George Mason University researchers target breast cancer in three trials

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A malarial drug is showing promise in stopping breast cancer before it starts, Mason researchers are discovering during a clinical trial.

"The bold long-term goal is a short-term oral treatment that prevents breast cancer by killing the precursor cells that initiate breast cancer," says Lance Liotta, co-director of Mason's Center for Applied Proteomics and Molecular Medicine (CAPMM). "And it's looking hopeful."

The PINC trial (Preventing Invasive Neoplasia with Chloroquine) targets ductal carcinoma in situ, or DCIS, the most common type of pre-invasive breast cancer. Chloroquine is a drug given to prevent or treat malaria; it's showing promise in the early phase of the PINC trial.

CAPMM has three ongoing breast cancer research projects, including the PINC trial, which span the full scope of breast cancer's impact on patients.

In the PINC trial, DCIS is the focus. DCIS shows up as white spots in the MRI of a breast. Those white spots are calcifications that may mark the milk ducts where DCIS cells are growing, says Virginia Espina, assistant research professor at CAPMM. Not all DCIS becomes cancer, but all breast cancer goes through the DCIS stage, she says.

If the patient is diagnosed with DCIS after a biopsy, then she can enter the trial, says Espina, adding that the study doesn't interfere with standard medical treatment. Mason researchers are working with Kirsten

Edmiston, a surgeon at Inova Fairfax Hospital who recruits the patients and clinically directs the trial.

While patients are waiting between their diagnosis and the surgery, they take chloroquine once a week for four weeks, Espina says.

A significant reduction in the lesion's size is the sought-after outcome, says Espina, who can be seen in this video describing individual differences in cancer.The widely prescribed malaria drug chloroquine has few side effects—a rare rash is one, Espina says. There could come a day when chloroquine is taken by women worldwide to prevent breast cancer.

"We can imagine that in the future every woman will take chloroquine once a year," Espina says. "Chloroquine kills off the pre-malignant cells that are starting to accumulate. You'd do this periodically as a new type of chemo prevention."

Chloroquine works by stopping autophagy, which is used by cells to survive under stress. "When your cells realize they don't have enough nutrients, they eat themselves," Espina says. "It's a way to make energy when you don't have enough food."

And that's the spot the DCIS cells are in as they pile up in the milk duct. They're not getting enough oxygen and food and are squashed together.

"For all these reasons, they're under stress," Espina says. "When a cell is under stress, it's a life-and-death struggle. They're not just going to die. They're going to do what they can to survive. That's when they use autophagy to stay alive."

Chemotherapy, a common treatment for cancer, can rev up autophagy, Espina says. "A doctor selects a treatment to try to kill the cell, but the

cell is trying to survive; it's trying to do what it's programmed to do. We have to find a way to defeat this cellular process."

Chloroquine works like Pepto-Bismol; it alters the cell's digestive process and therefore autophagy. "But the chloroquine doesn't kill the normal cells because the normal cells aren't dependent on autophagy to survive," Espina says.

The second CAPMM study on breast cancer is funded by the Side-Out Foundation. Researchers are developing individualized treatment for women with metastatic breast cancer. These advanced tumors have spread to other organs, such as the liver, brain and bone, and have limited response to conventional therapies. Standard chemotherapy failed the 25 women Mason has worked with to pinpoint more effective treatments, says Mariaelena Pierobon, CAPMM assistant research professor.

Pierobon is using technology created by Liotta and Emanuel "Chip" Petricoin III to identify which drug targets are activated within each patient tumor. Pierobon's team is building on the promise of personalized medicine by focusing on the molecular profile of the metastatic lesions.

"We hope that by providing physicians with detailed information on the mechanisms that are driving our patients' tumors, we can facilitate the selection of the most appropriate treatment," Pierobon says. "We are trying to guide that decision by using the cutting-edge molecular technologies that were created in our laboratory to select among the FDA-approved drugs that might be the most promising for each patient."

In this approach, patients don't have to wait for new drugs to be developed. "By using drugs that are already approved, you don't have to study toxicity. That's a huge advantage," Pierobon says.

The third study is the I-SPY 2 TRIAL in which CAPMM researcher Julia Wulfkuhle is leading molecular profiling efforts developed uniquely in the Mason laboratory for women with stage II/III breast cancer. The FDA singled out I-SPY 2 as a leading trial design for accelerated drug approval.

The Side-Out Foundation raised $370,000 through volleyball tournaments to fund the metastatic breast cancer trial. The Side-Out Foundation is sponsoring the ongoing CAPMM research studies on the I-SPY 2 TRIAL through the FNIH Foundation for the National Institutes of Health. The Department of Defense Breast Cancer Research Project is funding the majority of the $2.1 million, three-year PINC grant, which started two years ago.

More information: www.ispy2.org/
www.clinicaltrials.gov/ct2/sho … 477?term=PINC&rank=1

Provided by George Mason University

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