Preventing triple negative breast cancer from spreading
17 April 2019, by Eric Stann

A breast cancer cell is like a house with three locks on the front door. Keys, or receptors, allow drugs to unlock the door and kill the cell. However, in triple-negative breast cancer, these keys are absent, thereby resulting in few options for drug therapy, until now.

A protein called p53 suppresses and kills cancer in people. However, a defective, mutant form of p53 helps cancer cells grow and multiply. Researchers at the University of Missouri have now found that a combination drug therapy reduces the spread of triple negative breast cancer to other locations of the body by 50 percent.

"Most people who succumb to breast cancer, and those in particular with triple-negative breast cancer, do so following metastasis, or spread of the cancer to other organs in the body," said Salman Hyder, the Zalk Endowed Professor in Tumor Angiogenesis and professor of biomedical sciences in the College of Veterinary Medicine and the Dalton Cardiovascular Research Center. "Triple negative breast cancer lacks ways to treat the cancer with chemotherapy. Therefore, people are administered toxic, non-specific drugs. We wanted to see if this combination therapy could provide a new, non-toxic targeted approach for treatment."

The study built on previous research by Hyder's lab and used mice that had human metastatic cancer, which had spread into the lungs. Researchers wanted to see if two previously discovered drugs—APR-246 that restores the p53 protein's ability to kill cancer cells and 2aG4 that targets the blood vessels in order to kill cancer cells—had an effect on metastatic triple negative breast cancer. Hyder says the results are promising.

"The number of metastatic colonies was reduced when both compounds were given separately, and a little more with the combination of the two," Hyder said. "More importantly, the incidents of breast cancer, that is the number of mice that got cancer, was reduced by 50 percent when both were combined."

Both APR-246 and 2aG4 are currently in human clinical trials. Researchers hope these findings will help enhance personalized treatment for breast cancer by reducing existing cancer cells and preventing the spread of the cancer to other parts of the body.

This research highlights the power of translational precision medicine and the promise of the proposed initiative at MU. The initiative will bring together industry partners, multiple schools and colleges on campus, and the federal and state government to enable precision and personalized medicine. Scientific advancements made at MU will be effectively translated into new drugs, devices and treatments that deliver customized patient care based on an individual's genes, environment and lifestyle, ultimately improving health and well-being of people.

Researchers involved with the study included Cynthia Besch-Williford, professor of veterinary pathobiology; Yayun Liang, a research associate professor of biomedical sciences in the College of Veterinary Medicine and the Dalton Cardiovascular Research Center at MU; Anthony Belenchia, a postdoctoral research assistant at the Dalton Cardiovascular Research Center and the College of Human Environmental Sciences; and Rolf Brekken, a professor at the University of Texas Southwestern Medical Center and principal investigator in the Hamon Center for Therapeutic Oncology Research.

The study, "Targeting mutant p53 alone or in combination with a phosphatidylserine specific antibody suppresses growth and metastasis of human breast cancer: a strategy towards enhancing personalized medicine," was presented.
by Hyder at the 2019 Annual Endocrine Society Meeting in New Orleans.

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