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Annual report

Give to MSK

aggressive forms of breast cancer. The findings were published in the journal Proceedings of the National Academy of Sciences in May [PubMed Abstract].

Triple-negative breast cancer (TNBC) is defined by its lack of expression of the receptor proteins for the hormones estrogen and progesterone and another receptor protein known as HER2. Targeting one or several of these receptors is the basis for the most-effective breast cancer therapies. However, for patients with TNBC, the only drug-treatment option is conventional chemotherapy, which has many side effects and often results in early relapse when used on its own.

PU-H71 inhibits heat shock protein 90 (Hsp90), which plays a role in several types of cancer, including breast cancer, by stabilizing other cancer-causing proteins. "We discovered this class of compounds at the Center about ten years ago and have been studying it since," said Memorial Sloan Kettering chemical biologist <u>Gabriela Chiosis</u>, the study's senior author. "When we created PU-H71, we realized it had all the properties to make it a good Hsp90 inhibitor. It stays in cancer cells a long time, but rapidly clears from normal cells, which means that we can give high doses with little toxicity to healthy tissue."

In the current study, investigators showed in the test tube that PU-H71 stopped the proliferation and invasion of TNBC cells and eliminated cancer cells through apoptosis (programmed cell death). In several mouse models of TNBC, the drug induced complete response at the highest dose level with no observable side effects or evidence of resistance build-up to PU-H71 treatment.

"We are partnering with the <u>National Cancer Institute</u> to further develop this drug," Dr. Chiosis explained. "We are now working on additional toxicity studies and hope to begin an early-stage clinical trial next year."

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