Existing drugs may hinder the development of bone metastasis in breast cancer patients

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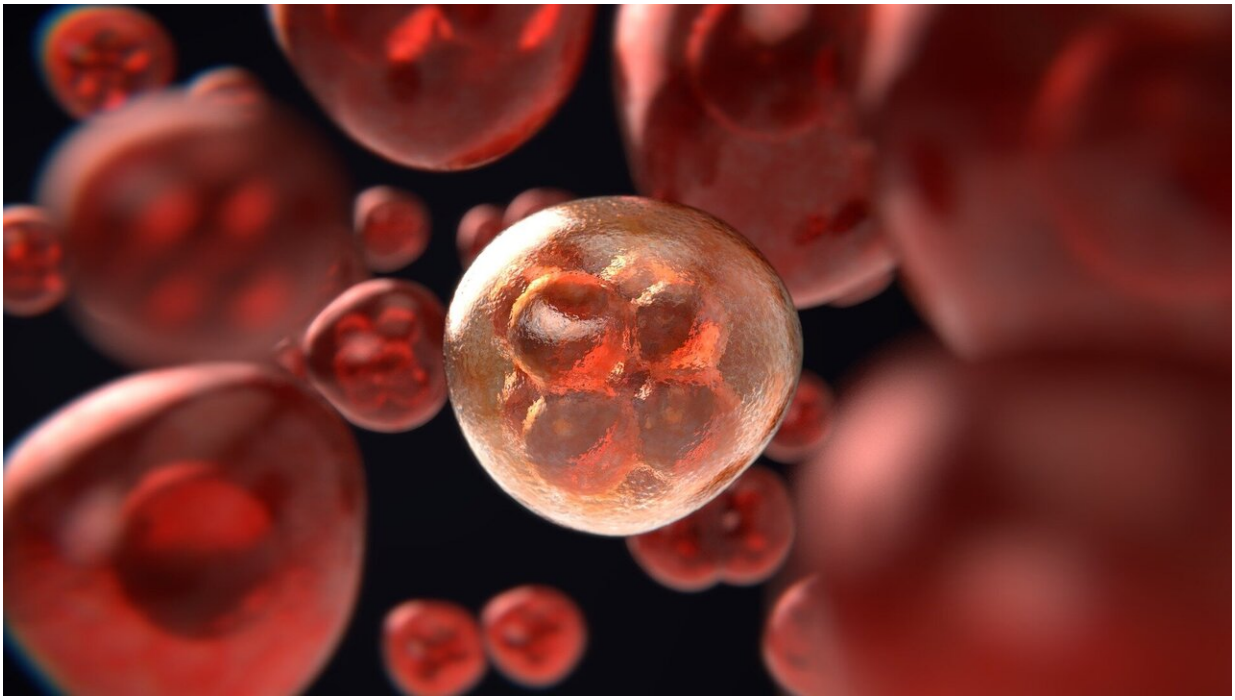

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Researchers at Tel Aviv University developed a new therapeutic strategy based on existing medications to inhibit bone metastasis in breast cancer patients. Using both an animal model and tissue samples from patients in Israel and the US, they demonstrated that a combination of drugs already available on the market can hinder bone metastasis and improve survival.

Based on their findings, the researchers predict that in the future, the treatment can be applied to human patients with breast cancer, as well as other types of cancer.

The study was led by Prof. Neta Erez and Dr. Lea Monteran at Prof. Erez's Laboratory for Tumor Biology at the Pathology Department, Faculty of Medical and Health Sciences, Tel Aviv University. The paper was published in Cancer Discovery.

The researchers explain that over 75% of patients with metastatic breast cancer suffer from bone metastases, which destroy bone tissues, causing fractures and a great deal of pain. Moreover, with today's technologies such as MRI or CT imaging, diagnosis of bone metastasis occurs in most cases when the disease cannot be cured. In this study, the researchers looked for a novel way to inhibit the progression of bone metastasis.

Prof. Erez says, "A tumor is more than a collection of cancer cells. Just like healthy tissues, a tumor is a whole ecosystem consisting of reciprocal interactions between different cell types, including cells of the immune system, connective tissues, blood vessels, etc."

"Moreover, cancer cells often 'corrupt' normal cells, causing them to 'collaborate' with the tumor and support the growth of cancer cells. Blocking the communication channels between cancer cells and healthy cells at an early stage can hinder the growth of cancer cells in the bones. To achieve this, the early stages of the process must be investigated."

To understand the process of bone metastasis, the researchers compared three types of bones from model mice: healthy, early-stage metastasis, and advanced metastasis. They found that when bone metastasis begins, T cells from the immune system arrive on the scene and penetrate the metastases but are unable to destroy them.

Next, the researchers discovered that the killing activity of T cells is inhibited by another type of immune cells and identified the proteins responsible for this effect. To neutralize these inhibitory proteins and reactivate the T-cells, they created a novel therapeutic combination that had never been tried before, a drug that counters the activity of the immune-inhibiting cells, along with an antibody that activates T cells.

This combination was administered to model mice, and the results were encouraging: the bone metastases were reduced, and survival was significantly improved compared to untreated model mice.

At the final stage of the study, the TAU research team collaborated with the Sheba and Ichilov (Tel Aviv) Medical Centers and the Baylor College of Medicine in Texas. They examined tissue samples from bone metastases taken from patients with breast cancer, as well as other types of cancer, and found that the immune cells inhibiting T cells express the same proteins as those found in the animal model.

Prof. Erez says, "Our findings suggest that the combined treatment—attacking the cells that inhibit T cells while activating the T cells—can be effective for treating bone metastasis resulting from breast cancer, as well as other types of cancer."

"The great advantage of our strategy is that both drugs are already available on the market, and consequently, the process of obtaining permits to use them against bone metastasis in humans can be relatively short. At the same time, clinical trials are needed to verify the effectiveness of the new therapeutic strategy."

More information: Lea Monteran et al, Combining TIGIT blockage with MDSC inhibition hinders breast cancer bone metastasis by

activating anti-tumor immunity, *Cancer Discovery* (2024). DOI: 10.1158/2159-8290.CD-23-0762

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