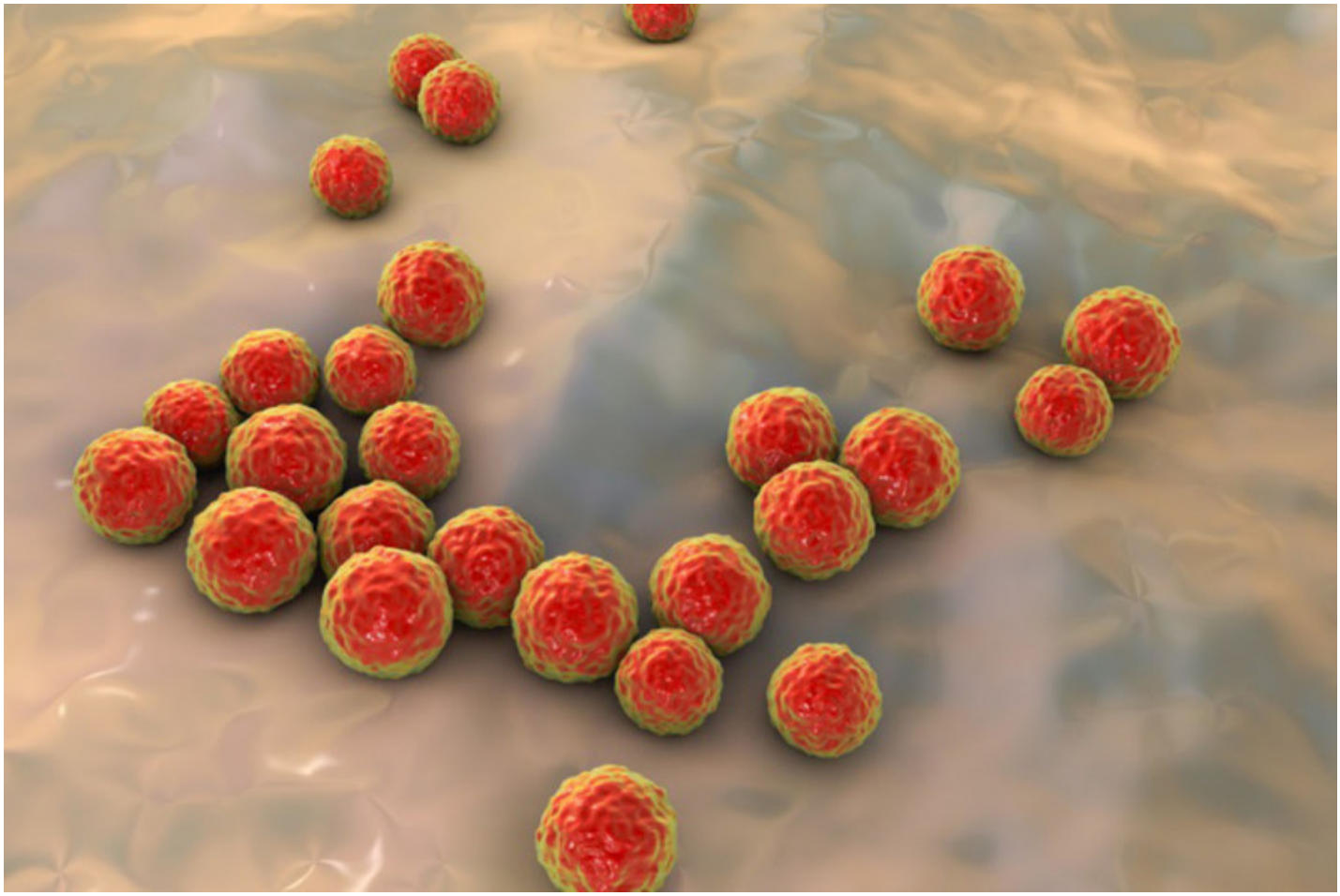
On Cancer

Study in Mice Suggests Lactose in the Diet Feeds Dangerous Gut Bacteria When the Immune System Is Compromised

By Julie Grisham, **Friday, November 29, 2019**



Infections with the Enterococcus bacterium are a major threat in healthcare settings. Credit: Katerna Kon/Science Source

Summary

> An international team led by scientists from MSK has shown for the first time that foods containing lactose, a sugar that's naturally found in milk and dairy products, help Enterococcus thrive in the gut, at least in mice.

Infections with the *Enterococcus* bacterium are a major threat in healthcare settings. They can lead to inflammation of the colon and serious illnesses such as bacteremia and sepsis, as well as other complications.

