Tumor Organoids Predict How Well Patients Respond to Cancer Drugs

Testing treatments on mini tumors may save time in identifying which therapies work best, a new study shows.

By Ruth Williams | February 22, 2018

For cancer patients with just months to live, time is short—too short to try drug after drug with the hope of finding one that slows the disease. But lab-grown mini tumors derived from patients’ cells could offer a way to test many drugs in parallel, saving time and possibly extending lifetimes. A report today (February 22) in *Science* brings this concept closer to clinical reality.

Previously, there has been “anecdotal evidence that observations in the clinic can be reproduced with organoids,” says stem cell and developmental biologist Hans Clevers of the Hubrecht Institute in Utrecht, the Netherlands, who was not involved in the research. “But, [the
authors] have now for the first time come up with a large number of cases like that and have statistical [results] that are very impressive.”

They have “shown definitively that these organoids are predictive of response,” Clevers continues. “I’m sure this is going to be one of the key papers in this field.”

In 100 percent of cases, if a drug didn’t work on a patient’s organoids, then it didn’t work in the patient, and in 90 percent of cases, if a drug did work on the organoids, then it worked in the patient.

Identifying the particular mutations present in a patient’s cancer is one approach to guiding treatment decisions, but in reality only a handful of mutations are known to confer sensitivity or resistance to certain drugs. And, even if such mutations are present, the tumors don’t always respond as expected.

Tumor organoids—model tumors grown in a dish from tumor biopsy cells—were originally developed for research into cancer physiology, says Valeri. But, he and his colleagues reasoned, if the organoids really do mimic the physiology of the original tumor, they might be suitable for testing candidate drugs before giving those drugs to patients.

“Nobody has ever compared how these organoids taken from the patient behave in the lab compared with how the patient responds in the clinic,” Valeri says, until now.

He and his colleagues collected 110 biopsies of metastatic tumors from 71 patients with gastroesophageal or colorectal cancers. Approximately 70 percent of the tumors were successfully grown into organoids. Comparing the genetic mutations and protein markers of the organoids with those of the parental biopsy material revealed “a 96 percent overlap in terms of molecular makeup,” says Valeri. And these similarities persisted long after the organoids were grown. “This proved to ourselves that the system was in fact very robust,” he says.

The patients who provided the biopsies were enrolled in a variety of clinical trials of new drugs, so the team tested those same drugs on the tumor organoids. Valeri and his colleagues found that in 100 percent of cases, if a drug didn’t work on a patient’s organoids, then it didn’t work in the patient, and that in 90 percent of cases, if a drug did work on the
organoids, then it worked in the patient, too.

The team also tested a panel of 55 drugs that are in either clinical or preclinical development on the organoids. For drugs where the effectiveness can differ depending on tumor-specific mutations, the researchers found the organoids almost always responded as would be expected for their genotype.

This study shows it is technically possible to use a patient’s organoids for screening candidate cancer treatments, says childhood cancer expert Sam Behjati of the Wellcome Sanger Institute in the U.K. who was not involved with the project. “It begins to paint a picture whereby you could envision that in the future . . . we can actually find a way of doing this routinely for patients.”