

'Self-seeding' of cancer cells may play a critical role in tumor progression

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Cancer progression is commonly thought of as a process involving the growth of a primary tumor followed by metastasis, in which cancer cells leave the primary tumor and spread to distant organs. A new study by researchers at Memorial Sloan-Kettering Cancer Center shows that circulating tumor cells - cancer cells that break away from a primary tumor and disseminate to other areas of the body - can also return to and grow in their tumor of origin, a newly discovered process called "self-seeding."

The findings of the study, published in the December 25 issue of the journal *Cell*, suggest that self-seeding can enhance [tumor](#) growth through the release of signals that promote angiogenesis, invasion, and metastasis.

"Our work not only provides evidence for the self-seeding phenomenon and reveals the mechanism of this process, but it also shows the possible role of self-seeding in [tumor progression](#)," said the study's first author Mi-Young Kim, PhD, Research Fellow in the Cancer Biology and Genetics Program at Memorial Sloan-Kettering.

According to the research, which was conducted in mice, self-seeding involves two distinct functions: the ability of a tumor to attract its own circulating progeny and the ability of circulating tumor cells to re-infiltrate the tumor in response to this attraction. The investigators identified four genes that are responsible for executing these functions: IL-6 and IL-8, which attract the most aggressive segment of the

circulating tumor cells population, and FSCN1 and MMP1, which mediate the infiltration of circulating [tumor cells](#) into a tumor.

The findings also show that circulating breast [cancer cells](#) that are capable of self-seeding a breast tumor have a similar [gene expression](#) pattern to [breast cancer](#) cells that are capable of spreading to the lungs, bones, and brain, and therefore have an increased potential to metastasize to these organs. Additional experiments revealed that self-seeding can occur in cancer cells of various tumor types in addition to breast cancer, including colon cancer and melanoma.

"These results provide us with opportunities to explore new targeted therapies that may interfere with the self-seeding process and perhaps slow or even prevent tumor progression," said the study's senior author, Joan Massagué, PhD, Chair of the Cancer Biology and Genetics Program at Memorial Sloan-Kettering and a Howard Hughes Medical Institute investigator.

The concept of self-seeding sheds light on clinical observations such as the relationship between the tumor size, prognosis, and local relapse following seemingly complete removal of a primary breast tumor. "We know there is an association between large tumor size and poor prognosis. This was always thought to reflect the ability of larger cancers to release more cells with metastatic potential. But this association may actually be caused by the ability of aggressive cancer cells to self-seed, promoting both local [tumor growth](#) and distant metastases by similar mechanisms," said study co-author Larry Norton, MD, Deputy Physician-in-Chief for Breast Cancer Programs at Memorial Sloan-Kettering.

Source: Memorial Sloan-Kettering Cancer Center

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