

# Decoding the microbial signature of aggressive form of breast cancer

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Micrograph showing a lymph node invaded by ductal breast carcinoma, with extension of the tumour beyond the lymph node. Credit: Nephron/Wikipedia

Cancer is a result of normal cellular functions going wildly awry on a genetic level. That fact has been known for some time, but increasing evidence is showing that the human microbiome, the diverse population of microorganisms within every person, may play a key role in either setting the stage for cancer or even directly causing some forms of it. A new study from the Perelman School of Medicine at the University of Pennsylvania, led by Erle S. Robertson, PhD and James C. Alwine, PhD, has identified, for the first time, an association between two microbial signatures and triple negative breast cancer (TNBC), the most aggressive form of the disease. The work was published online this week in *Scientific Reports*.

"Viruses and other microorganisms probably have much more to do with [cancer](#), at least the propagation of cancer and promotion of it, than is really known," said Alwine, a professor of Cancer Biology and associate director for core services at the Abramson Cancer Center. Using a microarray technology called PathoChip containing 60,000 molecular probes to identify all known viruses and pathogenic bacteria, fungi, parasites, and other microorganisms, Robertson, a professor of Microbiology and his colleagues screened tissue samples from 100 TNBC patients.

They also examined 40 matched and non-matched controls (matched controls are non-tumor tissue from TNBC patients; non-matched controls are breast tissue from healthy patients).

The team found a distinct microbial signature distinguishing TNBC tissue from normal samples, which could be further delineated into two broad clusters, one predominantly viral and the other predominantly bacterial, with some fungi and parasites.

"If we look at this closely, we may also find some smaller clusters within those major groups that could give us some insights to unique identifiers

for individuals in these clusters," stated Robertson, who is also associate director for global cancer research and co-leader of the tumor virology program at the Abramson Cancer Center. He explains that the team found "about 30 organisms that provide a specific type of signature to give us clues for developing a diagnostic tool." Co-authors Sagarika Banerjee, PhD, and Kristen Peck, from the Robertson lab, screened the organisms, and Michael Feldman, MD, PhD, and Natalie Shi from the department of Pathology and Laboratory Medicine, performed the pathology examinations to identify the TNBC cases.

Among the most prevalent viruses detected were Herpesviruses, Parapoxviruses, Retroviruses, Hepadnaviruses, Polyomaviruses, and Papillomaviruses. Significant bacterial signatures included *Arcanobacterium*, *Brevundimonas*, Sphingobacteria, and *Geobacillus*, while fungal species *Pleistophora* and *Piedra* and parasitic organisms *Foncecaea* and *Trichuris* were among the prominent ones identified.

Alwine emphasizes that the detection of these and the other pathogens in TNBC tissues does not necessarily mean that they actually cause cancer. "There are a lot of different ways to look at this," he pointed out. "It's possible that some of the organisms we're looking at have a causative effect, but we don't know that. We can't say until it's been thoroughly tested by many more experiments." One possibility is that the organisms could be adding something to the cellular microenvironment that helps damaged cells to become malignant or pushes them over the edge into cancer. Alternatively, certain organisms may simply find tumor tissue a favorable environment, without having any direct involvement at all with the cancer. "They might just be there because it's a good place to hang out," Alwine said.

In either case, finding a distinct microbial signature associated with cancer raises the prospect of new diagnostic possibilities. "We're looking at the signature as a potential for being able to diagnose cancer, possibly

at an earlier stage," Alwine explained.

"We're looking at different cancers to find out whether or not there are specific signatures that go with specific cancers." Robertson said. "We are also trying to come up with ways in which we can look at blood samples to see if we can potentially develop a test to detect these signatures, which might provide an early surveillance system for identifying patients who might be prone to developing these malignancies."

"The microbial signatures may also have therapeutic implications," Robertson said. "Many of these microorganisms can metabolize drugs and so their presence might diminish the effect of some drugs and might guide the ability to decide what to use for treatment of cancer," Alwine said. The research team next plans to explore these intriguing prospects in conjunction with the breast oncology group at Penn Medicine.

"We're not trying to say that any of these organisms are directly causing cancer," Alwine said. "We're trying to identify the specific cancer signature, so that we can figure out ways to treat, control, or modify the cancer or treat the tumor-associated microbes, to prevent these malignancies in the first place. We've now opened up the doors to look more specifically at what these organisms are actually doing."

Provided by University of Pennsylvania School of Medicine

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