A possible explanation for recurring breast cancer

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Credit: Texas A&M University

In October, we mourned those who died of breast cancer and celebrated all of the women (and men) who have survived. What many of those survivors worry about, though, is that their breast cancer may come back. It has puzzled scientists and health care providers that cancer can suddenly reappear, often with a vengeance, months or years after treatment is over.

Now, researchers at the Texas A&M College of Medicine have found that these dormant tumor cells might have become latent because they cannibalized—basically ate—the body's own stem cells. The study was published this month in the *Proceedings of the National Academy of Sciences* (*PNAS*).

The team had been working on teaching adult stem cells from bone marrow, called mesenchymal stem/stromal cells (MSCs), to fight cancer when they noticed that the MSCs were disappearing from the cell cultures.

"We actually thought we made a mistake or were witnessing an anomaly or negative result," said Thomas J. Bartosh, PhD, assistant professor at the Texas A&M College of Medicine and first author of the study. "We eventually realized that the breast cancer cells were eating the stem cells. What was really interesting was what happened next: The breast cancer cells that had taken in the stem cells went dormant—essentially became 'sleepy'—but at the same time they became much more difficult to kill."

Bartosh and the team realized that if breast cancer cells in the body behave the same way, it might explain cancer recurrence.

The cancer cells that have cannibalized MSCs are highly resistant to chemotherapy and nutrient deprivation that fairly effectively kills other cancerous cells. Because there are only a few of them, the surviving cells are not detected with existing scanning methods. "Then one day, when conditions are right, the cells 'wake up' and start growing again," Bartosh said. "This is when the cancer recurs, and because the cells are treatment-resistant, the recurrence can be very difficult to combat."

The hope is that now a possible mechanism for recurrence has been explained, a treatment could be found that would keep those cannibalistic cells dormant, and doing no harm, for the rest of the

person's life. Another possible avenue for drug development would be something that would stop breast cancer cells from eating MSCs in the first place. Bartosh and the team are also working on exploiting the cannibalistic activity of some cancer cells to potentially feed them toxic agents, using MSCs as the delivery vehicle that can target cancer cells specifically, like a tumor-seeking missile.

"The biology of the process is intriguing. It's one mysterious phenomenon—cell cannibalism—that might help explain another mysterious phenomenon: tumor dormancy," Bartosh said. "If these findings do translate to humans, the implications for patients would be enormous."

More information: Thomas J. Bartosh et al. Cancer cells enter dormancy after cannibalizing mesenchymal stem/stromal cells (MSCs), *Proceedings of the National Academy of Sciences* (2016). DOI: 10.1073/pnas.1612290113

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