HealthManagement
Promoting Management and Leadership

Suppressing Breast Cancer Metastasis

Researchers studying proteins that regulate alternative splicing events linked to metastasis report breakthrough findings that could lead to better treatments for metastatic breast cancer.

You might also like: Dense Breasts: Supplemental Screening Trends

Alternative splicing is a natural cellular process that helps cells perform many functions such as wound healing. Previous research has shown that alternative splicing can functionally control tumour metastasis. About 95% of all genes in the human body are processed through alternative splicing, which only recently has been shown to play a role in cancer metastasis.

In this study published in the journal Nature Communications, researchers screened cells looking for proteins functioning as alternative splicing modulators that prevented cells from becoming metastatic. They found that AKAP8, a protein naturally produced in the body, could suppress breast cancer metastasis in animal models of human tumours.

Additionally, the researchers led by Baylor College of Medicine observed that high levels of AKAP8 in the body predict a better survival for breast cancer patients.

"We studied AKAP8 in metastatic breast cancer animal model systems of cancer cells from human patients," said corresponding author Dr Chonghui Cheng. "We found that depletion of the AKAP8 protein in patient cancer cells promoted breast cancer metastasis in these mouse models. Furthermore, providing an external source of AKAP8 inhibited metastasis."

Dr Cheng, associate professor at the Lester and Sue Smith Breast Center, of molecular and human genetics and of molecular and cellular biology at Baylor, and colleagues further discovered that AKAP8 also regulated the alternative splicing of another protein called CLSTN1.

There are two forms of CLSTN1, called CLSTN1S and CLSTN1L. In the current study, Dr Cheng et al. found that AKAP8 tipped the balance towards the production of CLSTN1S, which was associated with preventing cells from progressing towards a metastatic state. This was a previously unknown function of CLSTN1, the research team noted.

Modulators of alternative splicing, the researchers continued, participate in a delicate balancing act of many different cellular proteins such as CLSTN1. Notably, two types of modulators play a part in keeping the balance. One type, like AKAP8, modulates alternative splicing towards the production of proteins that help cells remain in a normal state. The other type tips the balance towards proteins that promote metastatic transformation.

"If the balance is disturbed, tumour progression can be promoted," Dr Cheng points out. "By investigating how the balance is kept and the factors that disturb the balance, we hope to understand a new layer of regulation of tumour metastasis and gain insights that could lead to treatments for metastatic cancer, a deadly disease."

Source: Baylor College of Medicine
Image credit: Pixabay

Reference: Hu X, Cheng C et al (2020) The RNA-binding protein AKAP8 suppresses tumour metastasis by antagonizing EMT-associated alternative splicing. Nat Commun 11, 486. https://doi.org/10.1038/s41467-020-14304-1

Published on : Tue, 3 Mar 2020