Breast cancer drug shows promise for treating, preventing progestin-dependent tumors

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Recent studies suggest that human breast cancer risk is increased by outside exposure to the hormone progestin, such as during hormone replacement therapy. Now, a University of Missouri study suggests that PRIMA-1, a small molecule drug that targets the most common mutated gene, p53, in human cancer cells, has potential as a novel chemotherapeutic treatment for progestin-accelerated human breast cancer.

"We demonstrated that PRIMA-1 was an effective drug to treat and prevent emergence of progestin-accelerated mammary tumors in rats," said Salman Hyder, professor of biomedical sciences in the College of Veterinary Medicine and the Dalton Cardiovascular Research Center. "The results of this study may have significant implications for the treatment and prevention of human breast cancer because such a large fraction of human breast cancers are dependent on estrogens and progestins for growth."

Mutated p53 plays a key role in promoting tumor cell survival and tumor cell resistance to chemotherapeutic drugs. In more than 50 percent of breast cancer cases, mutated p53 is present. Previous research has indicated that when p53 is functionally abnormal, tumor cells are prolific and develop quickly. PRIMA-1 targets and returns normal function to the mutated p53.

In the study, researchers examined the ability of PRIMA-1 to suppress growth of progestin-accelerated, mammary tumors in an animal model. When tumors reached a certain size, researchers administrated PRIMA-1 twice a day for three days. The researchers found that PRIMA-1 caused regression of approximately 40 percent of progestin-accelerated mammary tumors. However, the drug did not induce regression of native, non-progestin accelerated tumors. PRIMA-1 also suppressed the emergence of any new progestin-accelerated tumors in the animal model.

"Postmenopausal women worldwide are exposed to exogenous progestin in the form of hormone replacement therapy, and clinical studies have associated combined exposure to progestin and estrogen with an increased incidence of human breast cancer in this population," said Hyder, who is also the Zalk Endowed Professor of Tumor Angiogenesis. "Because PRIMA-1 blocked the formation of new tumors following progestin stimulation in this experimental model, it is tempting to speculate that this agent could be used to prevent progestin-accelerated tumors in women on hormone replacement therapy. However, this needs to be tested thoroughly in a clinical setting."

Source: University of Missouri-Columbia