Potential new therapeutic target for a subset of aggressive breast cancers

March 1 2012

Scientists from the Max Planck Institute for Heart and Lung Research in Bad Nauheim have now discovered that they can prevent the formation of metastases by blocking the receptor protein Plexin B1.

In particularly aggressive forms of breast cancer, cancer cells can settle in other organs and form metastases there. Once such metastases form, complete recovery is rare. Consequently, it is enormously important to prevent the metastasisation of the breast cancer cells. The success, however, achieved by using existing forms of therapy is limited. Scientists from the Max Planck Institute for Heart and Lung Research in Bad Nauheim have now discovered that they can prevent the formation of metastases by blocking the receptor protein Plexin B1. They hope that their discovery will provide a new approach to preventing the metastasisation of aggressive forms of breast cancer, and thus improve the prognosis for patients.

Breast cancer is by far the most common form of cancer in women. Around one in ten women will suffer from the disease at some point in their lives. Around one quarter of all patients suffer from a particularly aggressive form of breast cancer, in which the tumour cells frequently metastasise in other organs. This aggressive form of breast cancer is characterised by the fact that the tumour cells produce the protein ErbB-2. If ErbB-2 is detected in the tumour cells in the tissue sample taken routinely from all breast cancer patients, they must undergo special and complicated therapy. Despite this treatment, it is not always possible to prevent the emergence of metastases.

Scientists from the research group of Stefan Offermanns, Director of the Max Planck Institute for Heart and Lung Research, have now discovered precisely what it is that makes ErbB-2-producing tumours so aggressive. "It was already known from tests on the nervous system that ErbB-2 forms a complex with the receptor protein Plexin-B1 which controls the movement and migration of cells," explains Thomas Worzfeld, leader of the research study. "For this reason we specifically looked for interaction between these two proteins in breast cancer cells." The Bad Nauheim researchers struck gold. When they switched off Plexin-B1 in breast cancer cells, the cells became incapable of migrating.

"We concluded from this observation that it should be possible to prevent the formation of metastases by switching off Plexin-B1," said Worzfeld. To verify this, they switched off the Plexin-B1 in mice with ErbB-2-producing breast cancer. The effect they observed was very clear: "We were able to establish a drastic reduction in the lung metastases in the animals without Plexin-B1. The effect could even be observed with the naked eye."

The next question to be resolved by the scientists concerned the extent to which this observation could be applied to humans. In a test on tissue from breast cancer patients, the Max Planck scientists noted a link between the Plexin-B1 content of the tumour tissue and the patients' prognoses: patients with very low Plexin-B1 content in their tumour tissue had a considerably better chance of survival.

The scientists are hopeful that these findings will provide a basis for the development of a new treatment. "We want to switch Plexin-B1 off specifically using an antibody and in this way suppress the emergence of metastases," said Worzfeld. The antibody, for which a patent has been filed, is now being tested in the animal model. Offermanns is cautiously optimistic: "With Plexin-B1 we believe we have found a crucial location where the formation of metastases can be blocked. However, we still

have a very long way to go until our antibody can be successfully used in clinical practice."

More information: Thomas Worzfeld, Jakub M. Swiercz, Mario Looso, Beate K. Straub, Kishor K. Sivaraj, Stefan Offermanns: ErbB-2 signals through Plexin-B1 to promote breast cancer metastasis. J Clin Invest 2012; doi: 10.1172/JCI60568

Provided by Max-Planck-Gesellschaft