New test aids personalized cancer care

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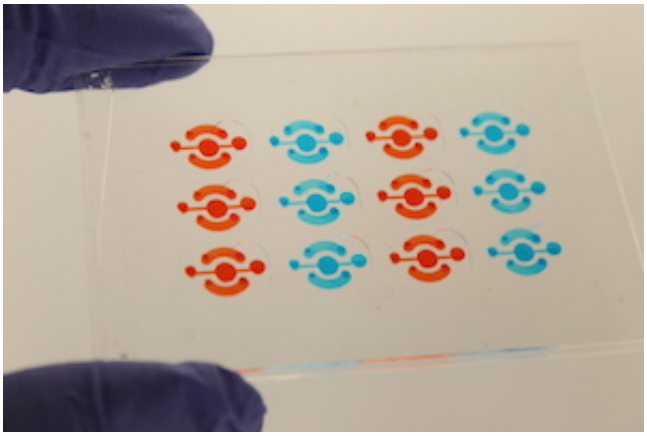

This microfluidic petri dish provides a highly accurate ex vivo testing environment.

In a highly successful, first-of-its-kind endeavor, a multidisciplinary team of University of Wisconsin-Madison researchers have created a "tumor in a dish:" an ex vivo microenvironment that can accurately anticipate a multiple myeloma patient's response to a drug.

The advance could mean a giant step forward in efforts to tailor medical treatment plans to individual patients.

Led by Shigeki Miyamoto, a professor of oncology at UW-Madison, and David Beebe, the John D. MacArthur Professor and Claude Bernard professor of biomedical engineering at UW-Madison, the researchers published news of the advance May 1, 2015, in the Royal Society of

Chemistry journal *Integrative Biology*.

"We're taking the first steps toward mimicking the body in a dish," Beebe says.

Much of the research was led by Chorom Pak, who previously was a graduate student working in Miyamoto's lab.

Pak and Edmond Young (now at the University of Toronto) and the other researchers produced an assay, or testing process, which involves co-culturing multiple myeloma tumor cells with their surrounding non-tumor cells, all from the same patient, in a microscale Petri dish. The researchers then treated the tumor cells with bortezomib, a drug commonly used in multiple myeloma therapy. And, after only three days, the researchers could determine whether the drug was effective—or not.

They compared the results of their ex vivo tests with the success or failure rates of actual patients who had received the drug—and an unprecedented 100 percent of the ex vivo test results matched the results of the patients.

Multiple myeloma is a universally fatal cancer. Rising in the blood marrow due to an accumulation of abnormal, or cancerous, plasma cells, myeloma is treatable but incurable.

"The median survival rate has improved, but is only about five to seven years," Pak says.

The new assay could save many multiple myeloma cancer patients the psychological stress of having to try multiple drugs until they find the most effective one. The assay reduces clinicians' need for this trial-and-error approach while treating a patient, and it also lowers the cost of treatment.

The fundamental idea behind the research was to focus on everything surrounding a tumor, not just the tumor itself. These surroundings can include bone marrow stromal cells, macrophages and other immune cells, all of which represent an integral part of the tumor's environment. By including these components in a microfluidic Petri dish—a device developed by Beebe and Miyamoto's lab a few years ago—the researchers' ability to accurately gauge results increased dramatically.

Beebe says scaling down the testing environment in the group's research is akin to moving from a lake to a bathtub: While the huge area of a standard-sized Petri dish dilutes all the extra cells, the micro-scale Petri dish the team used allows cancer cells to continue interacting with their usual surroundings, but outside of the body.

The researchers essentially created a miniaturized external model of an individual's cancer, says Pak.

She has founded a service-based company called Lynx Biosciences based on these findings, and the company was recently a finalist in the 2015 Wisconsin Governor's Business Plan Contest. Pak and fellow researchers are looking to conduct a prospective trial, which, instead of simply matching the results of patients with that of the ex vivo tests, will actually use the ex vivo tests to identify responsive and non-responsive patients. In addition, they are starting to consider what this discovery means for other cancer types, and other drugs.

The researchers' results could have interesting and wide-ranging implications for the future of cancer treatment and therapy, although their work is long from over.

"This is only one type of cancer, one particular drug, and we're a long way from implementing this and helping patients in a widespread way," Beebe says. "But it's happening. This is an exciting time in this area, and

we're definitely going to see more of this."

Funding for the research came from the National Cancer Institute of the National Institutes for Health and a collaborative grant funded by the Trillium Fund of the UW Carbone Cancer Center. Other authors on the paper include Hematology Associate Professor Natalie S. Callander and Assistant Professor Fotis Asimakopoulos, biomedical engineering alumnus Edmond W.K. Young, medical physics alumnus Benjamin Titz, Biostatistics and Medical Informatics Professor KyungMann Kim, associate researcher Sandeep Saha, and undergraduate student Kenny Chng.

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