Non-invasive blood test can detect cancer four years before conventional diagnosis methods

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An international team of researchers has developed a non-invasive blood test that can detect whether an individual has one of five common types of cancers, four years before the condition can be diagnosed with current methods. The test detects stomach, esophageal, colorectal, lung and liver cancer.

Called PanSeer, the test detected cancer in 91% of samples from individuals who had been asymptomatic when the samples were collected and were only diagnosed with cancer one to four years later. In addition, the test accurately detected cancer in 88% of samples from 113 patients who were already diagnosed when the samples were collected. The test also recognized cancer-free samples 95% of the time. ß

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The study is unique in that researchers had access to blood samples from patients who were asymptomatic and had not yet been diagnosed. This allowed the team to develop a test that can find cancer markers much earlier than conventional diagnosis methods. The samples were collected as part of a 10-year longitudinal study launched in 2007 by Fudan University in China.

"The ultimate goal would be performing blood tests like this routinely during annual health checkups," said Kun Zhang, one of the paper's corresponding authors and professor and chair of the Department of Bioengineering at the University of California San Diego. "But the immediate focus is to test people at higher risk, based on family history, age or other known risk factors."

Early detection is important because the survival of cancer patients increases significantly when the disease is identified at early stages, as the tumor can be surgically removed or treated with appropriate drugs. However, only a limited number of early screening tests exist for a few cancer types.

Zhang and colleagues present their work in the July 21, 2020 issue of *Nature Communications*. The team includes researchers at Fudan University and at Singlera Genomics, a San Diego and Shanghai based startup that is working to commercialize the tests based on advances originally made in Zhang's bioengineering lab at the UC San Diego Jacobs School of Engineering.

The researchers emphasize that the PanSeer assay is unlikely to predict which patients will later go on to develop cancer. Instead, it is most likely identifying patients who already have cancerous growths, but remain asymptomatic for current detection methods. The team concluded that further large-scale longitudinal studies are needed to confirm the potential of the test for the early detection of cancer in pre-diagnosis individuals.

Taizhou Longitudinal Study

Blood samples in the *Nature Communications* study were collected as part of the Taizhou Longitudinal Study, which has collected plasma samples from over 120,000 individuals between 2007 and 2017. Each

individual gave blood samples over a 10-year period and underwent regular check-ins with physicians. In all, over 1.6 million specimens have been collected and archived to date.

Once a person was diagnosed with cancer, the researchers had access to blood samples taken one to four years before these patients even started to show symptoms.

The team was able to examine samples from both healthy and sick individuals from the same cohort. The authors performed an analysis on plasma samples obtained from 605 asymptomatic individuals, 191 of whom were later diagnosed with cancer. They also profile plasma samples from an additional 223 diagnosed cancer patients as well as 200 primary tumor and normal tissue samples.

DNA methylation based diagnosis method

Zhang and his lab have been developing for over a decade methods to detect cancer based on a biological process called DNA methylation analysis. The method screens for a particular DNA signature called CpG methylation, which is the addition of methyl groups to multiple adjacent CG sequences in a DNA molecule. Each tissue in the body can be identified by its unique signature of methylation haplotypes. They did an early-stage proof-of-concept study that was published in a 2017 paper in *Nature Genetics*.

Zhang cofounded Singlera Genomics, which licensed technology he developed at UC San Diego. In the past few years, Singlera Genomics has been working to improve and eventually commercialize early cancer detection tests, including the PanSeer test, which was used in the *Nature Communications* study. Zhang is now the company's scientific advisor.

Zhang, Singlera Genomics and additional collaborators have been

working to make a formal demonstration that cancer can be detected in the blood prior to conventional diagnosis. The July 2020 *Nature Communications* publication is the outcome of that effort.

More information: Chen, X., Gole, J., Gore, A. et al. Non-invasive early detection of cancer four years before conventional diagnosis using a blood test. *Nature Communications* (2020). DOI: 10.1038/s41467-020-17316-z

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