THE UNIVERSITY OF QUEENSLAND

Communicating with Journalists Assignment

SCIE3001

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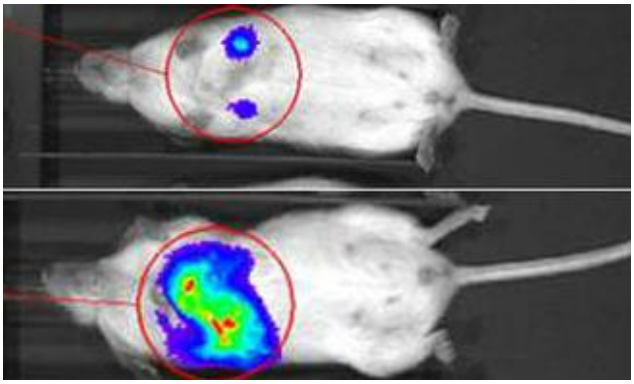
9/15/2014

The enzyme behind breast cancer metastasis has been identified

Researchers in the University of California, San Diego School of Medicine identified an enzyme called Ubc13 that is involved in breast cancer metastasis.



A tumour with reduced activity of the enzyme Ubc13 (top) and a tumour with higher activity of Ubc13 which spread into lungs (bottom)

Breast cancer is the leading invasive cancer which leads to death in women. Breast cancer deaths are related to distant metastasis than primary tumours.

Metastasis is the spread of cancer cells from the primary tumour into other distant organs. It is a multistep process which involves cancer cells invading the extracellular matrix, disseminating into blood stream, surviving in the circulation and successfully colonizing distant sites.

According to the American Cancer Society, an estimated 40,000 women in America will die of breast cancer in 2014. However this study sheds a light to tackling this problem.

This study has discovered "a way to target breast cancer metastasis through a pathway regulated by an enzyme."

The enzyme, Ubc13 is involved in regulating healthy immune system function and normal cell growth. Though this has been well documented previously, this is the first study to show its link to breast cancer. The enzyme was found to be expressed in breast cancer cells at two to three times the levels of healthy cells.

The researchers found that the enzyme regulates the activity of a protein called p38 which then regulates cancer cells' ability to transmit signals which stimulate their growth and survival. When the gene encoding for the protein is silenced, metastasis of breast cancer cells decreases significantly. Hence it is important to target the enzyme (Ubc13) which regulates its activity.

On a side note, the study also mentioned that, a compound which prevents the activity of p38 protein is being tested in treating patients with rheumatoid arthritis and so far, it has been successful.

The experiments in this study were carried out by taking human breast cancer cells which can spread into lungs. The expression of genes encoding for Ubc13 and p38 proteins were then silenced. These biologically altered cell lines were then injected into the mammary tissues of mice and were compared to non-altered breast cancer cell lines (normal breast cancer cell lines).

The non-altered cell lines showed a tenfold lung metastases than the altered cell lines showing the major role of Ubc13 and p38 in metastasis. The researchers observed the growth of primary tumours in the altered cell lines but the cancer did not spread. Hence the enzyme has an effect only in the metastasis stage and not during the primary tumour.

In order to make sure the reduction in metastasis was purely due to the loss of Ubc13, the activity of the enzyme was restored and any changes were noted. The researchers observed successful colonization of cancer into the lungs confirming the lack of spread in the Ubc13 silenced cell lines was due to the lack of the enzyme.

Silencing p38 also causes the blockage of metastatic spread of cancer and attenuates the growth and survival of already established lung colonization. Its activity was restored in order to make sure the results were purely due to the silencing of this protein and showed a positive result. Hence the researchers concluded that loss of p38 also leads to an anti-metastatic effect. Since in normal conditions, p38 is regulated by Ubc13, it is important to target the activity of Ubc13.

The researchers also observed down regulation of some genes such as CNN2, PLTP and IGFBP3 in Ubc13-deficient cells. Those genes have been previously associated with breast cancer metastasis. Hence the down regulation of the enzyme has another benefit.

As mentioned above, primary tumour is not much of a problem. It becomes very challenging and in most cases, lethal when metastasis comes into play. Hence this study provides a hopeful direction in designing therapeutics targeting the enzyme behind the breast cancer cell metastasis.

Reference

Wu, X., et al. "Ubiquitin-Conjugating Enzyme Ubc13 Controls Breast Cancer Metastasis through a Tak1-P38 Map Kinase Cascade." *Proc Natl Acad Sci U S A* (2014). Print.