DBT-NII scientists pave way for treatment for triple-negative breast cancer

New Delhi, May 27: Breast cancer is the second leading cause of cancer related deaths in women worldwide. Breast cancer patients whose tumors are estrogen receptor (ER) / progesterone receptor (PR)-positive are much more likely to respond to hormone therapy than patients that are ER/PR-negative. Likewise, breast cancer patients who are found positive for human epidermal growth factor receptor 2 (HER2) are treated with anti-HER2 antibodies and have prolonged life span.

There is a third type of breast cancer patients: Triple-negative breast cancer (TNBCs) patients. They do not express ER or PR and lack HER2 overexpression. They are the most difficult to treat. TNBC patients' accounts for 15%–20% of all breast cancer patients with a disproportionate number of metastatic cases and breast cancer deaths.

The standard treatment for metastatic TNBC is a combination of paclitaxel and other cytotoxic drugs. However, to date, they have failed to demonstrate significant activity in metastatic breast cancer. Researchers at the Department of Biotechnology's National Institute of Immunology (DBT-NII), New Delhi investigated the potential role of a novel protein named AKAP4 [A-kinase anchor protein].

Breast cancer growth occurs because of uncontrolled cell division, evasion of programmed cell death and acquisition of cell migration and invasion abilities. AKAP4 protein was found to promote breast cancer cell growth. It was shown also that AKAP4 was involved in breast cancer cell migration and invasion abilities to go to the other parts of the body that is termed as TNBC metastasis. Interestingly, down regulation of AKAP4 protein production by gene silencing approach [short hairpin RNA (shRNA)] in cancer cells resulted in reduced uncontrolled cell division, increased cell death and reduced migratory and invading abilities.

Further studies were carried-out by developing breast cancer in a mouse model. These animals were treated with AKAP4 shRNA to down regulate AKAP4 protein production in cancer cells. This resulted in reduced tumor burden.The scientists further found that when they down regulated AKAP4 protein and used Paclitaxel in combination, there was a synergistic cytotoxic effect of paclitaxel.

These findings suggest that AKAP4 down regulation inhibits various malignant properties and enhances the cytotoxic effect of paclitaxel, and this combinatorial approach could be useful for triple-negative breast cancer treatment. In summary, the scientists have demonstrated that AKAP4 plays an important role in TNBC cell growth. Their findings suggest that AKAP4 may be a potential therapeutic target and may have clinical application for the TNBC management.

Reference:

Jagadish N, Devi S, Gupta N, Suri V, Suri A. Knockdown of A-kinase anchor protein 4 inhibits proliferation of triple-negative breast cancer cells in vitro and in vivo. Tumour Biol. 2020. Apr; 42(4):1010428320914477. doi: 10.1177/1010428320914477.

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