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Researchers developing drug for recurring ER-positive breast cancer

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Researchers at UT Health San Antonio and two partner institutions are developing a new, first-in-class agent that has stopped the growth of estrogen receptor-positive (ER-positive) breast cancer in its tracks. The new agent is a molecule called ERX-11 that has blocked the growth of recurring breast cancer tumors.

Ratna Vadlamudi, Ph.D., is principal investigator of a study describing the new findings, published Aug. 8 in the journal *eLife*. He is professor of obstetrics and gynecology in the Joe R. & Teresa Lozano Long School of Medicine and is a member of the Cancer Development & Progression Program (CDP) at the UT Health Cancer Center.

"Most breast cancers in women require estrogen or progesterone - the two female hormones—to grow. To treat hormone-dependent cancers, you must either block the hormone or block the receptor that receives the hormone to prevent the development of the cancer. However, in many patients, tumors become resistant to the current therapy and tumors recur. Our team at UT Health discovered a new molecule that blocks the estrogen receptor signaling that occurs in resistant tumors and tested a drug based on the molecule in preclinical studies in the lab," Dr. Vadlamudi said.

"Developing this drug is important because it targets a unique site on the estrogen receptor and blocks its interactions with critical proteins that contribute to breast cancer progression. This drug will be useful in treating breast cancers that are sensitive to current therapies and that are

resistant to therapy," he said.

Researchers at UT Dallas led by Jung-Mo Ahn, Ph.D., were involved in synthesizing the drug that blocked the interaction, and scientists at UT Southwestern led by Ganesh Raj, M.D., Ph.D., are involved in mechanistic studies and in studies involving primary human breast tumors.

"Implanting mice with the human breast cancer cells usually causes them to develop the breast tumors, but when we gave the mice ERX-11 as an oral medication, the cancer growth was dramatically reduced," Dr. Vadlamudi said. The studies in mice showed no toxic effects, indicating the drug based on the ERX-11 molecule would be a good candidate for human trials.

"The next steps are to synthesize the drug under the FDA's drug development guidelines and conduct formal toxicity studies to ensure the drug can be safely tolerated," Dr. Vadlamudi said. "Additional work needs to be done before we can move forward with Phase I clinical trials. We expect human trials to begin soon."

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