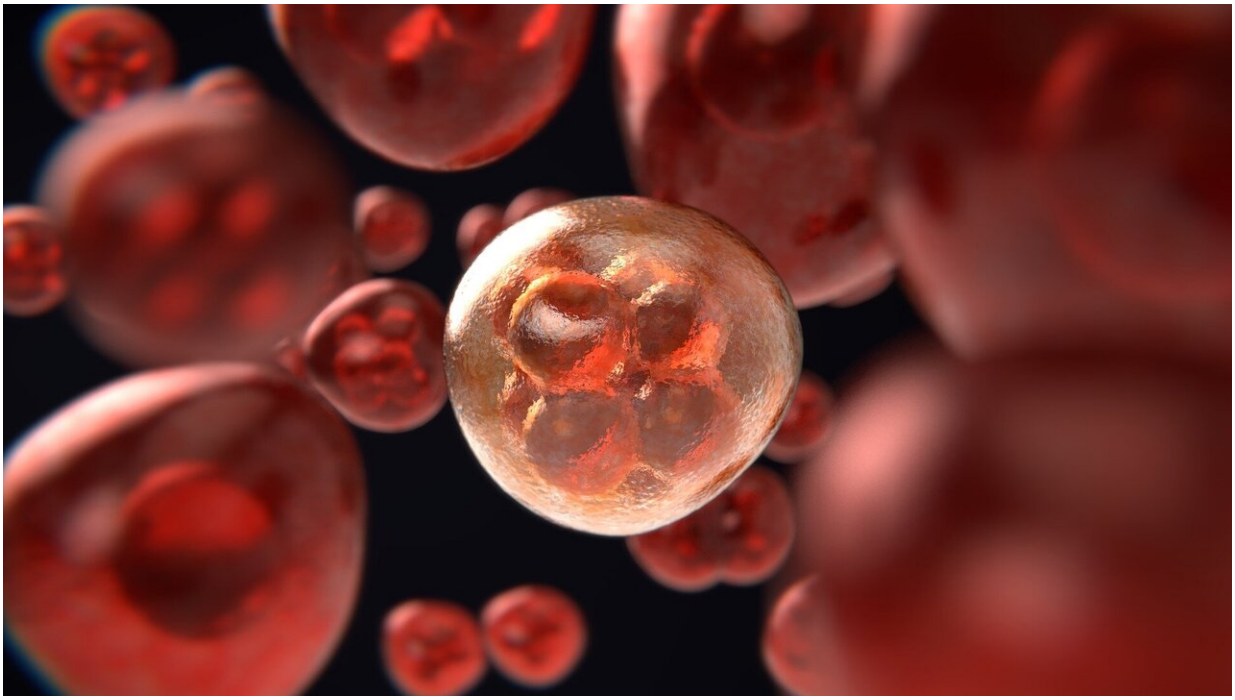
Medical Xpress

Researchers identify biomarkers in blood to predict liver cancer

May 1 2024



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Early detection has the potential to transform treatment and outcomes in cancer care, especially for cancers like liver cancer, which is typically diagnosed at a late stage with limited options for cure. A new study led by investigators from Mass General Brigham and Beth Israel Deaconess Medical Center suggests that proteins detectable in the blood could improve predictions about risk of liver cancer years before typical

diagnosis.

Results are published in *JNCI: Journal of the National Cancer Institute*.

"Liver cancer rates are rapidly increasing, and liver cancer has a high mortality rate, but if we can diagnose it early, therapeutic interventions can be potentially curative," said lead author Xinyuan (Cindy) Zhang, Ph.D., of the Channing Division of Network Medicine at Brigham and Women's Hospital. "We need to have a way to detect this form of cancer early enough to intervene with surgery or liver transplantation to treat the disease before it becomes metastatic."

Liver cancer, or hepatocellular carcinoma (HCC), ranks as the third leading cause of cancer worldwide and the second leading cause of cancer-related deaths globally, with its incidence rate nearly tripled since the 1980s in the US. Detection of liver cancers often occurs at advanced stages, where life expectancy typically spans less than 12 months.

Certain high-risk populations, such as individuals with cirrhosis and hepatitis, stand to benefit from early detection tests significantly. Currently, there is a notable deficiency in accurate, sensitive, and specific tools for the early detection of liver cancer. Many existing methods are relatively expensive, invasive, or limited in accessibility, primarily confined to major hospitals.

The research team included investigators from Mass General Brigham's founding members, Brigham and Women's Hospital and Massachusetts General Hospital, Harvard T.H. Chan School of Public Health, Beth Israel Deaconess Medical Center, and Yale University. The team utilized proteomics (profiling of proteins) to develop a prediction model aimed at diagnosing or screening for liver cancer at an earlier stage.

They used the SomaScan Assay Kit, a high-throughput proteomics

platform that measures protein levels in biological samples, available through the Beth Israel Deaconess Medical Center Genomics, Proteomics, Bioinformatics and Systems Biology Center. The SomaScan platform allowed them to detect minute levels of circulating proteins that may be present at an early stage of the disease, measuring 1,305 proteins simultaneously in the blood.

"It's always been challenging to identify highly specific disease biomarkers in the blood using traditional tools, but this new technology allows us to detect a broad and dynamic range of both high and low abundant proteins," said co-senior author Towia A. Libermann, Ph.D., of the Division of Interdisciplinary Medicine and Biotechnology, Beth Israel Deaconess Medical Center.

"New insights into the biological mechanisms underlying liver cancer development emerge from our data that may lead to the identification of novel therapeutic targets. Most importantly, we were able to validate these early detection biomarkers using alternative protein analysis techniques and in an independent population cohort from the UK."

The study team used SomaScan to analyze plasma samples from participants in both the Nurses' Health Study and the Health Professional Follow-Up Study, two longitudinal, ongoing, prospective cohorts in the U.S. Notably; they examined blood samples obtained from individuals an average of 12 years before their liver cancer diagnosis to pinpoint protein biomarker signals.

After examination, the researchers cross-referenced medical records to confirm whether these patients ultimately developed liver cancer.

From the blood samples, the researchers identified 56 plasma proteins that showed significantly elevated levels in individuals with liver cancer compared to matched control individuals without hepatocellular cancer.

The team selected four of these proteins to create a predictive model, which they tested on the UK Biobank Pharma Proteomics dataset, comprised of 50,000 individuals, 45 of whom were diagnosed with liver cancer.

Their model had greater accuracy in predicting liver cancer compared to traditional risk factors.

The authors caution that their study included a limited number of liver cancer cases, and further validation in larger, more diverse patient populations and in high-risk populations is needed.

"Even though further investigation in additional populations is absolutely needed, our results reveal a robust circulating protein profile associated with liver cancer years before diagnosis, which is remarkable," said co-senior author Xuehong Zhang, MBBS, ScD, who conducted work on this study while at the Channing Division of Network Medicine at the Brigham. Zhang is now at Yale.

The study team also aims to extend their methodology to uncover additional plasma protein biomarkers utilizing the more expanded SomaScan assay measuring 11,000 proteins, explore biomarkers linked with different cancer types, and gain deeper insights into the role of hepatocellular cancer risk factors across specific patient populations.

With further progress, the protein biomarkers investigated in the study could potentially hold clinical significance as a non-invasive test for assessing liver cancer risk.

More information: Xinyuan Zhang et al, Pre-diagnostic plasma proteomics profile for hepatocellular carcinoma, *JNCI: Journal of the*

National Cancer Institute (2024). DOI: 10.1093/jnci/djae079

Provided by Mass General Brigham