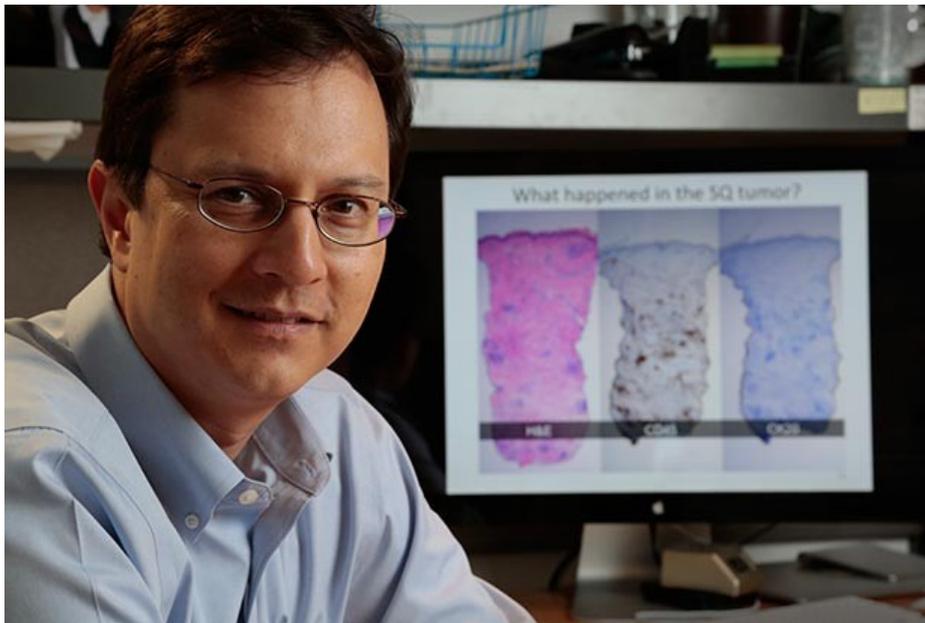


HUTCH NEWS

A new blood test detects recurrence of rare skin cancer

\$200 assay can accurately signal return of Merkel cell carcinoma — in some cases catching tumors earlier than expensive imaging

Dec. 12, 2016 | By Rachel Tompa / Fred Hutch News Service



Dr. Paul Nghiem, an expert in the rare skin cancer Merkel cell carcinoma, has led a study describing a new blood test that can pinpoint the cancer's return.

Photo by Robert Hood / Fred Hutch News Service

project at first, she said. But within just a few years of that conversation, the discoveries she, Nghiem and their colleagues at Fred Hutch and UW made would take another turn, and lead to the development of an inexpensive blood test for Merkel cell carcinoma recurrence.

In a **study published last week** in the journal *Cancer*, Nghiem, Galloway and their colleagues report their findings on 219 Merkel cell carcinoma patients whose cancer was followed over time using the blood test. For about half of those patients — those who produce a certain type of immune protein — the test is able to accurately predict if their cancer is coming back, the researchers found.

Galloway said she initially just wanted to know whether people with this cancer made any of these immune proteins, known as antibodies, to the cancer-causing virus.

“We didn’t know what the answer was,” she said. “A lot of research is like that — it turns out to be clinically useful, but in the beginning you don’t know whether it will be or not.”

The test signals the presence of antibodies specific to one viral protein. Among those patients who produce those antibodies, it can quickly and inexpensively signal to clinicians whether a patient’s Merkel cell carcinoma is recurring in

It began eight years ago, when a newly published scientific paper caught Dr. Denise Galloway’s eye.

The paper described the discovery of a new virus, Merkel cell polyomavirus, that drives the majority of cases of **Merkel cell carcinoma**, a rare but aggressive skin cancer.

Within days of that publication, the Fred Hutchinson Cancer Research Center virologist was on the phone to her colleague, University of Washington and Fred Hutch skin cancer researcher **Dr. Paul Nghiem**, a **specialist** in Merkel cell carcinoma.

Galloway wanted to know how the human immune system reacts to that virus. It was a purely curiosity-driven

the body — in some cases even earlier than traditional imaging tests such as CT scans. That specific antibody is found in about half of patients with the cancer, but curiously doesn't occur in healthy people, even though nearly all of us carry the polyomavirus on our skin.



Fred Hutch virologist Dr. Denise Galloway's curiosity about the human immune response to a cancer-causing virus ultimately led to the development of the clinical test.

Photo by Robert Hood / Fred Hutch News Service

For the half of Merkel cell carcinoma patients who produce these antibodies, the rise and fall of that protein in their blood can be a powerful predictive tool, the researchers found. In their study, they showed that 98 percent of patients with decreasing levels of antibody in their blood over time had no recurrence of their cancer, while 88 percent of those with rising amounts of antibody did have their cancer return soon after the test.

The blood test, which is performed in a clinical laboratory at UW and costs about \$200, is already in routine use for all Merkel cell carcinoma patients at Seattle Cancer Care Alliance, where Nghiem treats patients with the carcinoma and other skin cancers. Physicians from other institutes around the U.S. have begun ordering it for their patients as well, Nghiem said, and he hopes the team's recent publication will spur more doctors and patients to adopt the test.