Enterococcus infections are particularly risky for people having **stem cell and bone marrow transplants (BMTs)** to treat blood cancer. Studies have suggested that high levels of *Enterococcus* increase the incidence of **graft-versus-host disease (GVHD)**, a potentially fatal condition in which immune cells from the donor's stem cells attack the recipient's organs.

Now, an international team led by scientists from Memorial Sloan Kettering has shown for the first time that foods containing lactose, a sugar that's naturally found in milk and dairy products, help *Enterococcus* thrive in the gut, at least in mice. They also studied changes in the bodies of people having BMTs. The **study** was published November 29 in *Science.*

"These findings hint at a possible new way to reduce the risk of GVHD as well as dangerous infections," says MSK physician-scientist and GVHD expert **Jonathan Peled**. "But they are still preliminary, and it's too early to suggest cutting out lactose in the diets of people undergoing BMTs or other hospitalized patients who are at risk from *Enterococcus*."

Focusing on the Microbiota

For several years, Dr. Peled and **Marcel van den Brink,** head of MSK's **Division of Hematologic Malignancies**, have been studying the relationship between GVHD and microbiota — the community of microorganisms that inhabit the body. The two of them are co-senior authors of the new study.

Their previous research has shown that when harmless strains of microbes are wiped out, often due to treatment with antibiotics, *Enterococcus* and other harmful types of bacteria can take over due to lack of competition. As part of the new study, which included analysis of microbiota samples from more than 1,300 adults having BMTs, the team confirmed the link between *Enterococcus* and GVHD.

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Jonathan Peled
physician-scientist

The investigators conducted further *Enterococcus* research in cell cultures and in mice. “Mouse models are very helpful for understanding the mechanisms in the gut that lead to GVHD,” says Dr. van den Brink, who is also Co-Director of the **Parker Institute for Cancer Immunotherapy** at MSK and leads a **lab** in the Sloan Kettering Institute’s **Immunology Program.** “We studied mice that had been given BMTs and found that the cells lining their intestines, called enterocytes, were no longer able to make lactase, the enzyme that breaks down lactose. The high levels of undigested lactose in turn led to a total domination of *Enterococcus*. It was shocking to see how one type of bacteria completely takes over.”

Dr. van den Brink adds that on top of the defective enterocytes, the loss of competing healthy strains of bacteria caused by antibiotic treatment makes problems in the gut even worse. “It’s a double whammy,” he says.

A Trip to the Pharmacy Leads to a Surprising Discovery

To study whether higher lactose levels were boosting the growth of *Enterococcus*, or whether the connection was only a coincidence, visiting researcher and first author Christoph Stein-Thoeringer went to the pharmacy to buy Lactaid®. These lactase-containing pills break down lactose, helping people who are lactose intolerant to eat dairy products without side effects.

The researchers discovered that when lactase was added to lab cultures of *Enterococcus*, the bacterial growth was blocked. So, they began to feed lactose-free chow to lab mice that had been given BMTs and found that mice on the special diet were protected against *Enterococcus* domination.

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The investigators have not yet tested the new findings in humans, but existing data suggests that the same connection between lactose and *Enterococcus* seen in the mice may be at play in people who have had BMTs. “We know which gene variants are associated with being lactose intolerant,” Dr. Peled notes. “We looked at our records and found that people who had these gene variants tended to have a harder time clearing *Enterococcus* from their guts than others did.”

He adds that many BMT recipients become temporarily lactose intolerant, likely due to the loss of enterocytes caused by **chemotherapy**. “We are considering doing a trial in which people eat a lactose-free diet or take Lactaid during their cancer treatment to see if the growth of *Enterococcus* is blocked,” Dr. Peled says.

A Global Effort

Another important aspect of the new study is that it didn’t just look at people treated at MSK. It also included patient samples from Duke University School of Medicine in Durham, North Carolina; Hokkaido University in Sapporo, Japan; and University Hospital Regensburg in Germany. Researchers from those three institutions also contributed to the *Science* paper.

“Researchers who study the microbiome know that the environment in which a person lives is a major factor,” Dr. van den Brink says. “We’ve made a major effort to collect samples from all over the world, so we know that when we find common features, they are likely to hold up worldwide.”

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Dr. Peled reports research funding, intellectual property fees, and travel reimbursement from Seres Therapeutics and consulting fees from DaVolterra. Dr. van den Brink has received research support from Seres Therapeutics; has consulted, received honorarium from, or participated in advisory boards for Seres Therapeutics, Flagship Ventures, Novartis, Evelo, Jazz Pharmaceuticals, Therakos, Amgen, Magenta Therapeutics, WindMIL Therapeutics, Merck & Co. Inc., Acute Leukemia Forum (ALF), and DKMS Medical Council (Board). He also has IP licensing with Seres Therapeutics and Juno Therapeutics and stock options from Smart Immune.

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