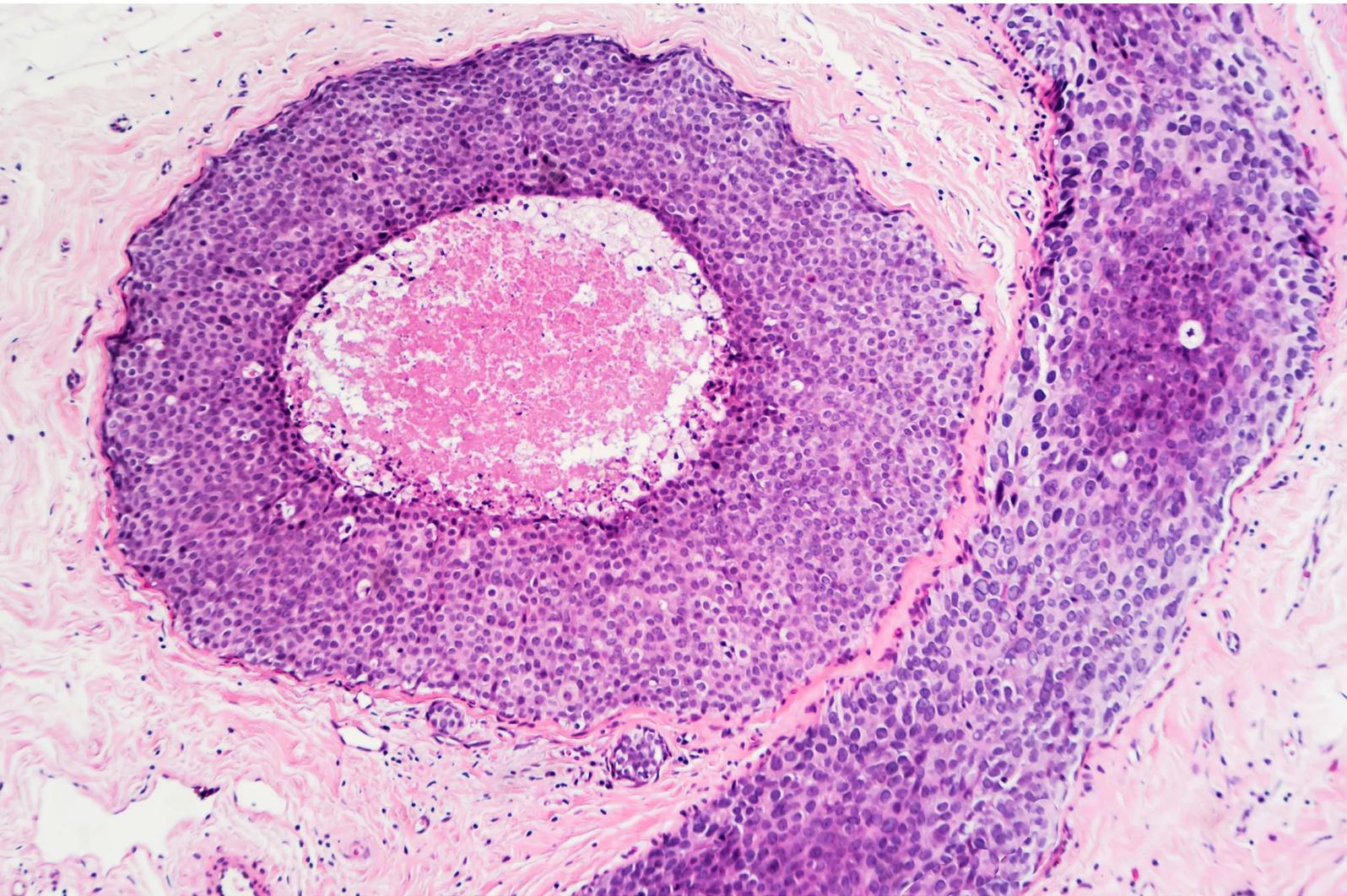


# To Test Cancer Drugs, These Scientists Grew ‘Avatars’ of Tumors

Growing organoids in dishes and xenografts in mice lets scientists recreate a living person’s tumor—and test dozens of drugs against them at the same time.



In a historic first, the team returned results in time to recommend a treatment that was used to attack a living patient’s breast cancer. PHOTOGRAPH: GETTY IMAGES

**IN 2018, ALANA** Welm found herself in an exciting, yet burdensome, position. The University of Utah [breast cancer research lab](#) where she leads joint projects with her husband, Bryan Welm, had created lab-grown versions of real tumors isolated from living cancer patients. Each cancer had been translated into two kinds of biological models: xenografts, made by implanting tissue into mice, and organoids, miniature clumps of tissue grown in plastic dishes.