That's important because Merkel cell carcinoma, though rare, is a very aggressive cancer. Only about 2,000 new cases of the cancer are diagnosed every year in the U.S. — but more than 40 percent of those with the cancer will have a recurrence after their initial treatment, and **close to a third** will die of their disease. The cancer is about three times deadlier than the more well-known rare skin cancer melanoma.

But there's hope, especially if the recurrence is caught early. Nghiem and his colleagues published a **study** earlier this year showing that the immunotherapy drug pembrolizumab, or Keytruda, shows promise in keeping metastatic Merkel cell carcinoma in check — about half of the patients treated on their trial had lasting remissions. Historically, only 10 percent of patients with metastatic Merkel cell carcinoma treated with chemotherapy had lengthy remissions.

Evidence from other cancers indicates that the earlier a recurrence is caught, the better immunotherapies such as pembrolizumab will work.

"We really think it's better to treat a grape-sized tumor instead of a grapefruit-sized tumor for lots of reasons, including that the larger cancer gets, the more tricks it has figured out to evade bodily controls, including the immune system," Nghiem said. "We want to find it early and yet we don't want to expose people to too many unnecessary scans."

If the test signals cancer's recurrence, it's important for clinicians to follow up with imaging tests to pinpoint and assess the new tumor and decide how to proceed with treatment, Nghiem said. And the approximately 50 percent of patients who don't produce the antibody still need to be followed with traditional imaging. In their study, the researchers found that those who don't produce the antibodies are more likely to have their cancer recur, meaning they should be followed with even more careful screening tests. But for those patients whose tests show falling antibody levels, they may be spared the exposure to radiation and expense of traditional CT scans.

Detecting hidden tumors

In some cases in their study and in Nghiem's practice at SCCA, the newly-developed blood test signaled a recurrence that imaging tests had yet to capture, meaning that it could herald cancer's return earlier than conventional scans.

Ludy Escobedo was one of those cases. The 61-year-old from San Jose, California, was first diagnosed with Merkel cell carcinoma just over a year ago. She thought the small, red lump on her right elbow was an ingrown hair.

The bump hurt occasionally, but "I didn't think anything of it," said Escobedo — until about two months after the lump had first made its appearance, when her son pointed out that her arm was bleeding.

“I look and it’s running down my arm and hand and in my clothes, and it was from that little thing,” she said.

A visit to the doctor, a referral to a dermatologist and a biopsy soon followed, and then the diagnosis — all of which felt like a whirlwind to Escobedo.

“It is so hard to go through this so fast,” she said. “You don’t have time to breathe. You don’t even know what’s hitting you.”

Her diagnosis was a surprise to her not only because Merkel cell carcinoma is so rare — rare enough that there were no specialists in the disease near her — but because when it does occur, it’s more likely to occur in Caucasian men. Escobedo is Hispanic.

She and her son visited an oncologist who suggested that, if at all possible, Escobedo try to make it up to Seattle to see Nghiem. So she did.

She had the tumor removed surgically and radiation treatment last spring, and, as is now the norm at SCCA for Merkel cell carcinoma patients, began receiving regular blood draws every few months to follow her antibody levels. By the summer, her antibody levels started climbing. Nghiem recommended she have CT scans of her torso to track down the tumors he was sure had come back somewhere in her body.

The scans didn’t find anything, so Nghiem asked Escobedo if she was having any unusual pain anywhere. Her elbow where her original tumor was removed felt a bit weird, she said. The doctor couldn’t feel anything there, but Nghiem decided to order an elbow MRI, just in case.

And they found a new tumor there, just a few inches from the original.

They also found evidence that the cancer was just beginning to spread to the lymph nodes in the armpit on the same side. It was a clear example of the blood test catching what could be considered “subclinical disease,” Nghiem said, a recurrence that traditional screening methods couldn’t find.

It’s too soon to say what Escobedo’s next treatment steps will be, but in some cases, the blood test is catching recurrences early enough that they can be treated locally with surgery and radiation, said Dr. Kelly Paulson, an oncology fellow at Fred Hutch and researcher in Nghiem’s lab who helped develop the blood test.

For some of these patients, “the cancer can be stopped before it spreads systemically, before it’s metastasized,” said Paulson, who was first author on the study published last week.

Escobedo said she’s glad she had access to the blood test. She’s sure her cancer’s return was caught far earlier than it would have been otherwise.

“It was hiding all along inside of my arm,” she said. “Because of [the test] I really think we caught it in good time.”

Rachel Tompa, a staff writer at Fred Hutchinson Cancer Research Center, joined Fred Hutch in 2009 as an editor working with infectious disease researchers and has since written about topics ranging from nanotechnology to global health. She has a Ph.D. in molecular biology from the University of California, San Francisco and a certificate in science writing from the University of California, Santa Cruz. Reach her by email at rtompa@fredhutch.org or follow her on Twitter at [@Rachel_Tompa](https://twitter.com/Rachel_Tompa).

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Ludy Escobedo of San Jose, California, was recently treated in Seattle for Merkel cell carcinoma.

Photo courtesy of Ludy Escobedo

TAGS: cancer recurrence, Clinical Research, Denise Galloway, Human Biology, immunotherapy, merkel cell carcinoma, Paul Nghiem, pembrolizumab, virus

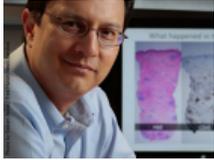
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