



The Gut Microbiome

What is the gut microbiome?

The gut microbiome is best thought of as a metabolically active organ made up of trillions of microorganisms—primarily bacteria, but also viruses, fungi, archaea and bacteriophages—plus their collective genes and metabolites. The microbiome is not only important for digestion but is also plays a major role in immune development, maintenance of the intestinal barrier, nutrient metabolism, bile-acid signaling, drug metabolism, as well as the development and treatment of cancer.

The microbiome and the immune system

The intestine is one of the body's major interfaces with the outside world and contains one of the largest concentrations of immune cells in the body. The intestinal epithelium is not simply a physical wall. It is a highly regulated immune barrier containing mucus, tight junctions, antimicrobial peptides, and immune cells. One of the most important concepts is immune tolerance. The immune system must tolerate trillions of commensal organisms without becoming chronically inflamed while remaining capable of mounting a rapid response to an invading pathogen.

Fiber, bacteria and short-chain fatty acids

Some dietary fibers reach the colon without being fully digested. Gut bacteria ferment these fibers and produce **short-chain fatty acids (SCFAs)**, especially acetate, propionate and butyrate. Colonocytes use butyrate as a major energy source. It also promotes epithelial integrity, mucus production and tight-junction function. Butyrate and other short-chain fatty acids can influence regulatory T cells, effector T cells, macrophages, B cells and dendritic cells. These effects can actually influence **gene expression and epigenetic regulation in human cells**.

That leads to an important concept: Fiber does not simply “keep the bowel moving.” Fiber provides metabolic substrate for organisms that manufacture signaling molecules capable of regulating immunity.

The microbiome trains the immune system

Development of the immune system begins very early in life. Birth mode, breast feeding, antibiotic exposure, diet and environmental microbial exposure influence early microbial colonization. These organisms help educate developing T-cell and B-cell populations and establish immune tolerance.

The interaction continues throughout life. This is one reason microbiome disturbances are being investigated in conditions as diverse as:

IBD, food allergy, asthma, autoimmune disease, metabolic disease and cancer

The microbiome and cancer

Cancer is not caused by a single 'bad bacterium.' Cancer develops through complex interactions among genetics, age, environment, lifestyle and other factors. However, research shows that certain microorganisms and microbial products can influence conditions that favor or oppose cancer development.

Possible mechanisms include:

- Chronic inflammation and injury to the intestinal lining.
- Production of chemicals that can damage DNA.
- Changes in normal cell growth and metabolism.
- Alteration of immune surveillance against abnormal cells.
- Changes in the local environment surrounding a tumor.

Colibactin-producing *E. coli*

Some strains of *Escherichia coli* contain genes that allow them to produce a genotoxin called **colibactin**. Colibactin can damage DNA. Researchers have identified characteristic mutation patterns associated with colibactin exposure in human colorectal cancers, providing an important example of how a microbial product may contribute directly to cancer-related genetic damage.

Fusobacterium nucleatum and colorectal cancer

Fusobacterium nucleatum, a bacterium commonly associated with the mouth, is enriched in some colorectal cancers. Research suggests that certain strains may promote inflammation, interact with tumor cells and alter the immune environment around a tumor. Its possible roles in cancer progression, metastasis and treatment response remain active areas of investigation.

Bacteroides fragilis

Enterotoxigenic ***Bacteroides fragilis***, or ETBF, produces *Bacteroides fragilis* toxin. This toxin can damage the epithelial barrier and activate inflammatory signaling pathways. The result can include: increased intestinal permeability, inflammation and epithelial proliferation.

ETBF, pks-positive *E. coli* and *Fusobacterium* are therefore among the organisms most consistently investigated as potential contributors to colorectal carcinogenesis.

The microbiome and cancer immunotherapy

Immune checkpoint inhibitors help the immune system recognize and attack cancer cells. These treatments include drugs targeting receptors on T cells. Researchers have repeatedly found differences in the intestinal microbiomes of patients who respond to checkpoint inhibitors and those who do not.

This has led to an important question: **Can deliberately changing the microbiome improve the response to cancer immunotherapy?** Early human trials suggest that microbiome manipulation

may eventually become part of cancer treatment, although it remains investigational.

Fecal microbiota transplantation (FMT) and cancer

FMT transfers an intestinal microbial community from a carefully screened donor to another person. FMT has an established role in selected patients with recurrent *Clostridioides difficile* infection. Its use in cancer therapy is experimental.

In a 2026 phase 2 trial, 20 patients with non-small-cell lung cancer and 20 with melanoma received healthy-donor FMT before immune checkpoint therapy. Objective response rates were 80% in the lung cancer cohort and 75% in the melanoma cohort. Because this was a small, open-label study without a randomized control group for these cohorts, the results are promising but do not establish FMT as standard cancer treatment.

Antibiotics and the microbiome

Antibiotics can substantially change the intestinal microbiome. Another clinically important observation is that exposure to broad-spectrum antibiotics near initiation of checkpoint therapy has frequently been associated with worse outcomes but these results can be difficult to interpret because patients who need antibiotics may differ in other important ways.

Patients should not avoid necessary antibiotics. Bacterial infections should be treated appropriately. The practical goal is to avoid antibiotics when they are not medically indicated.

What can you do to support a healthy microbiome?

There is no single scientifically defined 'perfect' microbiome. Healthy people can have very different bacterial communities. For most people, the safest way to support a healthy intestinal ecosystem is through diet and overall lifestyle rather than unproven microbiome products.

- **Eat a variety of plant foods:** vegetables, fruits, beans, legumes, whole grains, nuts and seeds.
- **Include fiber regularly:** different fibers provide substrates for different microbial communities.
- **Limit excessive ultraprocessed foods and processed meats** as part of an overall healthy dietary pattern.
- **Exercise regularly and obtain adequate sleep.**
- **Use antibiotics appropriately** and avoid unnecessary antibiotic exposure.
- **Follow recommended colorectal cancer screening guidelines.**

What about probiotics?

Probiotics can be useful in selected medical situations, but an over-the-counter probiotic containing a few strains is very different from the complex ecosystem of the human intestine. There is currently

no convincing evidence that a general probiotic prevents colorectal cancer or universally 'boosts' immunity.

Should I have my microbiome tested?

Commercial stool tests may report bacterial diversity, 'good' and 'bad' bacteria, gut age or individualized food and supplement recommendations. The technology is interesting, but clinical interpretation remains limited. A 2025 international consensus statement concluded that evidence supporting routine clinical microbiome testing is still scarce and that greater standardization is needed.

The future of microbiome medicine

The field is moving away from simply labeling individual bacteria as good or bad. Researchers increasingly focus on **what microbial communities are doing** - which metabolites they produce, which immune pathways they influence and which harmful functions might be removed or replaced.

Future strategies may include:

- Precisely designed bacterial communities.
- Targeted dietary and prebiotic interventions.
- Microbial metabolites or 'postbiotics.'
- Bacteriophages that selectively remove specific bacteria.
- Engineered bacteria.
- Targeted approaches to bacterial toxins such as colibactin.
- Carefully standardized microbiota transplantation.

THE BOTTOM LINE

The gut microbiome is an important partner in digestion, intestinal barrier health and immune regulation. It is also increasingly linked to colorectal cancer biology and the response to some cancer immunotherapies. The science is advancing rapidly, but there is not yet one ideal microbiome, probiotic, supplement or commercial test proven to optimize immune health or prevent cancer.

References and further reading

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Patient Information: This handout is for general educational purposes and does not replace individualized medical advice, diagnosis or treatment from your physician or other qualified healthcare professional. Research on the gut microbiome is rapidly evolving. Updated October 2026.