

Side-effect avoiding treatment shows early promise against breast cancer in mice

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A medical illustration of *Clostridioides difficile* bacteria, formerly known as *Clostridium difficile*. Credit: Public Health Image Library, Centers for Disease Control and Prevention (CC0 1.0, creativecommons.org/publicdomain/zero/1.0/)

New experimental evidence suggests that substances known as narrow-spectrum Wnt signaling inhibitors—which could have fewer side effects

than other related substances—are capable of suppressing the growth of breast cancer tumors in mice. Aina He of Shanghai Jiaotong University Affiliated Sixth People's Hospital, China, and colleagues presented these [findings](#) November 9 in the open access journal *PLOS Biology*.

While certain subtypes of breast cancer can be targeted with special medications, others can only be treated with standard chemotherapy. For some patients, chemotherapy may lead to the growth of stem cell-like cancer cells that are drug resistant.

Previous studies suggest that medications that inhibit a specific biological process called Wnt signaling could potentially combat these cells, but so far, the potential benefits of Wnt signaling inhibitors have been hampered by their damaging side effects, particularly on bone density.

These side effects arise from the fact that humans have ten different versions of the Wnt signaling receptor, Frizzled, with distinct functions. Researchers have therefore recently developed new Wnt signaling inhibitors that could reduce side effects by targeting just three of these receptors. However, it has been unclear how effective these narrow-spectrum Wnt signaling inhibitors might be at treating cancer.

To shed new light on the subject, He and colleagues conducted a series of experiments with a specific narrow-spectrum Wnt signaling inhibitor known as TcdB^{FBD}, which was derived from a toxin found naturally in the bacterial species *Clostridium difficile*. They tested TcdB^{FBD} in several different mouse models that mimic different types of breast cancer—basal-like and luminal-like—found in humans.

The researchers found evidence suggesting that TcdB^{FBD} suppressed [tumor growth](#) and reduced the activity of stem cell-like cancer cells in the mice, without side effects on bone density. They also found evidence

that TcdB^{FBD} can synergize with the standard chemotherapy drug cisplatin to inhibit both basal-like and luminal-like breast cancer tumors in mice.

These findings provide preliminary evidence for the potential therapeutic promise of narrow-spectrum Wnt signaling [inhibitors](#) like TcdB^{FBD}. However, more research will be needed to investigate their effectiveness in humans, examine how they might synergize with other cancer treatments beyond cisplatin, and explore their effects in additional types of cancer—such as serous ovarian cancer and oral squamous cell carcinoma.

The authors add, "A bacterial toxin fragment targets and suppresses breast [cancer](#) tumor-initiating and chemo-resistant cells."

More information: Targeted inhibition of Wnt signaling with a *Clostridioides difficile* toxin B fragment suppresses breast cancer tumor growth. *PLoS Biology* (2023). [DOI: 10.1371/journal.pbio.3002353](https://doi.org/10.1371/journal.pbio.3002353). journals.plos.org/plosbiology/.../journal.pbio.3002353

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