

DBT-NIBMG scientists working to find better treatments for Breast Cancer

New Delhi, Jan 07: Estrogen, or oestrogen, is one of the two most main sex hormones of women. It is responsible for the development and regulation of the female reproductive system and secondary sex characteristics. However, it is also a tumor promoter which mostly helps in cell proliferation and gene regulation.



Breast cancer is one of the most common cancers in women worldwide, both in developed and developing countries. According to the World Health Organization (WHO), there are about 1.38 million new cases and 458 000 deaths from breast cancer each year. It is a very heterogeneous cancer, mainly divided into two broad groups, that is, non-invasive breast cancers which include both ductal carcinoma in situ and lobular carcinoma in situ and invasive breast cancers which include invasive ductal carcinoma, invasive lobular carcinoma and metastatic breast cancer.

On the basis of hormone receptor expression, breast cancer is divided into three broad groups Hormone receptor positive breast cancer (ER +), HER2 positive breast cancer and Triple negative breast cancer

Approximately 70% of breast tumors are positive for estrogen receptor alpha (ER α , called here after ER+) expression. Due to ER's role in the growth of ER+ breast cancer, these tumors are generally treated with hormonal therapies. Endocrine therapy using selective estrogen receptor modulators (SERMs) such as tamoxifen (Tam) and/or aromatase inhibitors is the most common and effective treatment for ER+ breast cancer. But 5 to 10 years later, approximately 20% of these cancers develop insensitivity to hormone therapies. Although tamoxifen treatment is new, often effective, de novo insensitivity limits the success of this therapy.

JMJD6 that is Jumonji domain containing-6 (JMJD6) is a nuclear protein. Higher expression of JMJD6 was consistently associated with poor prognosis. JMJD6 increases proliferation and motility of breast cancer cells. JMJD6 has some enzymatic activity like, lysyl hydroxylase and arginine demethylase activity. More recently, JMJD6 was shown to phosphorylate H2Ax and have a kinase activity. JMJD6 small interfering RNA (siRNA) treated cells showed expression profiles which were significantly similar to those observed in tamoxifen resistant cells and xenografts. This indicated that JMJD6 may have some role in response/resistance to endocrine therapy. Secondly, ER+ women treated with Tamoxifen that have high expression of JMJD6 tend to have poorer survival than those who have lower levels of JMJD6. Next, cells that over express JMJD6 have expression patterns similar to estrogen treated breast cancer (MCF-7) cells. So, it may behave like Estrogen to induce a subset of Estrogen regulated genes- and a constitute signature for Tamoxifen resistance that are altered by JMJD6. Researchers at DBT- National Institute of Biomedical Genomics (DBT-NIBMG), Kalyani are investigating the role of JMJD6 in Tamoxifen insensitivity in breast cancer.

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