# Ready for relapse: Molecule helps breast cancer cells to survive in the bone marrow

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Patients who survive an initial diagnosis of breast cancer often succumb to the disease years later when the cancer shows up in a different part of the body. Now, scientists have identified key signals that support the long term survival of breast cancer cells after they have spread to the bone marrow. The research, published by Cell Press in the July issue of the journal *Cancer Cell*, may lead to development of treatment strategies that decrease the likelihood of breast cancer recurrence in the bone and other organs.

Metastasis, the ability of cancer cells to spread from the initial site of origin to other parts of the body, occurs frequently in breast cancer. Although it is clear that the majority of late-onset relapses after breast cancer arise in the bone, the mechanisms that contribute to cancer cell survival in the bone marrow environment are unknown.

"We sought to identify signaling pathways that support the survival of metastasized breast cancer cells and thereby extend the period during which metastasis may emerge after the diagnosis and removal of a breast tumor," explains senior study author Dr. Joan Massague from the Cancer Biology and Genetics Programs at Memorial Sloan-Kettering Cancer Center and the Howard Hughes Medical Institute.

Dr. Massague and colleagues used a sophisticated gene profiling technique link specific signaling pathways with late-onset relapse after breast cancer. In an investigation of samples from over 600 breast tumors, the researchers discovered that activity of a cancer-related

enzyme called Src was associated with late-onset bone metastasis. Interestingly, this link was independent of breast cancer subtype and was selective and specific for cell survival in the bone marrow.

The researchers went on to identify Src-regulated signaling molecules that were expressed in the bone marrow and promoted cell survival. Further, Src increased the resistance of metastasized breast cancer cells to a key cell death-inducing signal that was abundantly expressed in bone metastasis tissue. These results demonstrate that Src hyperactivity provides breast cancer cells with a superior ability to survive in the bone marrow.

"The link between Src-dependent signaling and metastatic cell survival provides mechanistic insights into metastasis latency, and suggests strategies to hasten the attrition of disseminated breast cancer cells," concludes Dr. Massague. "Recently, a number of pharmacological Src inhibitors have been developed that may be worthy of consideration in this respect."

Source: Cell Press (news : web)