Chemical tests of cell growth enter third dimension

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Ohio State University researchers have developed two new technologies for measuring cell growth in the laboratory.

The first patent-pending technology provides a way for researchers to easily tell if cancer cells in the laboratory are responding to an anti-cancer drug. The second -- because it tests several sets of cells at once -- allows for the simultaneous testing of different dosages, or the effect of a single drug on different kinds of cells taken from the body.

Shang-Tian Yang, professor of chemical and biomolecular engineering at Ohio State, and his colleagues described the two technologies Wednesday and Thursday at the American Chemical Society Fall National Meeting in San Francisco.

For more than a decade, Yang's team has been developing three-dimensional methods for growing cells for laboratory testing. His fibrous-bed bioreactor (FBB) is a device that allows cells to grow in natural 3D bundles. In the body, cells cling to supportive tissues as they grow; inside the FBB, they cling to strands of polyester fibers.

For the first of the two new technologies, Yang took the basic concept behind the FBB and combined it with laboratory testing methods that normally only grow cells in two dimensions.

Such tests are normally done on cells in trays containing many tiny wells. Each well contains a growth medium and some cells, and a protein that

will cause growing cells to fluoresce. Researchers test a drug by adding it to a well. If the cells continue to fluoresce, that means that the cells are still reproducing, and the drug isn't effective at controlling growth.

The problem is how to measure the amount of fluorescence, to quantify how much the cells are growing. Fluorescing cells don't look very bright in the well, because they grow as a thin film layer that is essentially two-dimensional. Researchers get around this problem by removing the cells from the well and counting them one by one under a microscope.

It's a long and tedious process.

"Our idea is very simple," Yang said. "We wanted to intensify the signal so that it could be read inside the well, by cultivating the cells in three dimensions."

Yang and his team created a device that uses standard well plates in a new way. In one well, they plant cells on one of their 3D scaffolds. The surrounding eight wells contain only growth medium.

The 3D glob of cells in the middle well glows brighter than a 2D film, due to a specific optical effect, Yang said. The surrounding empty cells provide a darker background that lets the fluorescence signal be measured even more easily.

"You can use this as a device to monitor a drug's effect, whether you want to stimulate or inhibit cell growth," Yang said. "We have used it on colon cancer cells and mouse embryonic stem cells. And in both cases, we found a very good relation between cell growth and fluorescence intensity."

The device can be used with standard well plates, though nine wells are required for each test instead of one. He and his team are expanding the

technology from 96-well plates to 384-well plates, and are working on their own custom plate design.

There is an advantage to using more wells: The eight empty wells supply nutrients to the cells in the middle well, so tests can run for up to two weeks without researchers having to replenish the growth medium.

"If you replenish the medium, you could essentially grow cells indefinitely," Yang said.

The second new technology to come from Yang's lab is a microfluidics platform that allows for testing of many types of cells or drug dosages at once. Tiny pipes connect wells that contain cells growing in 3D. The drug to be tested is pumped from a common reservoir into the pipes.

Each well could receive a different dosage of the same drug. Or, researchers could plant cells from different organs in each well, and see how each kind of cell reacts to the same dosage -- a quick way to detect a drug's potential side effects on the body.

"The trick is to use one pump for everything, and control the fluid distribution though all the channels," Yang said. While he has worked out an initial design, he would like to join with a commercial microfluidics manufacturer to develop the technology further.

The university is expecting to license both technologies.

Source: Ohio State University