cell Transplantation at UKR, and Prof. Hendrik Poeck, executive senior physician at UKR's Clinic and Polyclinic for Internal Medicine, describe in the journal *Nature Cancer* how the gut microbiome must be composed to provide protection.

The researchers studied stool samples from 78 patients at the two university clinics and tracked them over two years following stem cell transplantation. They used the results to develop a risk index indicating the probability of a rejection reaction. "Instead of counting bacteria, we measured the quantities of certain metabolites produced by the microbes," says Orberg.

These immuno-modulatory microbial metabolites (IMMs) influence the immune system and the body's regenerative capacity. "It is remarkable that a positive prognosis does not depend only on IMMs from bacteria," says Dr. Elisabeth Meedt, a physician at UKR and co-first author of the

article. "We demonstrated that certain viruses in the gut—the bacteriophages—also play a role. This alone offers an impressive insight into the complex world of our gut microbiome."

"Patients with a low IMM risk index had a higher chance of survival, showed fewer graft vs. host reactions, and experienced fewer relapses," says Poeck. The metabolites are formed mainly by bacteria from the families Lachnospiraceae and Oscillospiraceae in combination with the bacteriophages.

In the next step, the researchers at TUM and UKR want to predict and actively improve patients' chances at a cure. "By precisely controlling the composition of fecal microbiota transplants, the gut could be colonized with specific consortia of bacteria and bacteriophages," says Poeck. "In the coming years, we want to find out whether we can use this approach to prevent graft vs. host reactions as well as relapses."

Initial experiments with mice have been successful. As a result, the procedure could now be tested in clinical trials with human patients.

More information: Erik Thiele Orberg et al, Bacteria and bacteriophage consortia are associated with protective intestinal metabolites in patients receiving stem cell transplantation, *Nature Cancer* (2024). DOI: 10.1038/s43018-023-00669-x

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