'Engineered' breast aims to improve nanoparticle testings

February 23 2011

Researchers from Purdue University has reproduced portions of the female breast in a tiny slide-sized model dubbed "breast on-a-chip" that will be used to test nanoparticle-based approaches for the detection and treatment of breast cancer. The model mimics the branching mammary duct system, where most breast cancers begin, and will serve as an "engineered organ" to study the use of nanoparticles to detect and target tumor cells within the ducts.

Sophie Lelièvre and James Leary led the team of investigators that created the breast-on-a-chip model. The details of their work appear in the journal *Integrative Biology*.

"We've known that the best way to detect this cancer early and treat it effectively would be to get inside the mammary ducts to evaluate and treat the cells directly, and this is the first step in that direction," said Dr. Lelièvre. The ultimate goal of this project is to introduce magnetic nanoparticles through openings in the nipple, use a magnetic field to guide them through the ducts where they would attach to cancer cells, and then reverse the magnetic field to retract any excess nanoparticles. The nanoparticles could carry contrast agents to improve mammography, fluorescent markers to guide surgeons, or anticancer agents to treat the cancer, Dr. Leary said.

Physicians have tried to access the mammary ducts through the nipple in the past, injecting fluid solutions to try to wash out cells that could be examined and used for a diagnosis of cancer. However, this approach

could only reach the first third of the breast due to fluid pressure from the ducts, which branch and become smaller and smaller as they approach the glands that produce milk, Dr. Leary said. "The idea is that nanoparticles with a magnetic core can float through the naturally occurring fluid in the ducts and be pulled by a magnet as opposed to being pushed with pressure," he said. "We think they could reach all the way to the back of the ducts, where it is believed most breast cancers originate. Of course, we are only at the earliest stages and many tests need to be done."

Such tests could not be done using standard models that grow cells across a flat surface in a plastic dish, so the team created the artificial organ-like model in which living cells line a three-dimensional replica of the smallest portions of the mammary ducts. Dr. Leary's group used standard lithographic techniques to build a mold of branching channels out of a rubberlike material called polydimethylsiloxane. The channels are about 5 millimeters long of various diameters from 20 microns to 100 microns, roughly the diameter of a human hair, that match what is found near the end of the mammary duct system. Then, Dr. Lelièvre, whose group is one of the few in the world able to successfully grow the complicated cells that line the mammary ducts, coaxed the cells to grow within the mold and behave as they would within a real human breast.

"The cells within the breast ductal system have a very specific organization that has proven difficult to obtain in a laboratory," Dr. Lelièvre said. "The cells have different sides, and one side must face the wall of the duct and the other must face the inner channel. Reproducing this behavior is very challenging, and it had never been achieved on an artificial structure before."

The team coated the mold in a protein-based substance called laminin 111 as a foundation for the cells that allows them to attach to the mold and behave as they would inside the body, Dr. Lelièvre said. And

because injecting the delicate cells into the finished channels of the mold caused too much damage, the team created a removable top for the channels. "The design of the U-shaped channels and top was necessary for us to be able to successfully apply the cells, but it also allows us to make changes quickly and easily for different tests," she explained. "We can easily introduce changes among the cells or insert a few tumor cells to test the abilities of the nanoparticles to recognize them. The design also makes it very easy to evaluate the results as the entire model fits under a microscope."

This work is detailed in a paper titled, "Breast on-a-chip: mimicry of the channeling system of the breast for development of theranostics. An abstract of this paper is available at the journal's website.

Provided by National Cancer Institute