Helio Health
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Identifying epigenetic modifications leads to earlier cancer detection

A highly sensitive, multi-analyte blood test from Helio Health points to earlier detection of hepatocellular carcinoma and shows promise for a future of widely accessible cancer detection.

Helio Health, a pioneer in cell-free DNA methylation analysis and artificial intelligence (AI) for cancer detection, is proving that the key to unlocking earlier detection in cancer lies in a simple blood draw. With a proprietary platform to identify epigenetic modifications in blood caused by cancerous cells, the company's flagship product, HelioLiver, has been shown to significantly outperform other modalities in finding early-stage liver cancer.

The test is anticipated to improve liver cancer survival rates by detecting malignancies earlier, when curative treatment is available. In the USA, data suggests that when liver cancer is found early (localized), patients have a 5-year survival rate that is 13-fold higher compared to patients whose cancer is found late (distant)[1]. Early cancer detection can reduce healthcare costs and provide curative options, while advanced cancers require multiple rounds of costly chemotherapy and may be palliative at best.

Advances in AI and sequencing

"For the first time in a very long time, we are seeing a technological revolution in early cancer detection," said Justin Chen Li, CEO of Helio Health. "Sequencing at scale and advanced AI/deep-learning techniques have enabled valuable insights from biomarkers in our blood. Helio has proven this with its first test, HelioLiver, which can detect small-lesion hepatocellular carcinomas (HCC) where traditional imaging tools fall short."

Ultrasound is the standard of care for liver cancer surveillance, yet is widely perceived by physicians as inadequate. Its performance can be variable, depending on the technician operating the equipment and the radiologist interpreting the results. Studies have shown that as few as 20% of patients receive regular surveillance, owing to the cost and inconvenience of imaging[2]. With HelioLiver—a more accessible and reliable option—this number could dramatically increase.

"Ultrasound is only 21% sensitive for very early-stage cancers where lesions are about 2 cm wide. The quality of results is operator-dependent, it doesn't work as well in patients with a high body mass index, and it requires multiple visits," Li said. "That's why we decided to pursue a more sensitive and convenient solution for patients who are at high risk."

HelioLiver is a multi-analyte test that interrogates 77 methylation sites and 3 proteins, delivering superior performance compared to other clinically available tests. The test captures cell-free DNA (cfDNA) floating in the blood and examines its DNA methylation patterns to detect cancer.

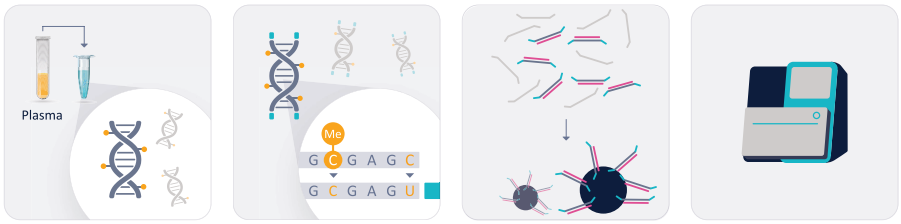

Fig. 1 | Helio Health's ECLIPSE platform. ECLIPSE enables the accurate and efficient detection of cell-free DNA methylation patterns from blood samples and uses next-generation sequencing to identify unique biomarkers that indicate if a cancer is present.

Tests for colon, breast and lung cancer are in Helio's pipeline.

Unlocking insights from the epigenome

Helio has developed the ECLIPSE platform to enable accurate, efficient detection of cfDNA methylation patterns through targeted next-generation sequencing (NGS).

Generally, if the regulatory regions (promoter and enhancer) of a gene are heavily methylated, the gene is turned off or down. If these regions are unmethylated, the gene is turned on or up. Extensive alterations in CpG methylation profiles—sites in the genome where cytosine is adjacent to guanosine—have been noted during malignant transformation and consistently occur in nearly all cases of specific cancer types.

ECLIPSE revolutionizes the cfDNA methylation capture process by combining several innovative approaches and optimizing each step—automated cfDNA extraction, library generation and enzymatic conversion, targeted capture, and NGS—combined with a customized bioinformatics pipeline (Fig. 1). The gentler, enzymatic conversion approach yields a higher quantity and quality of converted DNA compared to traditional bisulfite conversion, which is notoriously known to significantly damage the DNA and signal. The process is further enhanced with CHALM (cellular heterogeneity-adjusted clonal methylation), which identifies methylation patterns more accurately and improves test diagnostic performance compared to standard methods[3].

"When looking at millions of potential biomarkers, both the amount and type of data used for discovery and model development is extremely important to create an accurate and robust diagnostic test," said David Taggart, Helio's CSO. "Not only do we have to find the most predictive markers for a cancer, but we need to train a model that combines all of those markers together in a meaningful way to correctly differentiate patients with cancer from patients without cancer."

"This becomes even more difficult when developing tests to detect cancers within a background of benign, chronic or inflammatory diseases that may also produce distinctive cfDNA methylation patterns. Diagnostic tests that are intended to be used within patient populations with pre-existing diseases must be carefully developed to reduce potential noise or variability from these diseases," he added. "It is very uncommon for diagnostic tests developed for a general, relatively healthy population to have great performance characteristics when applied to high-risk populations with chronic and/or inflammatory diseases. Tests intended for relatively healthy populations often produce many more false positives or false negatives when used in these high-risk populations."

Helio and its partners have analyzed hundreds of thousands of samples through discovery and training, using the newest and most innovative AI and deep learning techniques. Helio's company mission is to apply its superior technology and platform across multiple cancer types, allowing for more cancers to be detected early and cured.

1. National Cancer Institute: Cancer Stat Facts – Liver and Intrahepatic Bile Duct Cancer (2020). https://seer.cancer.gov/statfacts/html/livibd.html
2. Wang, C. et al. *Medicine (Baltimore)* **95**, e4744 (2016).
3. Xu, J. et al. *Nature Commun.* **12**, 400 (2021).

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