

STAT

A cancer researcher races to find a cure — for his own incurable cancer



Courtesy Tom Marsilje Tom Marsilje has tried to give other colon cancer patients the same advantages he has, as he searches for a cure.

By [Rebecca Robbins](#) @rebeccadrobbins

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SAN DIEGO — With two decades of cancer research under his belt, Tom Marsilje is no stranger to project deadlines. But he's never faced one quite like this before.

He's racing against the clock in an improbable quest to cure his own incurable colon cancer before it takes him away from his wife and their two little girls.

Marsilje, 44, knows that if he does nothing, the tumors he's keeping in check with chemotherapy will eventually burst forth into growth mode. It's a question of when, not if.

So he's doing all he can to outwit his cancer before it's too late. He's enlisted help from a small team of scientists who think they might have identified a new approach to revving up his immune system. If it works, it could open new paths for other patients with hard-to-treat cancers.

It hasn't been easy. Two of the most commonly used therapies for his type of cancer have stopped working. An unrelated health condition shut him out of tantalizing clinical trials. His pursuit of his own genetic information recently left him with a (very minor) collapsed lung.

And it's still not certain that his team of advisers will be able to turn their research into an experimental therapy for Marsilje — or that it will work.

Researchers and doctors who spend their days fighting cancer point to Marsilje's story as a model for other patients. Everyone, they say, should learn to take [command of their own care](#)¹ and insist that they get every possible shot to stay alive.

But if his story is an inspiration, it's also a cautionary tale.

Marsilje (pronounced mar-SIL-ya) is a medicinal chemist who knows how to decipher his own genetic data, how to read the scientific literature, and who to ask for help. He even lives in the right place: San Diego, where medical research institutes and biotech companies are about as common as ocean views and taco stands.

"I'm the most empowered patient possible, probably," Marsilje said.

And yet even he has faced huge challenges, familiar to many patients: It's hard to get into the most promising clinical trials, and there aren't many of them for certain cancers. Just getting a tumor sample can be a quest of its own. And while new discoveries raise excitement, it's a very long road between the "aha!" moment in the lab and an actual treatment.

A few times, it seemed as though Marsilje had hit the end of the road — only to have his hope revived thanks to chance meetings with prominent scientists. That's part of his story, too: It's clear just how important dumb luck can be when you're fighting steep odds.

A soft-spoken and easygoing man who can spend hours parsing data, Marsilje now has a clear glimmer of hope: Plans are in motion for a clinical trial at the University of California, San Diego, cancer center where he's already receiving treatment. He and his team are hoping he'll be able to join.

If he's accepted, he would receive a [personalized vaccine](#)², programmed to stimulate his immune cells to attack his tumors' most vulnerable mutations. If it worked, it could turn his cancer into a manageable chronic disease or, in a best-case scenario, even melt it away.

The approach is called a neoantigen vaccine because it prompts the immune system to home in on red flags, known as neoantigens, planted on the surface of malignant cells. It's part of the hot new wave of [immunotherapies](#)³, which have generated considerable excitement — even though they've helped just a fraction of cancer patients.

Experts see real promise in personalized neoantigen vaccines, but caution that it could take years to see benefits. And that the promise could still fizzle upon further testing. There are plenty of reasons, after all, why there aren't any such therapies on the market yet.

Marsilje is clear-eyed about the long odds he faces. But he's also unabashedly optimistic.

"I can pin my hopes on a 10 or 20 percent chance," he said, "because that's certainly better than zero."



Courtesy Tom Marsilje Tom Marsilje with his wife, Veronica, and daughters, Eleni and Amelie, in San Diego in 2012.

Waiting to get cancer

Marsilje had expected to get cancer at some point in his lifetime. He just didn't expect it would be this soon.

Growing up, he was already "abnormally serious" about pursuing cancer drug discovery because he had seen many family members afflicted. His photographic memory and fascination with science helped propel him through his scientific training.

Then, when Marsilje was 27 and finishing up his PhD in medicinal chemistry at the State University of New York at Buffalo, his mother was diagnosed with advanced pancreatic cancer at age 54. He and his sister cared for her in the last months of her life. He emerged ever more determined to use science to fight cancer.