Each simulated cancer was a way to test which of about 45 drugs, some experimental and others approved by the US Food and Drug Administration, might perform best for the real patient. During testing on one patient’s organoids, the researchers isolated a drug that effectively killed its cancer cells. That was the exciting bit. The burden: Welm had no right to do anything about it. She couldn’t tell the patient or her doctor. “We were just doing this for research,” says Welm.

This particular drug had already earned FDA approval to be used against breast cancer, but it wasn't approved for this patient's type of cancer. So Welm dialed up her university's Institutional Review Board, an ethics oversight group. "We called them and said: We found this, we really think we need to let them know," Welm recalls. The board agreed; the team could bring the patient's physician into the loop. "That really was an eye-opener," Welm says. "Wow, we can actually make a difference!"

Yet by the time Welm reached the physician, it was too late. The patient passed away shortly after. "It was heartbreaking," she says. But it was also motivating: The Welms' team doubled down on efforts to refine their methods and turn their research into a clinical tool.

Last month, writing in *Nature Cancer*, the team reported the next step. After creating a "bank" of xenografts and organoids from real patient tumors, they validated, for the first time, that these accurately capture how such diverse and dangerous cancers respond to drugs in humans. And in another first, the team returned results in time to recommend a treatment that was used to attack a living patient's breast cancer.

This is a big deal, particularly for the people battling the kinds of cancer this lab studies—the most lethal forms, which tend to recur and metastasize. "Having cancer in the breast doesn't kill anyone," Welm says. "It's because it spreads to the brain and the lungs and the liver and the bones." Although these cancers remain incurable, there are drugs that can fight them, for example by stopping cancer cells from replicating, thereby slowing tumor growth. But it's impractical—and *toxic*—to blow through all of them. (Stacking treatments can also breed drug resistance.)

One option is to sequence the genome of the cancer tissue to find which gene mutations are causing the problem. But that doesn't guarantee that there's a drug that targets cells with that mutation. A 2017 study reported that tumor genetics revealed a recommended treatment in fewer than 10 percent of 769 patients. In a 2018 clinical trial for people with metastatic breast cancer, 46 percent of participants had tumors with mutations that *are* targeted by a drug—but none saw any benefit from being matched with drugs on that basis.

The Welms' approach, called functional precision medicine, posits that you can find answers by growing organoids and xenografts as tools for trial-and-error drug testing. Both are like "avatars," says Elgene Lim, a medical oncologist with the Garvan Institute of Medical Research in Sydney, Australia. "Having the confidence that your avatar is truly an *accurate* avatar could potentially cut down the billions of dollars spent on drug development barking up the wrong tree only because your model is wrong."

The Welms' team isn't the only group betting on this idea. The London startup Vivan Therapeutics is trying a similar idea by screening drugs on genetically modified fruit flies. Companies like SEngine, Certis, and Champions Oncology have offered organoids or xenografts for cancer. And other labs have created collections of breast cancer tissue, and monitored drug response over the span of a week. The Welms' team wanted to zero in on the most lethal versions of the disease—and to study the avatars for months.

They also took the dual approach of using xenografts *and* organoids because they provide different glimpses into what's happening in the body. Organoid tests can—quickly and in parallel—find out which drugs disarm the cancer. The mouse tests can predict metastasis and whether a drug slows recurrence. Xenografts offer more comprehensive information, but organoids are easier to scale, faster, and more humane.

Since 2007, the Welms have partnered with hospital physicians at the Huntsman Cancer Institute and have built a bank of cells, taken from 40 patients. Then they grew organoids and created xenografts. They stowed the prepared tissue away in a lab freezer set to minus-320 degrees Fahrenheit. (They also stowed the biological details of each online for any researcher to study.)

Next, to prove that their models actually represented a patient's cancer, they compared the organoids and the xenografts to each other and to the real tumor: Were the same genes active? Did they grow as quickly? Did they respond the same way to drugs? Yes, yes, and yes. The team felt confident that they had built high-fidelity avatars. "Now," asks Welm, "can we actually use it to help?"

