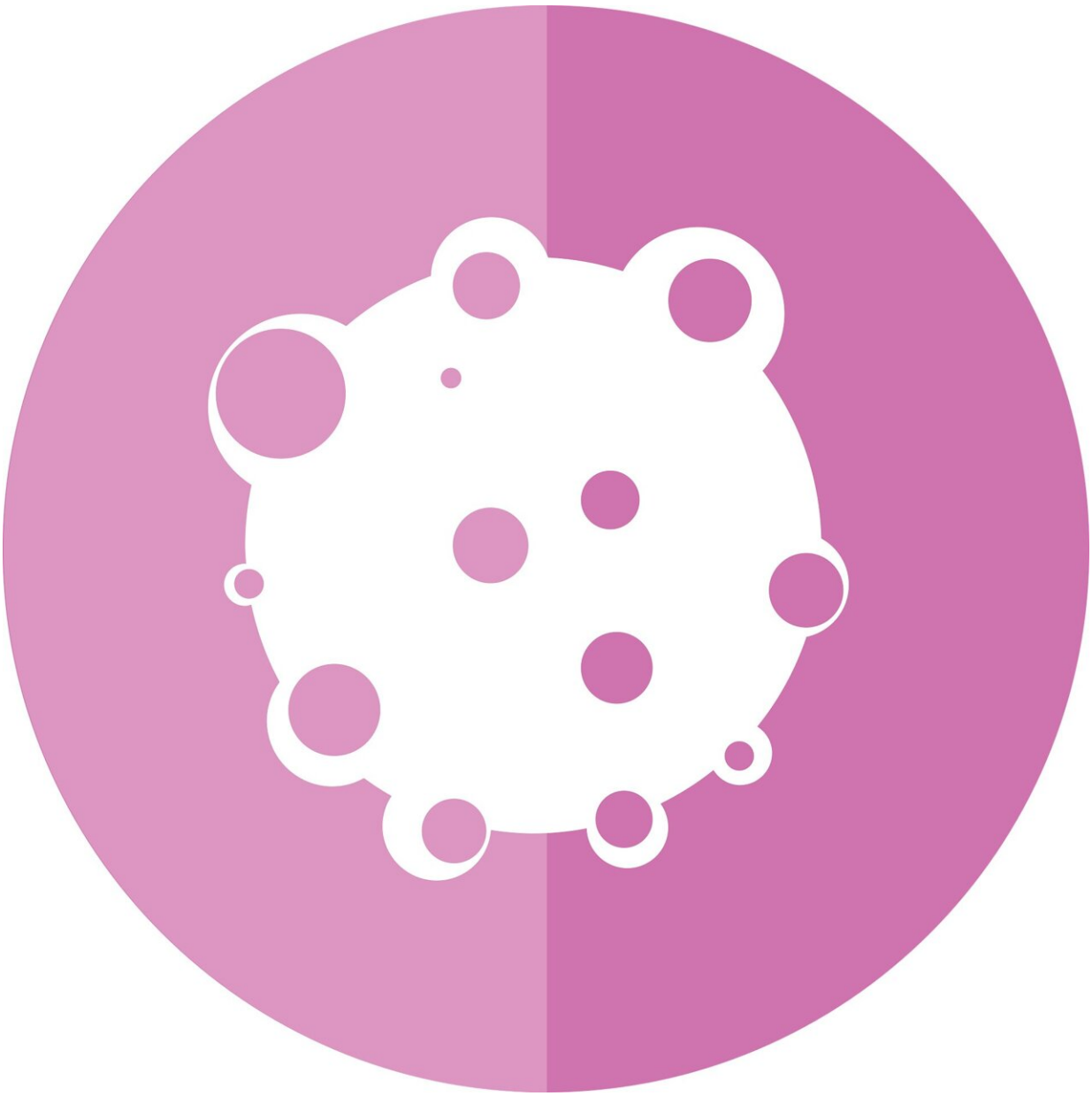
Fine-tuning 3D lab-grown mini tumors to help predict how patients respond to cancer therapies

June 6 2023



Credit: Pixabay/CC0 Public Domain

Scientists from the UCLA Jonsson Comprehensive Cancer Center have developed a new method to bioprint miniature tumor organoids that are designed to mimic the function and architecture of real tumors. The improved process allows researchers to use an advanced imaging method to study and analyze individual organoids in great detail, which can help researchers identify personalized treatments for people with rare or hard-to-treat cancers.