Marsilje built a busy and fulfilling life in San Diego, where he's worked for Novartis's corporate research arm since 2003. He married a woman who's as technically minded as he is — an electrical engineer. By

the end of his 30s, they had a toddler and a baby and spent as much time as they could in the redwood forests in Northern California.

Because of his family history of cancer, Marsilje had planned to start getting colonoscopies after he turned 40.

Then, at age 39, he started having some gastrointestinal problems. For a while he'd thought he might be gluten intolerant. He wondered if he had a parasite. Finally, he scheduled a colonoscopy⁴.

The morning of his appointment, Marsilje scored a huge professional victory when an experimental cancer drug that he had first synthesized had its breakout moment at a scientific meeting. The results from the first tests in humans were promising: The drug (now sold as Zykadia) seemed to work.

It looked like he had finally helped strike a blow against cancer.

Still “walking on air” six hours later, Marsilje went in for his test. He woke up to hear the doctor tell his wife: Your husband has colon cancer. We need to schedule surgery immediately.

Surgery and chemotherapy gave him months of remission and the hope that he'd dodged a bullet. He started running regularly.

But more than a year after he was first diagnosed, devastating news: The cancer had spread to his lungs and distant lymph nodes. It would be too dangerous to operate. And surgery couldn't catch all the cancer cells, anyway.

His disease was incurable.



Ariana Drehsl for STAT
Tom Marsilje attends a meeting with a team of physicians and scientists helping him seek a cure for his cancer.

A diagnosis lights a fire

The day Marsilje got the first hints that his cancer had spread, he put on his running shoes and managed, for the first time, to run a half-marathon without stopping to rest.

Then he really got to work.

As Marsilje's friend and former colleague Eric Murphy put it: "You take that hardcore researcher and you light a fire under him, and that's what's happened here."

He went vegan. He started running six miles every other day. He read everything relevant he could find in the scientific literature. He peppered his oncologist with questions. He emailed the many cancer researchers he'd met over the years, asking what they'd been hearing about colon cancer.

And he started researching clinical trials, making Excel flowcharts of which he wanted to try first, and where he'd go next if each subsequent therapy failed.

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Tom Marsilje

He spent hours on the task, working on his laptop at home or while munching on a salad at his desk during extended lunch breaks at work, where his bosses encouraged him to spend time focusing on his own health.

He started by scouring clinicaltrials.gov, the [database of clinical trials](#)⁵ that's notoriously hard to navigate, "even for a scientist," he said. Marsilje came up with an initial list of several dozen trials, and then whittled it down, focusing on the immunotherapies that seemed most aggressive.

"When the game clock's ticking, and you're behind, you take the big shots," he said.

Soon he and his oncologist found what seemed like the perfect immunotherapy trial: It was at home in San Diego, and the experimental treatment would be used on top of, rather than instead of, therapy already on the market.

But at a meeting for him to sign the paperwork, it came up in an offhanded way that Marsilje had a small melanoma, unrelated to his colon cancer, removed a few weeks earlier. The paperwork was taken out of his hands; he wouldn't be allowed to join this trial or others with the same restriction. (Patients with secondary cancers are often excluded from trials for three to five years, out of fear that their secondary cancer might confound the trial results.)

Marsilje was out of options.

Fighting past 'chemo brain'

He wasn't out of time, though.

He's joined the many patients with incurable cancer who undergo chemotherapy or take targeted drugs to prolong life. Many with his type of cancer are living for multiple years on these regimens, and a small fraction can live longer than five years.

That strategy is still working for Marsilje. He did six months on one targeted therapy, and once his tumors started growing, switched over to a combination of chemotherapy and a different targeted therapy that has been keeping his cancer under control for nearly a year now.

But chemo has been hard: Family trips to the redwoods aren't practical anymore. He can't normally run long distances. He gets easily fatigued. And he suffers what's known as "chemo brain." Having no memory of an email he sent or forgetting where to turn on his daily commute is a stark adjustment for a man who normally can recall information in a flash. But chemotherapy never seems to interfere with his ability to talk about or remember scientific concepts.

Marsilje has never stopped working full-time for Novartis, though he no longer works in the lab. He's shifted to a consultant role, for oncology projects.

