A team of researchers has taken a major step toward one of the hottest goals in cancer research: a blood test that can detect tumors early. Their new test, which examines cancer-related DNA and proteins in the blood, yielded a positive result about 70% of the time across eight common cancer types in more than 1000 patients whose tumors had not yet spread—among the best performances yet for a universal cancer blood test. It also narrowed down the form of cancer, which previously published pancancer blood tests have not.

The work, reported online today in *Science*, could one day lead to a tool for routinely screening people and catching tumors before they cause symptoms, when chances are best for a cure. Other groups, among them startups with more than $1 billion in funding, are already pursuing that prospect. The new result could put the team, led by Nickolas Papadopoulos, Bert Vogelstein, and others at Johns Hopkins University in Baltimore, Maryland, among the front-runners.

“The clever part is to couple DNA with proteins,” says cancer researcher Alberto Bardelli of the University of Turin in Italy, who was not involved in the work. The researchers have already begun a large study to see whether the test can pick up tumors in seemingly cancer-free women.

Genetic mutations drive the growth of cancer cells, and dying cells shed some of this mutated DNA into the blood. The Johns Hopkins group and others have shown that so-called liquid biopsies of blood-borne tumor DNA can reveal, for example, whether a patient’s cancer should respond to a specific drug. But detecting the scant DNA released by early stage tumors is still challenging. Companies such as the $1 billion Grail, launched in 2016 by sequencing giant Illumina, are using a big data approach, sequencing hundreds of genes in thousands of patients’ blood in search of a definitive set of DNA markers.

The Johns Hopkins researchers and collaborators found that gains in the detection rate tailed off when they added more genes to their test. They decided to sequence parts of just 16 genes often mutated in different types of cancer. They then added eight known protein biomarkers characteristic of specific kinds of cancer. This bumped up sensitivity and allowed the team to home in on the tissue type of the tumor.

In blood samples from 1005 patients with eight types of tumors that had evidently not yet metastasized, the test detected between 33% and 98% of cases, depending on the tumor type (see graph, below). The sensitivity was 69% or higher for ovarian, liver, stomach, pancreatic, and esophageal cancers—all types that are difficult to detect early.

The test rarely found cancer that wasn’t there. Only seven of 812, or less than 1%, of healthy controls tested positive. And the test, called CancerSEEK, narrowed the origin of the cancer to two possible sites in about 80% of patients. The team, which is applying for patents on CancerSEEK, estimates the cost at less than $500 per sample. “That’s a very attractive number,” says molecular pathologist Anirban Maitra of the MD Anderson Cancer Center in Houston, Texas, because it is in the range of other cancer screening tests such as colonoscopy.

Maitra and others point to caveats, however. One is that the cancer-related proteins used by the test reflect tissue damage and can also appear in people with inflammatory diseases such as arthritis. That means the 1% false positive rate will likely be higher in less healthy populations, notes proteomics researcher Lance Liotta of George Mason University in Manassas, Virginia. What’s more, the 1005 patients already had cancer symptoms; CancerSEEK probably won’t work as well in asymptomatic patients whose smaller tumors may shed less DNA. In fact, the test picked up only 43% of very early, stage 1 cancers. “We’re still not there yet,” Bardelli says.

The Johns Hopkins team thinks CancerSEEK is ready for testing as a screening tool. “A test does not have to be perfect to be useful,” Papadopoulos says. In collaboration with Johns Hopkins, the Geisinger Health System in Pennsylvania has already begun to use CancerSEEK on blood samples from female volunteers between ages 65 and 75 who have never had cancer. The planned $50 million, 5-year study of up to 50,000 women is being funded by a private philanthropic group, The Marcus Foundation.

For those who test positive twice, the next step will be imaging to find the tumor. But that will bring up questions raised by other screening tests. Will the test pick up small tumors that would never grow large enough to cause problems yet will be treated anyway, at unnecessary cost, risk, and anxiety to the patient? Papadopoulos thinks the problem is manageable because an expert team will assess each case. “The issue is not overdiagnosis, but overtreatment,” he says.

Still, others working on liquid biopsies say that it will take time to figure out whether widespread screening of healthy people with a universal blood test can reduce cancer deaths without doing harm. “If people expect to suddenly catch all cancers, they’ll be disappointed,” says cancer researcher Nitzan Rosenfeld of the University of Cambridge in the United Kingdom. “This is exciting progress,” he says. “But evaluating it in the real world will be a long process.”

**A screening scorecard**

A new cancer blood test worked better for some types than others, and caught only 43% of stage 1 cancers. (Error bars represent 95% confidence intervals.)

![A screening scorecard](https://example.com/scorecard.png)
'Liquid biopsy' for cancer promises early detection

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