The method is described in the journal *Nature Communications*.

"Tumor organoids have become fundamental tools to investigate tumor biology and highlight drug sensitivities of individual patients," said Alice Soragni, Ph.D., an assistant professor in the department of Orthopaedic Surgery at the David Geffen School of Medicine at UCLA and member of the UCLA Jonsson Comprehensive Cancer Center. "However, we still need better ways to anticipate if resistance could be arising in a small population of cells, which we may not detect using conventional screening approaches. This is truly important, particularly as organoid-based drug predictions are starting to be leveraged clinically."

These miniaturized tumors, called organoids, can be grown in a lab using cell lines or patients' own cells to better understand human biology and diseases. By recreating patient tumors, researchers can test different drugs to see if the tumor will respond well or poorly to the treatment. This can make it easier for physicians to choose the best therapy for their patients.

While these mini tumors have helped improve drug modeling and are becoming invaluable tools for testing the efficacy and safety of potential drugs, it is still challenging for current models to capture underlying tumor heterogeneity which often drives clinically observed resistance to therapy. One of the main limitations of this approach is that current methods fail to capture changes or differences within the organoid samples that may be responsible for the resistance to therapy that is observed in clinical settings.

To overcome these challenges, the team of researchers created a method that uses a bioprinting technique to print cells in a thin layer of support extra-cellular proteins to give rise to 3D mini-tumors without altering the tissue histology and gene expressions. The team combined bioprinted cells with high-speed live cell interferometry (HSLCI), an imaging system that is a non-destructive approach used to observe and measure the weight of living cells in real-time. These methods are then combined with machine learning algorithms to analyze and measure individual organoids.

"By using this method, we are able to accurately measure the masses of thousands of organoids simultaneously," said Dr. Michael Teitell, director of the UCLA Jonsson Comprehensive Cancer Center and co-senior author of the study. "This information helps identify which organoids are sensitive or resistant to specific therapies, which can be used to quickly select the most effective treatment options for patients."

With the new method combination, researchers confirmed that they could measure the growth patterns of the bioprinted tumor cells over time to see how the cells responded to different drugs or treatments.

"The measurements were done in a way that did not damage or destroy the organoids, allowing for non-invasive analysis of their growth and drug responses," noted Teitell.

The researchers were able to identify an effect of certain drugs on cells as soon as six hours from adding the therapies. The team also identified small groups of cells that did not respond to the drugs, even within very homogeneous cell line samples consisting mostly of cells that were responsive to the treatment.

"This new pipeline has enhanced the quality and depth of information we can get from drug screening of 3D models of disease," said Soragni. "We are now applying the same approach to organoids established from hard-to-treat, rare cancers."

The researchers will leverage the new approach to uncover novel therapeutic avenues and mechanisms of resistance to eventually develop personalized treatment strategies.

The co-first authors are Peyton Tebon, Bowen Wang and Alexander Markowitz, all from UCLA. Other UCLA authors include Ardalan Davarifar, Brandon Tsai, Alfredo Gonzalez, Sara Sartini, Huyen Nguyen, Nasrin Tavanaie, Thang Nguyen and Paul Boutros.

More information: *Nature Communications* (2023). DOI: 10.1038/s41467-023-38832-8 , www.nature.com/articles/s41467-023-38832-8

Provided by University of California, Los Angeles