

How Bacteria May Promote Breast Cancer

Overabundance of certain pathogenic bacteria can increase the activity of a key metabolic enzyme, leading to tumor growth and metastasis.

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Researchers at the Johns Hopkins Kimmel Cancer Center have discovered how certain pathogenic bacteria in gut and breast tissue can promote breast cancer development and progression by hijacking a key metabolic enzyme known as spermine oxidase (SMOX).

In a study led by [Dipali Sharma](#), PhD, professor of oncology and a Fetting Fund scholar, investigators found that exposure to pathogenic bacteria such as *Bacteroides fragilis*, *Fusobacterium nucleatum*, and *Escherichia coli* significantly increased SMOX activity, leading to DNA damage, tumor growth, and metastasis in laboratory and animal models of breast cancer.

The work, published February 15 in [Cancer Research](#), reveals a novel link between microbial dysbiosis — the imbalance of good and harmful bacteria — and breast cancer, and identifies SMOX as a potential therapeutic target.

“Microbes don’t just reside in our gut. They can directly influence cancer behavior,” says Sharma. “We found that an overabundance of certain pathogenic bacteria triggers inflammation and activates SMOX, producing reactive oxygen species that damage DNA and fuel tumor growth. By blocking SMOX, we were able to dramatically reduce tumor formation in our preclinical models.”

The researchers focused on enterotoxigenic *Bacteroides fragilis* (ETBF), a strain known to secrete a potent toxin that can remodel bacterial communities and promote cancer. When breast cancer cells or mouse mammary tissue were exposed to ETBF or its toxin, SMOX levels surged, setting off a chain reaction that increased oxidative stress, inflammation and genomic instability.

Further experiments showed that *Fusobacterium nucleatum* and toxin-producing *E. coli* had similar effects, while nonpathogenic bacteria did not. The bacteria also triggered a rise in inflammatory cytokines interleukin-6 (IL6) and tumor necrosis factor-alpha (TNF-alpha), both of which further amplified SMOX expression and activity.

“This establishes a self-perpetuating loop,” says Deeptashree Nandi, PhD, a postdoctoral fellow working with Sharma and first author on the study. “Inflammatory cytokines stimulate SMOX,

SMOX generates oxidative stress, and the resulting DNA damage helps tumors grow and spread.”

To test whether this bacterial influence could be stopped, the investigators treated breast cancer cells in laboratory and animal models with two SMOX inhibitors — MDL72527 and SXG-1. Both agents effectively suppressed SMOX activity, reduced DNA damage markers, and halted tumor progression, even in the presence of pathogenic bacteria.

Mice colonized with ETBF developed more and faster-growing mammary tumors than uninfected controls, but those treated with SMOX inhibitors had markedly smaller tumors, fewer metastases, and lower markers of oxidative DNA damage.

“These findings suggest that pharmacologic inhibition of SMOX could be a viable strategy to counteract the cancer-promoting effects of microbial dysbiosis,” Sharma says.

The research also revealed that the SMOX-driven mechanism was not unique to *B. fragilis*. Pathogenic *F. nucleatum*, *E. coli*, and even *Mycobacterium tuberculosis* culture extracts also induced SMOX upregulation and DNA injury in breast cancer cells.

“This convergence across distinct bacterial species suggests that SMOX may represent a shared molecular hub through which microbes influence cancer biology,” says Sharma.

The findings suggest that evaluating SMOX activity or microbial composition could help identify women at higher risk for aggressive breast cancer. The researchers are now exploring SMOX inhibitors as potential adjuncts to standard therapies and investigating how microbe-induced inflammation affects tumor immune responses.

“Understanding how bacteria communicate with cancer cells opens entirely new avenues for prevention and treatment,” says Sharma. “If we can interrupt that conversation — particularly by targeting SMOX — we may be able to slow or even stop cancer progression in patients affected by microbial imbalance.”

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