Their frozen bank contained tissue from a 43-year-old who had been diagnosed in 2018 and started a course of surgery, chemo, and radiation. But her cancer came back a year later, and in her liver, too. A genomic test of the cancer came up empty: There weren't any drugs built to fight tumors with these genetic mutations. So, in 2019, the team began testing different FDA-approved compounds against organoids and xenografts grown from the woman's tissue. One called eribulin stood out. It killed the cancerous organoids. The mice went into remission and survived long enough to be put down for old age.

Welm brought the team's result to the patient's physician, who started her on eribulin. After the 2018 attempt to advise treatment didn't pan out, Welm was nervous. "I just remember the physician coming by. And they showed us the scans" of areas where the cancer had previously spread, she says. "Before, there were all these liver [metastases], and her abdomen was filled with fluid. And then—there's nothing. I remember looking at the scans with my mouth open, like: *Really?*"

The patient went into complete remission for nearly five months. But about eight months after she started eribulin treatment, the cancer returned and she passed away.

This is often true for the extremely aggressive cancers Welm studies. But she is encouraged by two key oncological metrics from this patient's treatment: "progression-free survival" (how long a drug keeps cancer from spreading) and "time to next systemic therapy" (how long until another drug is needed). Both numbers usually go down with each subsequent round of treatment. In this case, they went up. The patient's previous chemotherapy had stopped the cancer from growing for 41 days. The eribulin gave the patient 138 days before the cancer returned, and 197 days before she needed a new kind of treatment.

It's important to note that this is a proof-of-concept study, and it represents only one person. Still, says Lim, "it's certainly brought us one step closer to making these avatars more potentially useful to the clinical world."

Specifically, it shows that organoids are a reliable alternative to testing on mouse xenografts, which can be slow and expensive. That process can take up to a year, and it doesn't always work. "Patients who have late-stage disease don't have that time," Lim says. Organoids are faster to scale up, since they don't require animals. Welm is shooting to run these tests in about 12 weeks, start to finish. With organoids, says Lim, "the sky's your limit. You can test as many drugs as you want."

Still, there are other caveats. Whenever scientists study cancer *outside* the human, an immune system is missing. Welm uses immune-compromised mice, and organoids grow without immune challenge. For the time being, that makes these models incompatible with testing immunotherapies, or drugs that rally the natural immune system to combat cancer, Lim and Welm agree.

But that limitation is fading too, says Tony Letai, a professor at Harvard Medical School and the Dana Farber Cancer Institute. Researchers are learning to culture organoids in blood, or in tandem with immune cells. "The writing's on the wall that it ultimately will be possible," says Letai, who is also president of the [Society for Functional Precision Medicine](#). Just 20 years ago, growing real tumors in the lab was a crapshoot—they didn't reliably emulate the patient's. Today, not only are they accurate matches, but scientists can keep cultures alive for months, they have dozens of more potent drugs to screen, and they can analyze the biology of individual cells with mind-boggling accuracy. "This type of approach is, I think, the future of finding cancer patients the right drugs," Letai says.

The University of Utah team has begun enrolling patients in a related clinical trial, in which they will match people to drugs based on the organoid versions of their tumors. The trial includes a survey for physicians as well—Welm hopes to find out whether doctors would actually trust the tool. “It looks very promising, but we don't know till we know,” she says.

Welm remembers that even in 2019, when her team was awed by the medical scans showing the patient's improvement after receiving eribulin, they knew the likely outcome. “We have a *guarded* enthusiasm, just because we know that we need better therapies,” she says. “We have a lot of questions that we still need to answer.”

## More Great WIRED Stories

-  The latest on tech, science, and more: [Get our newsletters!](#)
- [Ada Palmer](#) and the weird hand of progress
- [YouTube's captions](#) insert explicit language in kids' videos
- [VR is here](#) to stay. It's time to make it accessible
- The future of [mental health](#) goes beyond the manual
- What it would take to bring [the ISS](#) down in one piece
-  Explore AI like never before with [our new database](#)
-  Upgrade your work game with our Gear team's [favorite laptops](#), [keyboards](#), [typing alternatives](#), and [noise-canceling headphones](#)

---

[Max G. Levy](#) is freelance science journalist based in Los Angeles, California writing about tiny neurons, vast cosmos, and all the science in between. He received a PhD in Chemical & Biological Engineering from the University of Colorado, Boulder.

CONTRIBUTOR 

---

TOPICS MEDICINE HEALTH CANCER GENETICS BIOTECH DISEASES PRECISION MEDICINE DRUG DEVELOPMENT

---

---

MORE FROM WIRED

---