New imaging technique could predict whether primary breast cancer will spread to the lung

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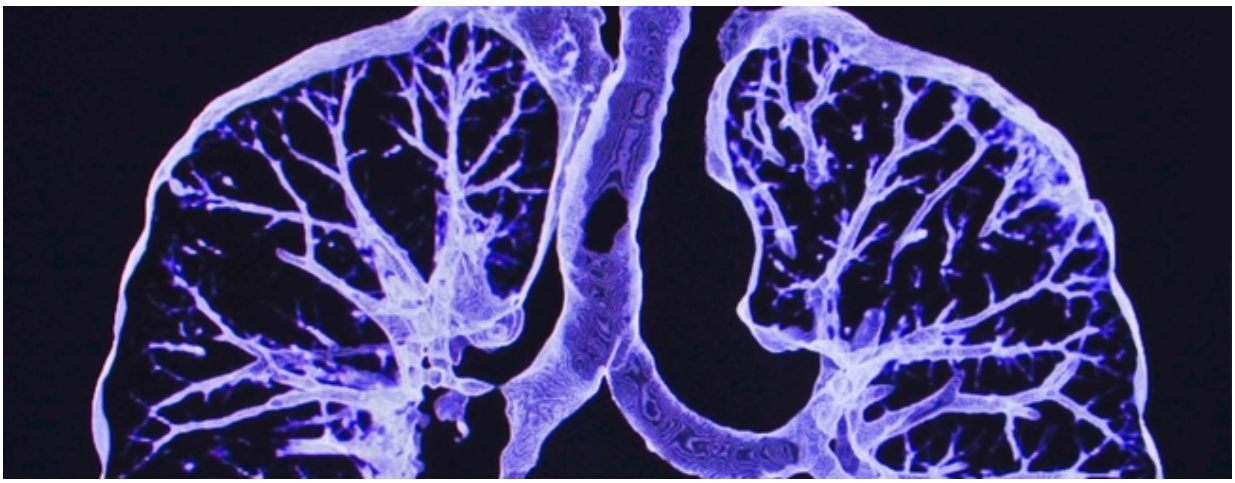

Credit: Medical Research Council

Scientists funded by the MRC, Breast Cancer Now and other collaborators have developed an innovative imaging technique that could predict whether breast cancer will spread to the lung.

In the study, published in *Theranostics* opens in new window, researchers have demonstrated in mice that a new non-invasive imaging method can be used to detect changes in the lungs that signal breast cancer may soon spread there – before any metastases are visible.

If validated in humans, this approach could enable patients to be offered more intensive therapy earlier, to potentially prevent breast cancer spread.

Previous research has shown that the gathering of a special type of immune cell called 'myeloid-derived suppressor cells' (MDSCs) – in locations such as the lung – prepares the ground for breast cancer metastasis, by suppressing the local immune system and promoting the formation of new blood vessels (angiogenesis).

Researchers at King's College London – in collaboration with teams at University College London and the University Hospital Muenster in Germany – have now developed a radioactive 'tracer' molecule to detect MDSCs accumulating in the lung in preparation for the arrival of breast cancer cells and the formation of metastases.

MDSCs are known to release a protein duo 'message' called S100A8/A9 which instructs the cells to gather in the lungs. The gathering of these MDSCs in the lung causes inflammation, which makes it a favourable location for cancer cells to metastasise to.

The research teams – led by Dr Michel Eisenblätter and Dr Fabian Flores-Borja at King's College London – hypothesised that, by making S100A8/A9 visible, it could be possible to identify when the lungs were being prepared for colonisation by breast cancer cells.

To test this theory, they developed a 'tracer' antibody able to attach itself to S100A8/A9, that can be detected using a special scan called SPECT (single photon emission computed tomography) – a 3D gamma-ray scanner. The tracer releases radiation which can be distinguished by the SPECT scanner, highlighting areas where S100A8/A9 molecules, and MDSCs, are accumulating.

The researchers tested the tracer with triple negative breast cancer cells that had been implanted in mice, and were able to show – using a miniature SPECT scanner – that the 'tracer' lit up the lungs of mice well before any tumour cells were visible in the lung.

Furthermore, the tracer could distinguish between highly aggressive breast cancer with a high tendency to spread to the lung and tumours without metastatic potential.

Currently, to assess the risk of a patient's breast cancer spreading, doctors use tools based upon the features of the primary tumour, such as tumour size and whether it has already invaded nearby lymph nodes.

With this early-stage study demonstrating the technique to be effective in mice, further studies are now required to develop a more effective 'tracer' molecule – better suited for use in humans – to be tested in clinical trials in future.

Dr Fabian Flores-Borja, Research Fellow at the Breast Cancer Now Research Unit at King's College London, said: "By combining cell biology and imaging techniques, we have established a method to predict, at an early time-point during tumour development, whether tumour invasion will occur.

"We envision this technique being used to help select patients for either further surveillance or intensified therapy, as well as aiding cancer research. The development of a test that is able to identify an increased risk of metastasis soon after a patient is diagnosed with breast cancer, would be very useful in helping choose the best treatment for patients."

Dr Mariana Delfino-Machin, MRC Programme Manager for Cancer, said: "This study in mice has demonstrated that immune cells can be used as a warning system for breast cancer metastasis in the lungs, and it

paves the way towards developing a similar warning system for use in the clinic.

"Innovative, non-invasive imaging methods like this, which can help predict and diagnose disease as early as possible and avoid the discomfort of current invasive tests, have the potential to greatly impact cancer treatment and outcomes. This promising, early-stage study is a great example of the kind of cancer research that the MRC proudly supports."

Baroness Delyth Morgan, Chief Executive at Breast Cancer Now, which helped to fund the study, said: "While more research is needed before this could be tested in patients, the prospect of a hospital scan which could predict whether breast cancer will spread to the lungs is incredibly exciting.

"More immediately, this study brings a brand-new method to the table that will help researchers unpick how the immune system is involved in the spread of breast cancer. Finding ways to predict and halt the spread of the disease will be crucial if we are to finally stop people dying from it.

"This is a promising step towards being able to use 3D imaging to help offer more personalised therapy. Ultimately, anything that could provide patients and their doctors with a more accurate picture of whether their breast cancer may spread will help us tailor treatments to stop this from happening."

More information: Michel Eisenblaetter et al. Visualization of Tumor-Immune Interaction - Target-Specific Imaging of S100A8/A9 Reveals Pre-Metastatic Niche Establishment, *Theranostics* (2017). DOI: 10.7150/thno.17138

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