



**ONE** in  
**EIGHT**

AN UNEXPECTED SOURCE OF BREAST  
CANCER RISK

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When it comes to breast cancer risk factors, researchers have long known the usual suspects. Age, family history, and inherited gene mutations, such as BRCA1 and BRCA2, fall into the category of unchangeable risk factors. Others, like obesity, lack of physical activity, alcohol or tobacco use, and exposure to toxins, are considered modifiable, or behaviors women can change to potentially reduce their breast cancer risk. What troubles scientists, however, is that even among women who carry the strongest known risk factors, not all develop breast cancer. Moreover, some women with no apparent risk find themselves with a diagnosis of breast cancer.

“Clearly, there are other factors at play,” says cancer prevention expert and former Fetting Fund scholar Dipali Sharma, Ph.D. “We knew we had to look beyond the established risks if we truly wanted to understand who is most vulnerable and how we can prevent this disease.”

With seed support from the Fetting Fund for Breast Cancer Prevention, Dr. Sharma and her colleagues have been pursuing high-risk, high-reward ideas that might not have been funded otherwise, but that hold the potential to change the way we detect and prevent breast cancer.

One of the team’s first projects looked to an unexpected place, the gut microbiota, i.e. bacteria. Although it has been an important area of research for gastrointestinal cancers, it seemed, on the surface, an unlikely culprit when it came to breast cancer.

However, in a Fetting Fund pilot project, Dr. Sharma’s lab discovered that *Bacteroides fragilis* (ETBF), a microbe previously linked to chronic diarrhea and colon cancer, was also present in malignant breast tissue. The finding opened a new line of inquiry for Dr. Sharma and team as they looked to see if the bacterium plays a role in breast cancer initiation or growth.

In a series of laboratory experiments, the team discovered that when ETBF was introduced to the gut or breast ducts of mice, it always induced growth and metastatic progression of tumor cells. The research earned international attention when it was published in the journal Cancer Discovery.

“We believe certain receptors on breast cancer cells may attract these bacteria, allowing them to enter and persist,” Dr. Sharma explains.

In clinical studies, the investigators have started looking for microbiota changes among breast cancer patients to see how this impacts tumor progression and response to therapy. The seed funding from the Fetting Fund allowed Dr. Sharma’s team to gather preliminary data, which they used to win a major Department of Defense (DoD) grant to expand the work and to secure a second DoD grant.

Their studies have the promise to lead to new strategies to detect the bacteria early, and potentially prevent or halt its impact on breast cancer development.

“Projects like these often face steep hurdles at major funding agencies like the NIH, where highly innovative but untested ideas can be difficult to push through,” says Dr. Sharma. “The Fetting Fund gives us the ability to take that first step and allows us to generate the evidence we need to compete for large-scale grants and move discoveries forward.”



Dr. Dipali Sharma