

Researchers and doctor collaborate on ovarian cancer screening tool

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Clemson University's Ken Marcus (left) and Terri Bruce are working with Prisma Health's Dr. Larry Puls to develop a screening process for ovarian cancer. Credit: Clemson University School of Health Research

A team of researchers from Clemson University and Prisma Health-Upstate are working to create a screening process to catch ovarian cancer in the early or pre-cancerous stages.

Their goal is to make this screening as simple and easy for women as getting a pap smear. The idea is to identify the pre-cancerous changes through the makeup of the cervical mucus.

Dr. Larry Puls, the director of Gynecologic Oncology at Prisma Health Cancer Institute; Terri Bruce, director of the Clemson University Light Imaging Facility and research assistant professor of bioengineering, and Ken Marcus, professor of chemistry at Clemson and 2019 university Researcher of the Year, have been working together for more than a year to create this process. Through their research of cervical mucus, exosomes and chromatography, they are working to find a way to detect and identify pre-cancerous changes in a diagnostic setting. And now they are

putting their screening tool to the test through trials.

According to the Centers for Disease Control and Prevention (CDC), there is no simple, reliable way to screen for [ovarian cancer](#), especially in women who do not show symptoms. And none of the usual [cancer](#) exams work as a screening tool to catch the disease in the pre-cancerous stage, Puls said.

"People have looked at pelvic exams, blood tests and transvaginal ultrasonography as screening tools and none of it has worked as we would like," Puls said. "To this day, there is no adequate screening protocol for ovarian cancer and that's part of the reason why it's such a lethal disease. We can't find it early enough."

Ovarian cancer is the fifth deadliest cancer for women, just behind pancreas, colon, breast and lung cancers according to the CDC. In 2015, the latest year for which data is available, nearly 14,000 women died of ovarian cancer in the United States, according to the CDC.

While there are ways to diagnose ovarian cancer in the [early stages](#), it can be difficult, because the term ovarian cancer can be used to describe cancer of the ovary, fallopian tube or peritoneum, Puls said. However, Puls said he believes the majority of cases of this type of cancer most likely originate in the fallopian tubes. One of the best ways to potentially impact survival with ovarian cancer is to screen for it before symptoms occur and treat it before it is advanced, Puls said.

"Of all the advanced stage ovarian cancer patients, which makes up about 75 percent of the cases, only 10-15 percent will survive," Puls said. "But if you can find it when it's confined to just the ovary alone, 90 percent of patients beat their cancer. If we could shift women out of stage 3 and into stage 1, we can make a huge impact on this disease. We can even make a bigger impact if we could find a pre-cancerous change."

Citing previous research, Puls said that researchers will evolve in the future to be used for a "dipstick" test, have begun to identify this change because of a genetic mutation that predisposes a woman to ovarian cancer. Bruce said.

If most ovarian cancer cases are actually fallopian tube cancer, Bruce, Marcus and Puls said precancerous changes could be identified using the cervical mucus because there's a direct conduit from the fallopian tube to the mucus. "We've been getting patient samples so we can really start looking at possible ways of isolating very specific exosomes to identify common marker proteins as well as mRNA messages to help identify early stage ovarian cancer," Bruce said.

To do this, they used Bruce's already established work with exosomes, which are small lipid droplets derived from a cell. Through private funding, Puls, Bruce and Marcus have started trials and will continue for several more months. They plan to use the data this preliminary study provides to apply for larger, federal grants from agencies such as National Institutes of Health, National Cancer Institute and the Department of Defense. With the data they've collected thus far, they are hopeful this could be a way to help identify ovarian cancer earlier.

"Exosomes were once simply dismissed as a way of eliminating 'trash' from cells, but researchers now realize that they may be the key to the development of liquid biopsies," Bruce said.

This is because exosomes are derived from virtually all cells, giving a snapshot of what is going on within the cell, and can be found in any liquid within the human body, such as cervical mucus. "The hope is to be able to come up with an early diagnostic test so that we can catch this deadly cancer much earlier and give women a fighting chance," Bruce said.

"You can tell a lot about somebody by looking through their trash, so it turns out that you learn a lot about a cell from their exosomes," Bruce said. "This can include an overview of the types of RNA and proteins that are being made within the cells. Changes in these profiles could hold the key to early diagnostics." Their research is a product of the mission of the Clemson University School of Health Research, a virtual school that works to bring researchers together for collaboration and advance the research initiative at Clemson.

To make this idea a reality, the exosomes first must be captured. Because they are so small, exosomes are routinely separated from body fluids using a two- to three-hour process of ultracentrifugation steps or kits that can leave behind contaminants. These methods are costly and time-consuming, making a simple diagnostic test based on these protocols unrealistic, Bruce said. Windsor Sherrill, associate vice president of health research at Clemson, brought Puls and Bruce together for this type of research because Puls had been looking to create a screening tool for ovarian cancer, and Bruce had been looking at [cellular communication](#) and [exosomes](#) in previous cancer and disease progression research. Because of previous collaboration, Bruce knew that Marcus' work with chromatography would be an asset in their project.

To separate the exosomes from the cervical mucus, the researchers used Marcus' method of the use of capillary-channeled polyester fibers and hydrophobic interaction chromatography, a process that takes eight to 10 minutes and leaves behind no appreciable contaminants. This method, which was studied by Bruce and Marcus and recently published in the journal *Electrophoresis*, could "This initiative illustrates the power of collaboration between Clemson faculty and clinical investigators at Prisma Health-Upstate and is the type of innovation we envisioned with the CU School of Health Research," Sherrill said. "Professors Bruce and Marcus bring unique expertise to the challenges of cancer care and working with Dr. Puls and the oncology team at Prisma Health, they are making great strides toward their goal."

More information: Terri F. Bruce et al. Exosome isolation and purification via hydrophobic interaction chromatography using a polyester, capillary?channeled polymer fiber phase, *Electrophoresis* (2018). DOI: [10.1002/elps.201800417](https://doi.org/10.1002/elps.201800417)

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