Dual role in breast tissue for a protein involved in leukemia

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A protein known to play a role in growth of some types of leukemia appears to have a mixed function in breast cancer development, say researchers from the Lombardi Comprehensive Cancer Center at Georgetown University Medical Center (GUMC).

The findings, presented at the annual meeting of the Endocrine Society in Washington, DC, indicate that the function of this protein, known as Stat5a, may be different in developing breast cancer cells that are estrogen receptor-positive as compared to estrogen receptor-negative. When estrogen receptor levels were overexpressed, loss of Stat5a reduced development of a lobular type of preneoplasia. However, when estrogen receptor levels were normal, loss of Stat5a not only had no effect on reducing preneoplasia, but increased susceptibility to carcinogen-induced breast cancer. The results illustrate the importance of breast cancer heterogeneity when testing new therapeutic targets.

The researchers say Stat5a could be a target for treatment of leukemia, but add, "If Stat5a is to be used as a drug target for leukemia or other cancers, it is important to fully understand how altering its function impacts the breast, especially since it appears it may play different roles in different types of breast cancer," says the study's lead author, Anne Miermont, MS, a doctoral graduate student in tumor biology at Georgetown University Medical Center.

Stat5a is a member of the STAT family of proteins, which are key to regulating cell growth and differentiation. Because they have been found

to be over-expressed in leukemia, Miermont and Priscilla Furth, MD, a professor of oncology, sought to see if they were important in breast cancer development. Estrogen receptors are over-expressed in more than half of human breast cancers, so the investigators set up studies to test if the function of Stat5a was the same or different in cells with estrogen receptor overexpression.

They found that Stat5a A is rather "two-faced" when it comes to its role in breast tissue. Previous studies had shown that mice born without the gene produce breast cells that are a little less differentiated than they should be, meaning that they are not fully developed enough to participate in milk production. Miermont found that when the animals were exposed to a cancer-causing chemical, they were more likely to develop breast cancer than mice with intact Stat5a genes. At the same time, however, Miermont found that when estrogen receptor was over-expressed, Stat5a collaborated with it to promote growth of a type of precancerous lesion of the breast termed a hyperplastic alveolar nodule.

"Our studies in in vivo mouse models illustrate a dual role for the Stat5a protein in breast tissue. While it can contribute to the growth of one type of precancerous lesion in the breast, this protein also appears to protects mammary cells from carcinogenic exposure," says Miermont.

These findings need to be validated and expanded, Furth says, but she adds that "while Stat5a is obviously a complicated protein that has many functions, the results underscore the need to specifically understand the mechanisms that regulate its different roles in breast cells and how changes in Stat5a activity may affect different types of breast cancer generation."

Source: Georgetown University Medical Center (news : web)