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New way to determine whether metastatic cancer cells in breast cancer patients are dormant or soon to turn deadly

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For the first time ever, Mount Sinai researchers have identified a protein as a marker that can indicate whether a cancer patient will develop a reoccurrence of lethal, metastatic cancer, according to a clinical study published in *Breast Cancer Research* in October.

The researchers found that when cells from a breast cancer patient's original tumor metastasized into the patient's bone marrow with none, or only a small amount, of the protein NR2F1, the patients all soon died. However, patients who had a high concentration of NR2F1 in the cancer cells in their bone marrow did not frequently develop this type of metastatic cancer, and lived longer. The presence of a high concentration of NR2F1 induced dormancy in the cancer cells, essentially deactivating them, so this research shows that survival in these patients is due to the dormancy of the disseminated cancer.

These findings suggest that the absence of this protein in cancer cells that have spread to a patient's bone marrow can reliably signal that the patient will relapse soon and that additional treatment is needed, while if the protein is present, the cancer cells are dormant and the patient can be monitored rather than undergo unnecessary treatment. This research is particularly important because the most common breast type of breast cancer, when it metastasizes, almost always goes to the bone.

The research is especially important in the United States because bone

marrow tests, called aspirates, are not used to monitor patients there. The study was a collaboration with physicians and scientists in Oslo, Norway, where bone marrow aspirates are used to monitor patients. The laboratory of Bjorn Naume from University Hospital of Oslo collaborated with the Aguirre-Ghiso and Sosa labs at the Icahn School of Medicine at Mount Sinai and conducted the analysis of the patients' samples from their clinical trials, thus contributing significantly to this research.

Using this research, physicians could monitor their patients with bone marrow aspirates. Tests for the protein could also help clinicians identify patients who may benefit from recently identified drugs that were shown to target cancer cells and render or keep them dormant. Studies have already shown that androgen deprivation treatment, an anti-hormone therapy used in prostate cancer, has been linked to increasing levels of the NR2F1 protein. Mount Sinai, through a trial funded by the V Foundation for Cancer Research and The Tisch Cancer Institute at the Icahn School of Medicine, has already begun recruiting prostate cancer patients for a test of the ability of two drugs to induce dormancy through NR2F1 upregulation. "This research shows that the survival advantage in these patients is due to high levels of this protein. Tests using this protein marker could further improve curative treatment of breast cancer, sparing patients from unnecessary treatments. Identifying patients with disseminated disease that is not yet symptomatic and characterizing it for potential dormancy or metastatic recurrence is a game changer," said lead researcher Julio Aguirre-Ghiso, Ph.D., Director of Solid Tumor and Metastasis Research, Director of Head and Neck Cancer Basic Research, and Professor of Oncological Sciences, Otolaryngology, and Medicine (Hematology and Medical Oncology) at The Tisch Cancer Institute at the Icahn School of Medicine. "Improved techniques to assess the population of patients with residual disease and their dormant or reactivating state will be key to identifying the risk of future metastasis despite undergoing standard treatment. This opens the way for testing

new treatments that prevent metastasis by inducing dormancy or eradicating the dormant disseminated cancer cells that have not yet initiated metastatic growth."

Provided by The Mount Sinai Hospital