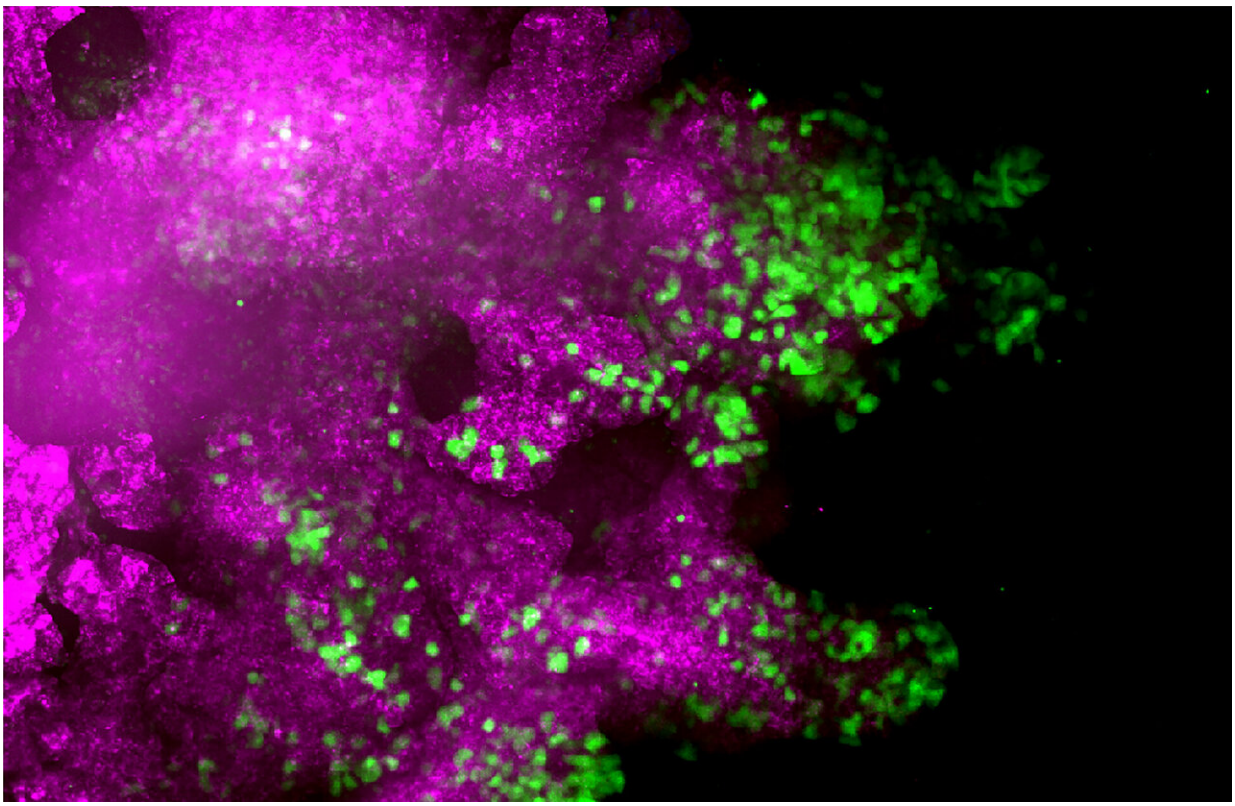
Cancer cells may promote metastases and resistance to therapy, depending on their state

November 29 2021



Malignant breast cancer cells that have undergone partial EMT (green) leave the original cell cluster (red) and migrate to the surrounding area. Credit: University of Basel, Department of Biomedicine

A type of cell transformation known as EMT enables cancer cells to break away from the tumor and form metastases elsewhere. However, this process does not always take place in full. Researchers at the University of Basel have now been able to show that tumor cells contribute differently to the formation of metastases and the development of therapy resistance, depending on whether they have undergone full or only partial transformation.

Most cancer patients do not die as a result of their primary tumors, but from metastases that destroy vital organs. Metastases occur when cancer cells detach from the original tumor and migrate into healthy tissue.

A multi-stage process called epithelial-mesenchymal transition (EMT) plays a crucial role in this process, enabling tumor cells to break away from their cell cluster and spread throughout the body.

In the short term, chemotherapy in combination with targeted therapy can inhibit cancer growth with high efficacy. But in the long term, cancer cells develop resistance to this treatment and the tumors and metastases grow all the more aggressively. Researchers suspect that EMT is responsible for cancer cells evading the therapy and continuing to metastasize.

Course of EMT makes all the difference

Not all cancer cells go through the EMT program in full, which is why they ultimately have different characteristics and properties. Professor Gerhard Christofori's research group in the Department of Biomedicine at the University of Basel has now investigated the way in which cells influence the progression of cancer depending on how the EMT proceeds.

In mouse models for breast cancer, the researchers were able to use

genetic changes to make cancer cells that had been subject to partial or full EMT visible. This showed that cells in different stages of an EMT process contribute differently to metastasis formation and chemo-resistance.

Metastasis requires partial EMT

Breast cancer cells that have undergone only partial EMT can switch between early stages of EMT and the starting point, the epithelial state. In contrast, cells can rarely return to their initial state following full EMT, as they are less adaptable.

The research team was able to show that breast cancer cells that have completed only individual stages of EMT have a key impact on the formation of lung metastases in mice. When the researchers eliminated these cells, this proved to inhibit the development of metastases.

The partial EMT breast cancer cells appeared to act as pioneer cells and lead the other breast cancer cells in a collective cell migration. In contrast, breast cancer cells that had undergone full EMT were rarely found in metastases, and their removal had no noticeable effect on metastasis.

Both EMT types promote resistance to therapy

Regardless of whether the transformation is full or only partial, both types of breast cancer cell contribute to the development of resistance to therapy. The results show that the various stages of EMT and the resulting cell plasticity of cancer cells play an important role in the formation of metastases and therapy resistance.

These experiments highlight the great potential of inhibiting EMT in the

development of novel therapeutic approaches against cancer metastasis and resistance to therapy.

The research was published in *Developmental Cell*.

More information: Fabiana Lüönd et al, Distinct contributions of partial and full EMT to breast cancer malignancy, *Developmental Cell* (2021). DOI: 10.1016/j.devcel.2021.11.006

Provided by University of Basel