

Novel therapy studied for inherited breast cancer

August 27 2019, by Will Sansom



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UT Health San Antonio researchers have discovered a novel way to kill cancers that are caused by an inherited mutation in BRCA1, the type of cancer for which actress Angelina Jolie had preventive double

mastectomy and reconstructive surgery in 2013.

"This represents a new treatment for inherited breast and [ovarian cancer](#), which are higher in our region," said Robert A. Hromas, M.D., FACP, professor and dean of the Joe R. and Teresa Lozano Long School of Medicine at UT Health San Antonio. Dr. Hromas is senior investigator on the research, published in the journal *Proceedings of the National Academy of Sciences*. (Reference: "MiR223-3p promotes synthetic lethality in BRCA1-deficient cancers," Aug. 8, 2019.)

A tiny molecule called microRNA (miR) 223-3p prevents [normal cells](#) from making mistakes while repairing their DNA. However, cancers with BRCA1 mutations repress miR223-3p to permit their cells to divide. Adding back miR223-3p forces the BRCA1-mutant [cancer](#) cells to die, said study co-author Patrick Sung, D. Phil. Dr. Sung, who joined UT Health San Antonio in 2019 from Yale, is a BRCA1 cancer expert who occupies the Robert A. Welch Distinguished Chair in Biochemistry.

Exploiting the cancer's Achilles' heel

MiR223-3p acts like a light switch, turning off proteins that BRCA1-mutant cancers need to divide properly. Without these key cell division proteins, BRCA1-mutant tumors commit suicide, Dr. Hromas said.

"It's kind of a cool way of thinking about treatment," Dr. Hromas said. "We are using the very nature of these BRCA1-deficient cancer cells against them. We are attacking the very mechanism by which they became a cancer in the first place."

There is evidence that restoring miR223-3p before cells convert to cancer can even prevent BRCA1-related disease, he said.

BRCA gene mutations affect 1 in every 400 people in the United States—an estimated 825,000. After Ashkenazi Jews, Hispanics have the second-highest prevalence of BRCA1 disease-causing mutations. The disease's burden in San Antonio and South Texas is therefore among the highest in the country.

More information: Gayathri Srinivasan et al, MiR223-3p promotes synthetic lethality in BRCA1-deficient cancers, *Proceedings of the National Academy of Sciences* (2019). [DOI: 10.1073/pnas.1903150116](https://doi.org/10.1073/pnas.1903150116)

Provided by University of Texas Health Science Center at San Antonio

Citation: Novel therapy studied for inherited breast cancer (2019, August 27) retrieved 5 May 2024 from <https://medicalxpress.com/news/2019-08-therapy-inherited-breast-cancer.html>

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