He's also become a vocal leader in the colon cancer patient community. He's well aware of the advantages that he has in navigating treatment options, and tries to pay it forward. As an advocate, he's given speeches and pressed lawmakers to increase research funding and make it easier to get

colonoscopies. As a blogger, he translates clinical trial results into plain English and advises fellow patients about how to advocate for themselves.

His tone is upbeat — underscored by the title of his [blog](#)⁶, “Adventures in Living Terminally Optimistic” — where he includes photos of himself jogging or jumping into his swimming pool, with the hashtag “#CannonballLife.”

For Marsilje, there’s something surreal about the tumors inside him lurking in wait. Since getting his initial colon surgery more than four years ago, he has had no disease symptoms. His illness is just spots on a CT scan.

“I joke that I’m a perfectly healthy guy,” he says, “except for one small problem.”

A lucky break

It turned out to be a series of lucky breaks that put Marsilje’s quest to cure his cancer back on track.

A few weeks after being shut out of the San Diego trial, Marsilje was in the audience at a panel discussion about cancer when his ears perked up: A prominent cancer biologist was talking about helping a patient get her [tumors sequenced](#)⁷ so doctors could understand her cancer’s genetic quirks — and potential weaknesses.

On his drive home that night, Marsilje couldn’t stop thinking about the talk. He cold-emailed the biologist, Geoffrey Wahl of the Salk Institute for Biological Studies, and asked for help.

To his surprise, Wahl answered right away. They met for lunch the next day, at a cafe overlooking the Pacific Ocean. Wahl promised to try to find a way to help Marsilje get his cancer sequenced, too.

Recalling that promise today, Wahl uses the Yiddish word *bashert*: It was meant to be.

“When the game clock’s ticking, and you’re behind, you take the big shots.”

Tom Marsilje

That same night, Wahl’s wife needed him to fill in for her at a dinner party attended by leading scientists and philanthropists preparing for a charity bike ride. Wahl happened to be seated next to [Craig Venter](#)⁸, the pioneering geneticist and entrepreneur who now runs a San Diego biotech that’s [building](#)⁸ the world’s largest operation devoted to sequencing the human genome.

Wahl barely knew Venter, but he looked him straight in the eye and made the appeal: What good is a charity bike ride if you can’t help someone like Marsilje?

“I just said, ‘Absolutely, get him over and get the tumor sample to us,’” Venter recalled responding. His company paid for Marsilje to get both his cancer and his blood sequenced. In exchange, Venter’s company, Human Longevity, got to keep Marsilje’s genetic data for further research.

Now Marsilje had his genetic information, but he still didn't have a way to do anything with it — until he met two researchers affiliated part-time with Human Longevity: immunologist Stephen Schoenberger and UCSD oncologist Dr. Ezra Cohen.

In their other jobs, they were working on neoantigens, focusing on cancer types like his, which have hardly benefited from the new wave of immunotherapies. Their project might be able to help him, they told Marsilje. At the very least, it would be scientifically interesting.

Would he want to join?



Ariana Drehsler for STAT
Stephen Schoenberger sits in his office at the La Jolla Institute for Allergy and Immunology, a nonprofit research organization in San Diego.

A shot at the jackpot

So far, immunotherapy's power seems to⁹ have a lot to do with the number¹⁰ of meaningful genetic errors in the cancer it's trying to take on. The more mutations a tumor has, the more red flags will go up in the form of neoantigens that the patient's immune cells can recognize and attack.

"The feeling in the field now is that it's a numbers game," Schoenberger said. "Each mutation is thought to be a ticket to the lottery. More tickets, more chances of a win."

Former President Jimmy Carter¹¹, whose cancer famously went into remission¹² with the immunotherapy drug Keytruda¹³ even after it had spread to the brain, had lots of lottery tickets: He had

melanoma, the type of cancer with the most mutations.

The type of colon cancer that Marsilje has, on the other hand, has relatively few mutations — suggesting his immune system probably wouldn't have much of a shot.

"People have been put off by the idea of having too few tickets to the lottery," Schoenberger said. He thinks they shouldn't be.

Immunotherapy researchers working on cancers with many mutations, like melanomas, typically use computer algorithms to predict which of those mutations might make juicy targets for the immune system. Schoenberger and his team worried that such an approach wouldn't work for certain cancers with few mutations, like Marsilje's type of colon cancer. But they found a workaround: Because there were so few mutations, they could test them all individually the old-fashioned way, in the wet lab.

