Purdue proves concept of using nano-materials for drug discovery

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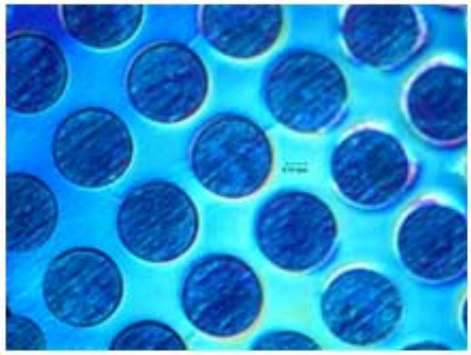

Researchers at Purdue University have built and demonstrated a prototype for a new class of miniature devices to study synthetic cell membranes in an effort to speed the discovery of new drugs for a variety of diseases, including cancer.

Image: This image, taken with an optical microscope, demonstrates the successful test of a prototype for a new class of miniature devices to study synthetic cell membranes in an effort to speed the discovery of new drugs for a variety of diseases, including cancer. Purdue University researchers created a chip about one centimeter square that holds thousands of tiny vessels sitting on top of a material that contains numerous pores. The

researchers tested the devices with an enzyme that produces a blue color when combined with a liquid that contains molecules small enough to easily pass through the pores. The enzyme was placed inside the vessels – on the inner surface of the "nanoporous" membranes – and the liquid was placed outside each vessel so that it covered the opposite side of the membranes. When the liquid diffused through the membrane's pores, it mixed with the enzyme, causing a reaction and turning blue in the process, which demonstrated that the device works. (School of Chemical Engineering, Purdue University)

The researchers created a chip about one centimeter square that holds thousands of tiny vessels sitting on top of a material that contains numerous pores. This "nanoporous" material makes it possible to carry out reactions inside the vessels.

The goal is to produce "laboratories-on-a-chip" less than a half-inch square that might contain up to a million test chambers, or "reactors," each capable of screening an individual drug, said Gil Lee, the project's leader and an associate professor of chemical engineering.

"What we are reporting now is a proof of concept," said Lee, one of three researchers who wrote a paper that details new findings in the current issue (Feb. 15) of the journal Langmuir. The two other researchers are Zhigang Wang, a postdoctoral fellow at Purdue; and Richard Haasch, a research scientist at the University of Illinois at Urbana-Champaign.

The work is part of overall research being carried out by an interdisciplinary team of scientists and engineers who are members of a Center for Membrane Protein Biotechnology. The center was created at Purdue in 2003 through a grant from the Indiana 21st Century Research and Technology Fund, established by the state of Indiana to promote high-tech research and to help commercialize innovations.

The vessels discussed in the research paper are cylindrical cavities that are open at the top and sealed at the bottom with a material called alumina, which contains numerous pores measured in nanometers, or billionths of a meter.

Researchers are working to duplicate how cell membranes function on chips in order to test the potential effectiveness of new drugs to treat diseases. Membranes, which surround cells and regulate the movement of molecules into and out of the cells, contain a variety of proteins, some of which are directly responsible for cancer's ability to resist anti-tumor chemotherapy drugs. These proteins act as tiny pumps that quickly remove chemotherapy drugs from tumor cells, making the treatment less effective. Cancer cells exposed to chemotherapy drugs produce a disproportionately large number of the pumps, causing the cells to become progressively more resistant to anticancer drugs.

Engineers and scientists in the Purdue center are trying to find drugs that deactivate the pumps, which would make the chemotherapy drugs more effective. The researchers are developing synthetic cell membranes to mimic the real thing and then plan to use those membranes to create chips containing up to 1 million test chambers. Each chamber would be covered with a membrane containing the proteins, and the chambers could then be used to search for drugs that deactivate the pumps, Lee said.

Such an advanced technology could be used to quickly screen millions of untested drug compounds that exist in large pharmaceutical "libraries." The chips could dramatically increase the number of experiments that are possible with a small amount of protein.

"It’s been very hard to study these proteins because they are difficult to produce in large quantities," Lee said. "The devices we have created offer the promise of making chips capable of running thousands of

reactions with the same amount of protein now needed to run only about 10 reactions."

Findings being reported in the paper detail how researchers created the device with the same "microfabrication" techniques used to make computer chips. The reactors range in diameter from about 400 to 60 microns, or millionths of a meter. Human hairs are about 100 microns wide.

"You can think of it as a micro-petri dish for studying biochemical reactions," Lee said.

The alumina contains pores smaller than 100 nanometers, and the total volume of the reactors varies from 1-10 nanoliters.

"What's unique about this device is that the surface has nanometer-scale pores in it," Lee said. "The concept is fairly simple – there is an inorganic porous membrane – in this case alumina, which separates the reaction chamber from a solution. The pores in this membrane are nanometer in scale, so they do not allow proteins to readily pass through the membrane but will allow smaller molecules to pass.

"This allows us to do separation right in the reactor, which means we can do reactions that could not be done before in such a small device. We can study membrane proteins in a fundamentally new way, which is very important because many future drugs to treat diseases will likely work by controlling proteins in cell membranes."

Researchers tested the devices with an enzyme that produces a blue color when combined with a liquid that contains molecules small enough to easily pass through the pores. The enzyme, which is a protein, was placed inside the vessels – on the inner surface of the alumina membranes – and the liquid was placed outside each vessel so that it

covered the opposite side of the membranes. When the liquid diffused through the membrane's pores, it mixed with the enzyme, causing a reaction and turning blue in the process, which demonstrated that the device works.

Source: Purdue University