MedicalXpress

An implantable microdevice has potential to identify suitable therapy for cancer patients

April 20 2016

A microdevice implanted into a tumor could release up to 100 individual cancer therapeutics or combinations, and upon retrieval from the tumor and analyses, could identify the best treatment option for that tumor, according to preclinical research presented here at the AACR Annual Meeting 2016, April 16-20.

The research team that developed this microdevice has initiated a clinical trial to test the safety and feasibility of placing and removing the microdevice in patients with early-stage HER-2 positive or triple-negative breast cancer.

"Currently, there are about 150 cancer drugs approved by the U.S. Food and Drug Administration, and many cancer patients have different drugs to choose from to treat their specific disease. However, patients respond differently to different drugs, and often, no two patients have the same response to a specific drug. It has been a major challenge to determine which drug or combination of drugs to give to which patient," said Oliver Jonas, a postdoctoral fellow appointed jointly in the laboratories of Robert S. Langer, ScD, the David H. Koch Institute Professor, and Michael Cima, PhD, a David H. Koch Professor of Engineering, at Massachusetts Institute of Technology.

"Being able to identify the right therapy that will work optimally for every patient will be a major advance," he added.

Jonas and colleagues engineered a small implantable microdevice that is

less than a millimeter in diameter and about 4 millimeters in length, which has multiple reservoirs to hold single agents and combination therapies. The device is implanted into the tumor through a small biopsy needle and left there for about 24 hours. The implant is then extracted along with a layer of surrounding tumor tissue, and the tumor tissue is analyzed to determine the effect of each of these drugs and combinations on the tumor.

"We published a study last year in *Science Translational Medicine*, in which we demonstrated that we can implant this microdevice into mouse tumors and that we can test 16 different therapies. We've increased that number to 100 since then," Jonas said. "We showed that the local readout that we can get from many agents in a single tumor is actually predictive of the drug sensitivity."

The researchers engineered the cylindrical microdevice, using biocompatible plastics. When implanted in a mouse tumor, the therapeutics, loaded in specific reservoirs within the device, were released in such a way that crosstalk between the different drugs was eliminated by taking into account the chemistry of drug and formulating the drugs appropriately to separate the reservoirs from each other. The researchers can also adjust the drug-release rates to mimic the concentration of the drug achieved by standard systemic delivery, Jonas explained.

In addition to further developing the device to hold up to 100 different drugs and combinations, they are now able to study the tumor at different time points while the device is still in place, by real-time imaging using optical fibers attached to each reservoir, Jonas added. "We are now able to measure how tumors adapt and change when they are treated locally or systemically, and how their sensitivity to different drugs changes when switched from standard-of-care therapy," Jonas said.

"Our study points to two important aspects," Jonas said.

He explained that traditionally, there are two approaches to systems biology; one approach is to study the effects of multiple drugs on one type of cells in the laboratory, and the other is to conduct whole mouse studies where one could only test one or two agents at a time, which takes a long time and comes at a high cost. "We are showing that there is a middle ground where one can work in vivo, so that we take into account the effects of the microenvironment, but can also screen 100 or more compounds efficiently and rapidly in a single tumor, such that we can prioritize therapy to a patient, in addition to being able to understand the cancer in a functional way that we haven't been able to do before," Jonas said.

As proof of principle, Jonas and his colleagues at MIT's Koch Institute for Integrative Cancer Research have so far tested the effects of many drugs in patient-derived xenograft (PDX) mouse models of melanoma, and prostate and breast cancer. In recent studies, they tested the sensitivity of estrogen receptor-positive breast cancer to single agents and combinations that target the ER, CDK4/6, PI3K, and other pathways.

"This microdevice also enables us to investigate the mechanisms behind drug resistance. Our results demonstrate new patterns of therapy evasion by cancer cells and adaptive signaling mechanisms, which offer clues for effective combination therapy," Jonas said.

More information: O. Jonas et al. An implantable microdevice to perform high-throughput in vivo drug sensitivity testing in tumors, *Science Translational Medicine* (2015). DOI: 10.1126/scitranslmed.3010564