

This is How to Beat the Tumor Cells That Survive Cancer Therapy

University of California San Francisco researchers built a robot system that treats thousands of mini tumors at once in the laboratory.

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Cancer drugs can shrink fast-growing tumors. But sometimes a few tumor cells survive. These “persister” cells seed new tumors, forcing cancer patients into arduous cycles of testing and treatment.

The problem is, persister cells are rare — as few as one in a thousand tumor cells — and they’re genetically identical to the tumor, which makes them hard to find. Plus, their tenacity can be temporary, and by the time a scientist can get them in a petri dish, the qualities that helped them survive may have faded.

To figure out how to beat them, researchers at UC San Francisco built a robotic system that treats thousands of mini tumors at once in the laboratory. The platform lets scientists systematically identify, track, and treat surviving cells. It revealed shared features among persister cells that could help explain why cancer comes back — features that could be exploited by future drug therapies to beat them.

“A few years ago, people were still asking whether persister cells were real,” said [Xiaoxiao “Vany” Sun](#), PhD, first author of the paper and an assistant researcher in the UCSF Department of Pharmaceutical Chemistry. “Now we can find them and test ideas for how to eliminate them.”

The [findings appear in Science Advances](#) on June 12.

The team gathered 94 drug candidates that other laboratories had flagged as potential persister therapies. They wanted to test each drug, at different doses, on persisters from two types of lung cancer that had been treated with standard therapies. It would require 10,000 painstaking, week-long experiments — so they built a robotic platform to eliminate the labor and inconsistency of

doing it by hand.

Thousands of miniature tumors sat in stacks of 384-well plates inside controlled incubators. A robotic arm, like those used in pharmaceutical drug screening, moved the plates between experimental stations.

One station used sound waves to deposit tiny, precise doses of drug onto each tumor (first, a lung cancer therapy; then, an experimental persister therapy). Other stations stained the tumors with antibodies and took microscopic images of each tumor or group of persisters.

Of the tested drugs, nine consistently weakened persister cells. It suggests that persister cells may share common vulnerabilities, even if they had emerged under different treatment conditions.

The team plans to expand the platform to include more tumor types and treatment conditions. They hope the resulting dataset will be a resource to help researchers eliminate persister cells before they can give rise to drug-resistant disease.

“We expected each tumor to behave as its own special case,” said [Steve Altschuler](#), PhD, professor of Pharmaceutical Chemistry at UCSF and co-senior author of the paper. “Instead, we found patterns that held up across many different samples, suggesting there may be underlying rules that can help predict which therapies are most likely to work.”

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