What determines whether breast cancer cells can form metastases?

In most cancers, it is not the growth of the primary tumor that determines the prognosis for the patient, but whether it will spread and form metastases. This process is very complex. There are often years between the development of the cancer and the aggressive growth of the metastases. Scientists from the German Cancer Research Center (DKFZ), the Stem Cell Institute HI-STEM*, the Ruhr University Bochum, Helmholtz Munich and ETH Zurich have studied and identified metastasis growth in breast cancer. They show: Not every breast cancer cell can lead to the development of metastases.

The scientists looked at a specific cellular mechanism called epithelial-mesenchymal transition (EMT). As a result, cancer cells, which are intrinsically sedentary, gain mobility and can first invade surrounding tissues and eventually be transported to distant organs via blood and lymph channels. In the process, as the term EMT describes, the cancer cells change their cellular identity from "epithelial" to "mesenchymal" and back, which can be detected using various markers.

Reprogrammed clones metastasize less

Both types of cancer cells were present in the metastasis biopsies. Subsequent experiments showed, surprisingly, that only those cancer cells that had retained their original epithelial identity were able to form new metastases, i.e., they drove the cancer. In contrast, a loss of epithelial features characterized cancer cell clones whose metastatic potential was suppressed. The researchers demonstrated that a complex cellular program protects the cellular identity of cancer cells and prevents them from losing their ability to proliferate.

"There are different and sometimes conflicting data on the importance of the EMT mechanism for metastasis in patients, which may also differ depending on the type of cancer," emphasized Martin Sprick of HI-STEM.

"Overall, our results suggest that complete and irreversible EMT surprisingly limits clonal spread of cancer cells, while epithelial identity of cancer cells is absolutely essential for disease spread. Our data in patient cells as well as in various metastatic breast cancer models are consistent with a model in which cancer cells with hybrid status, i.e., with epithelial and mesenchymal features, drive metastasis," said Andreas Trumpp, devision head at DKFZ and HI-STEM director.

"The process of metastasis growth is particularly important because cancers are fundamentally most difficult to treat at this stage," adds Christina Scheel of the Dermatological University Hospital in Bochum. It will now be the task of future research to find out how these experimental results can be used for a therapy of the most aggressive metastasis-forming cancer cells.

* The Heidelberg Institute for Stem Cell Technology and Experimental Medicine (HI-STEM) gGmbH was founded in 2008 as a public-private partnership between the DKFZ and the Dietmar Hopp Foundation.

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Further information

- German Cancer Research Center (DKFZ)