



All in the blood

Liquid biopsies are advancing the detection of early and aggressive cancers.

YOU COULD CALL THE BIRTH OF A LIQUID BIOPSY—a new blood test screening for about 50 forms of cancer—a potential lifesaver. You also could call it happenstance.



MICHELE MEYER

In 2015, biotech researchers at San Diego's Illumina, Inc., were working on a blood test to find fetal abnormalities early in pregnancy. But their DNA sequencing efforts also revealed an oddity: Blood samples from about 10 of 150,000 seemingly healthy pregnant women showed methylation patterns.

Those occur when abnormal cells and proteins shed fragments of DNA into the blood. Not only was this an early sign of cancer, but it was also an indication of where in the body it was occurring. Could these women have cancer—despite showing no symptoms?

Indeed, all 10 new mothers were diagnosed with cancer soon after. None of the other women were.

Finding a signal

“There was something about the peculiarity of that signal which was absolutely unique to the type of changes that characterize cancer,” says Josh Ofman, M.D., president at Grail, which later spun off from Illumina in Menlo Park, California. He recalls the details on the firm's podcast, *The Cancer Signal*.

The company is named for its mission, one of the

holy grails of research: to detect symptomless cancers throughout the body. Until now, screenings approved by the U.S. Food and Drug Administration only could detect colorectal, breast, cervical and lung cancer.

In June 2021, Grail launched its tumor tracker, Galleri. The multi-cancer early detection (MCED) isolates DNA fragments in the blood and sequences those fragments to identify tumor-specific markings.

Large-scale trials of hundreds of thousands of patients in the United States and the United Kingdom show promise, and the company expects to complete its FDA submission in early 2026. For now, the test only is available when prescribed by physicians and as an FDA-endorsed Investigational Device Exemption.

Revolutionary blood test

So far, Galleri can identify DNA shed by about 50 tumor types, each with its unique fingerprint in the blood.

“This is a tremendous opportunity to broaden the scope to include harder to detect, more aggressive and more likely to be fatal cancers,” says Betsy O'Donnell, M.D., co-director of Dana-Farber Cancer Institute's Centers for Early Detection and Interception.

The test also catches melanoma, leukemia, lymphoma and cancers of the bladder, liver, stomach, prostate, kidneys, bile ducts, adrenal glands and soft tissues of the head and neck.

Limitations

Galleri has room for improvement. At this point, the blood test's false positives top 57%, according to O'Donnell. Given how shattering a diagnosis of cancer can be, the FDA hasn't found those odds acceptable.

Megan Hall, Ph.D., Grail's vice president of medical affairs, points to a more promising statistic: When cancer is found, the test accurately pinpoints its location in the body about 90 percent of the time. Galleri only detects cancer DNA at the time of the test.

Another challenge, O'Donnell says, is that the number of DNA fragments shed by abnormal cells and proteins varies depending on how advanced a tumor is and where it's located.

"At Dana-Farber, MCEDs are something we're very interested in and continue to learn about," O'Donnell says. "But we cannot give guidance on how they should be administered because they're not FDA-approved. We await the agency's recommendations."

If the MCED is FDA-endorsed, it will complement current screenings, not replace them, she says.

Planning for the future

Without the FDA's blessing, a Galleri test costs about \$950 out-of-pocket. But Hall and O'Donnell both predict the agency will sign off on the blood test within two years.

While a number of studies and clinical trials are complete, a three-year trial that focuses on a diverse nationwide population is ramping up.

About 100 biotech firms also are working on liquid biopsies with the aim of finding two or more tumor types, O'Donnell says.

"The hope, the dream, is that these tests will be demonstrated to pick up more cancers consistently," she says. "They have great potential to broaden the range of cancers that are found in time to save more lives." •

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