Researchers identify nutrient metabolism that drives breast tumor metastasis

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A multinational group of scientists, led by professor Sarah-Maria Fendt (VIB-KU Leuven), have discovered that breast cancer cells that have invaded other organs rely on a different nutrient metabolism to produce energy than normal cells and non-metastasizing cancer cells. To demonstrate their findings, the researchers used mouse models to show that inhibiting energy production from this nutrient metabolism reduces the occurrence of metastases by more than 60%. This discovery could result in new breast cancer therapies that prevent metastases by targeting this metabolic process. These groundbreaking insights are published in the leading scientific journal *Nature Communications*.

Breast cancers that invade other organs almost always result in the patient's death. Even more, scientists have yet to discover a way to prevent cancer from spreading, or 'metastasizing'. As a result, no effective treatment has been developed for the approximately 25% of breast cancer patients who experience metastases. However, the work of the team of professor Sarah-Maria Fendt has revealed the importance of the nutrient proline in the energy production process of metastasizing breast cancer cells.

Investigating the role of proline

In order to spread, cancer cells must change the way they operate. However, the way cells' metabolism supports this process of adaptation is largely unknown. In this study, the researchers discovered that

metastasizing breast cancer cells rely on a different nutrient metabolism to generate energy than normal cells and non-metastasizing breast cancer cells.

Prof. Sarah-Maria Fendt (VIB-KU Leuven): "We observed that proline metabolism is increased in breast cancer metastases versus primary breast cancers in mice and patients. Not only that, but we inhibited the enzyme that drives proline metabolism, Prodh, successfully reducing the formation of lung metastases without harming healthy tissue or affecting organ function. Our results provide ample evidence that Prodh is a potential breast cancer drug target."

Two paths towards a clinical therapy

The team's finding is an exciting first step toward translating the inhibition of the identified metabolic enzyme into a real therapy. Prof. Fendt plans to move forward on two specific fronts in order to move the research from the lab into the clinic.

Prof. Sarah-Maria Fendt: "First, we plan to define how the inhibition of Prodh, and thus the energy production from proline in the cancer cell, can be combined with standard of care preventative chemotherapy to have the best possible efficacy against the occurrence of metastases. Second, we're searching for industrial partners that can help us identify a powerful compound that inhibits the enzyme. These steps are necessary to transform this compelling result into tangible benefits to cancer patients. With the right partner, this could result in clinical trials in as few as five years."

Qestions from patients

A breakthrough in research is not the same as a breakthrough in

medicine. The realizations of VIB researchers can form the basis of new therapies, but the development path still takes years. This can raise a lot of questions. That is why we ask you to please refer questions in your report or article to the email address that VIB makes available for this purpose: patienteninfo@vib.be. Everyone can submit questions concerning this and other medically-oriented research directly to VIB via this address.

More information: Proline metabolism supports metastasis formation and could be inhibited to selectively target metastasizing cancer cells. *Nature Communications* DOI: 10.1038/ncomms15267

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