Breast cancer medicines may force some cancer cells into “sleeper mode,” allowing them to potentially come back to life years after initial treatment.

These are the early-stage findings from scientists at Imperial College London, who studied human breast cancer cells in the laboratory.

The team, who studied hormone treatments, say their research opens avenues for finding ways of keeping the cancer cells dormant for longer, or even potentially finding a way of awakening the cells so they can then be killed by the treatment.

“For a long time, scientists have debated whether hormone therapies—which are very effective treatment and save millions of lives—work by killing breast cancer cells or whether the drugs flip them into a dormant ‘sleeper’ state,” explained Luca Magnani, PhD, lead author of the study from Imperial College London Department of Surgery and Cancer.

“This is an important question as hormone treatments are used on the majority of breast cancers. Our findings suggest the drugs may actually kill some cells and switch others into this sleeper state. If we can unlock the secrets of these dormant cells, we may be able to find a way of preventing cancer coming back, either by holding the cells in permanent sleep mode, or by waking them up and killing them.”

**Study Details**

In the study, published in the journal *Nature Communications* (2019; doi: 10.1038/s41467-019-11721-9) and funded by Cancer Research UK and the NIHR Imperial Biomedical Research Centre, the team studied around 50,000 human breast cancer single cells in the lab and found that treating them with hormone treatment exposed a small proportion of them as being in a dormant state.

The team noted the “sleeper” cells may also provide clues as to why some breast cancer cells become resistant to treatment, causing a patient’s drugs to stop working, and their cancer to return.

Hormone therapies are used to treat estrogen-receptor positive breast cancer. These make up over 70 percent of all breast cancers, and are fueled by the hormone estrogen. These cancers are usually treated with surgery to remove the tumor, followed by a course of targeted hormone therapy—usually either aromatase inhibitors or tamoxifen, which target estrogen receptors.

However, around 30 percent of breast cancer patients taking hormone therapies see their cancer eventually return—sometimes as long as 20 years after treatment. This returning cancer is usually metastatic and the tumors are often now resistant to medication.

Previous work by the same team has investigated why breast cancer cells become resistant to hormone treatment, with findings suggesting cells can make their own “fuel,” allowing them to avoid being “starved” by cancer treatment.

This new research provides another piece in the puzzle, explained Iros Barozzi, PhD, co-author of the study, also from the Department of Surgery and Cancer. “These sleeper cells seem to be an intermediate stage to the cells becoming resistant to the cancer drugs. The findings also suggest the drugs actually trigger the cancer cells to enter this sleeper state.”

The research also revealed cells in this dormant sleeper state were more likely to spread around the body, explained Sung Pil Hong, PhD, study co-author from Imperial, “Our experiments suggest these sleeper cells are more likely to travel around the body. They could then ‘awaken’ once in other organs of the body, and cause secondary cancers. However, we still don’t know how these cells switch themselves into sleep mode—and what would cause them to wake up. These are questions that need to be addressed with further research.”

The team added that hormone therapies remain one of the most effective treatments against breast cancer, and that further patient research will explore whether taking hormone therapies for longer after initial cancer treatment could prevent cancer cells from waking from their sleeping state.

“Although treatments for breast cancer are usually successful, cancer returns for some women, often bringing with it a poorer prognosis,” noted Rachel Shaw, PhD, from Cancer Research UK. “Figuring out why breast cancer sometimes comes back is essential to help us develop better treatments and prevent this from happening. This study highlights a key route researchers can now explore to tackle ‘sleeping’ cancer cells that can wake up years after treatment, which could potentially save the lives of many more women with the disease.”

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