So that's what they did. In Schoenberger's lab at the La Jolla Institute for Allergy and Immunology, they analyzed Marsilje's genetic data to come up with a short list — 32 tumor mutations — that they believed to be the most promising targets. They synthesized a bunch of little protein fragments, called peptides, so that each one included a mutation unique to Marsilje's data. Then they exposed those peptides to Marsilje's blood, and measured what happened.

The immune cells in his blood lashed out at about a dozen of the peptides. That's more than the computer algorithms would have predicted. It was a signal that cancer cells may not need a huge number of mutations for the immune system to recognize them as dangerous — meaning that Marsilje's tumors might be vulnerable to attack, too, if only his immune system could just get a boost.

That's where a personalized neoantigen vaccine would come in.

Marsilje's oncologist, Dr. Tony Reid of UCSD, said the science is not at a level where it's possible to predict the chances of such a therapy working for a given patient. But he and the rest of the team think the signal is strong enough to warrant seriously considering the approach for Marsilje.

"We feel confident that what we're seeing is real and of potential clinical value for Tom," Schoenberger said.

Hoping for a chance to be a guinea pig

The next big step: Getting Marsilje enrolled in a clinical trial where the lab work could be turned into a therapy.

The wheels are in motion for Human Longevity to sponsor a clinical trial where each enrolled patient would get a personalized vaccine. If Marsilje can't get into that trial, or if it doesn't come to fruition fast enough, the team will look elsewhere. Marsilje still checks the federal trial registry every Monday to update his spreadsheets with backup options.

Marsilje wants to try something as soon as possible. At a recent meeting with his team, someone suggested waiting until his tumors have grown enough so that researchers could easily get another

sample as another way of confirming their work.

Marsilje interjected right away.

“My concern is waiting too long,” he said. “I don’t know if [chemotherapy] will work another three years or another three months. I don’t know what it’s going to be.”

Marsilje is adamant that his quest to fight his cancer not get in the way of the time he spends with his family. (He concedes only that he doesn’t have the time to watch sitcoms anymore.)

It helps that he barely sleeps: He’s on his laptop working on his own project or trying to help other patients every night for a few hours after putting his daughters to bed, and then rises before the sun for a few more hours of work before they wake up.

His biggest driving force to live: wanting to be there for his daughters when they need him. When he first got his incurable cancer diagnosis, he entertained the idea of jetting off to see the world with his family while he still could, but opted against it. He’s less concerned about the big milestones than the small moments of everyday life.

He recently taught his 5-year-old daughter, Eleni, to play soccer.

And with his 9-year-old daughter, Amelie, he plays lots of Minecraft. It’s hard for her to see him fatigued from chemotherapy, which he explains to her as his “sleeping medication.”

To Amelie, he sums up his quest to design his own cure this way: “We’re trying to find a medicine that I can take where I won’t need to take the sleeping medicine anymore.”

Links

1. <https://www.statnews.com/2016/03/24/appendix-cancer-treatment/>
2. <https://www.statnews.com/2016/01/12/personalized-cancer-vaccines/>
3. <https://www.statnews.com/2016/07/15/cancer-patients-immunotherapy-trials/>
4. <https://www.statnews.com/2016/03/14/colonoscopy-colon-cancer-screening/>
5. <https://www.statnews.com/2015/12/13/clinical-trials-investigation/>
6. <https://adventuresinlivingterminallyoptimistic.com/>
7. <https://www.statnews.com/2016/01/26/gene-sequencing-medicare-tumors/>
8. <https://www.statnews.com/2015/11/05/geneticist-craig-venter-helped-sequence-the-human-genome-now-he-wants-yours/>
9. <http://www.bloomberg.com/news/articles/2016-07-07/more-cancer-mutations-may-be-good-for-immunotherapy-patients>
10. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3919509/figure/F1/>
11. <https://www.statnews.com/2016/08/22/jimmy-carter-cancer-fight/>
12. <https://www.statnews.com/2015/12/06/jimmy-carter-brain-cancer/>
13. <https://www.statnews.com/2015/12/18/jimmy-carter-cancer-drug-keytruda/>

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