

The newest precision medicine tool: Prostate cancer organoids

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Research led by investigators at Memorial Sloan Kettering Cancer Center has shown for the first time that organoids derived from human prostate cancer tumors can be grown in the laboratory, giving researchers an exciting new tool to test cancer drugs and personalize cancer treatment.

The researchers, whose results were published today in *Cell*, successfully grew six prostate cancer organoids from biopsies of patients with metastatic prostate cancer and a seventh organoid from a patient's circulating tumor cells. Organoids are three-dimensional structures composed of cells that are grouped together and spatially organized like an organ. The histology, or tissue structure, of the prostate cancer organoids is highly similar to the metastasis sample from which they came. Sequencing of the metastasis samples and the matched organoids showed that each organoid is genetically identical to the patient's cancer from which it originated.

"Identifying the molecular biomarkers that indicate whether a drug will work or why a drug stops working is paramount for the precision treatment of cancer," said Yu Chen, MD, PhD, Assistant Attending Physician in the Genitourinary Oncology Service and Human Oncology and Pathogenesis Program at MSK. "But we are limited in our capacity to test drugs—especially in the prostate cancer setting, where only a handful of prostate cancer cell lines are available to researchers."

With the addition of the seven prostate cancer organoids described in the



Cell paper, Dr. Chen's team has effectively doubled the number of existing prostate cancer cell lines.

"We now have a new resource at our disposal that captures the molecular diversity of prostate cancer. This will be an invaluable tool we can use to test drug sensitivity," he added.

The use of organoids in studying cancer is relatively new, but the field is exploding quickly according to Dr. Chen. In 2009, Hans Clevers, MD, PhD, of the Hubrecht Institute in the Netherlands demonstrated that intestinal stem cells could form organoids. Dr. Clevers is the lead author on a companion piece also published in *Cell* today that describes how to create healthy prostate organoids. Dr. Chen's paper is the first to demonstrate that organoids can be grown from prostate cancer samples.

The prostate cancer organoids can be used to test multiple drugs simultaneously, and Dr. Chen's team is already retrospectively comparing the drugs given to each patient against the organoids for clues about why the patient did or didn't respond to therapy. In the future, it's possible that drugs could be tested on a patient's organoid before being given to the patient to truly personalize treatment.

After skin cancer, prostate cancer is the most common cancer in American men—about 233,000 new cases will be diagnosed in 2014. It is also the second leading cause of cancer death in men; 1 in 36 men will die of the disease.

Despite its prevalence, <u>prostate cancer</u> has been difficult to replicate in the lab. Many mutations that play a role in its growth are not represented in the <u>cell lines</u> currently available. Cell lines can also differ from their original source, and because they are composed of single cells, they do not offer the robust information that an organoid—which more closely resembles a living organ—can provide.



Provided by Memorial Sloan-Kettering Cancer Center

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