New Delhi, Oct 01: Tamoxifen is the first line treatment for breast cancer. Development of resistance to the medicine is a major challenge in the treatment of estrogen receptor positive breast cancer. More than 70% of breast tumors express the estrogen receptor and respond to tamoxifen. However, a gradual resistance develops for tamoxifen during the treatment that poses a serious concern for the continuation of the therapy.

Apart from genetic influence, contribution of epigenetic modifications in the development of drug resistance is widely accepted. There is an oncogene called Enhancer of zeste homolog 2 (EZH2) which favors breast tumorigenesis by increasing proliferation and inhibiting apoptosis through its target molecules that include several tumor suppressor genes.

The cancer research group DBT- Institute of Life Sciences, Bhubaneswar (DBT-ILS) led by Dr Sandip Mishra has observed that EZH2 inhibition reverses the tamoxifen resistance cells
back to the sensitive state in breast cancer. They have listed proteins that were previously not recognized for their role in tamoxifen resistance. The genes encoding these proteins were significantly associated with breast cancer patient survival.

Further, they have identified the molecular players involved in EZH2-mediated effects on tamoxifen resistant MCF-7 cells. They have concluded that tamoxifen, an antagonist, is the wonder drug for estrogen receptor positive breast cancer that starts acting as an agonist once the resistance is established. EZH2 is one of the culprits that modulate its target molecular players leading to tamoxifen resistance. Thus, the research group suggests that targeting EZH2 or the molecules down the cascade might be helpful in re-acquiring sensitivity to tamoxifen in breast cancer. The study also suggests that more research in this area is anticipated and that the EZH2 inhibitors such as DZNepA might show promising effects against tamoxifen resistant breast cancer similar to its effect against nicotine-induced increased breast tumor growth as previously reported by the group of Dr Mishra.

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