血液検査が早期肺がんを検出できる可能性が示された(Abstract LBA8501)

CCGA：血液検体から得たゲノムシークエンシングは、早期および進行期肺がんのいずれも検出するのに成功した

CCGA: Genome sequencing from blood samples successfully identifies both early- and late-stage lung cancer

現在進行中の大規模試験Circulating Cell-Free Genome Atlas (CCGA) により、血液検査が早期肺がんを検出できる可能性があるとの予備的なエビデンスが得られる。このサブ解析で研究者らは、I～IV期肺がんを有する患者127人において、3つの異なるアッセイのがん検出能を調査した。肺がんの生物学的シグナルは、試験したアッセイ全てにおいて同等であった。このシグナルは、がんのステージとともに増加し、偽陽性率が低かった。580のコントロール検体のうち、5例（<1%）は3つ全てのアッセイにおいてがん様シグナルを有していた。これらのうち、2例はその後がんと診断されており、これらの検査が早期がんを検出する可能性を強調している。

Full Text

An initial report from the large, ongoing Circulating Cell-Free Genome Atlas (CCGA) study provides preliminary evidence that a blood test may be able to detect early-stage lung cancer. This is one of the first studies to explore blood tests analyzing free-floating or cell-free DNA as a tool for early detection of cancer.

The findings are featured at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting.

"We're excited that initial results from the CCGA study show it is possible to detect early-stage lung cancer from blood samples using genome sequencing," said lead study author Geoffrey R. Oxnard, MD, Associate Professor of Medicine at Dana-Farber Cancer Institute and Harvard Medical School in Boston, MA. "There is an unmet need globally for early detection tests for lung cancer that can be easily implemented by health care systems."

Survival rates are significantly higher when lung cancer is diagnosed early. Globally, low-dose computed tomography (LDCT) is not widely adopted due to cost and lack of health infrastructure. Having a blood test that can be done through a simple blood draw at the doctor's office may improve lung cancer screening rates, but before such a test could be widely used, additional validation in larger data sets and in studies with people who have not been diagnosed with cancer would be needed.

Analysis of cell-free DNA from blood is already used to help choose targeted therapies (e.g., the cobas EGFR mutation test), but such "liquid biopsies" are used only for people with advanced lung cancer. Until recently there has been limited evidence to show cell-free DNA analysis may be feasible for early detection of lung cancer.

The CCGA study has enrolled more than 12,000 of the planned 15,000 participants (70% with cancer, 30% without cancer), across 141 sites in the United States and Canada. This report is from the first pre-planned sub-study from the CCGA, in which three prototype sequencing assays were performed on blood samples from approximately 1,700 participants. Twenty different cancer types across all stages were included in the sub-study (additional early results from the sub-study, including breast, gastrointestinal, gynecologic, blood and other cancers will be presented separately at the 2018 ASCO Annual Meeting, see abstracts #536 and #12021, and #12003).

In this initial sub-analysis, researchers explored the ability of three different assays to detect cancer in 127 people with stage I-IV lung cancer. The three assays that were designed to detect mutations and other genomic changes that could be used in the development of an early cancer detection test are:

- Targeted sequencing to detect somatic mutations, such as single nucleotide variants and small insertions and/or deletions
- Whole-genome sequencing (WGS) to detect somatic gene copy number changes
- Whole-genome bisulfite sequencing (WGBS) of cfDNA to detect abnormal cfDNA methylation patterns (epigenetic changes)

Among the 127 participants with lung cancer, the biologic signal for lung cancer was comparable across the assays, and the signal increased with cancer stage. At 98% specificity, the WGBS assay detected 41% of early stage (stage I-IIIA) lung cancers and 89% of late-stage (stage IIIB-IV) cancers. The WGS assay was similarly effective, detecting 38% of early-stage cancers and 87% of late-stage cancers, whereas the targeted assay detected 51% of early-stage cancers and 89% of late- stage cancers.

Initial results showed that all three prototype assays could detect lung cancer with a low rate of false positive findings. Of the 580 control samples in the sub-study, five (<1%) had a cancer-like signal across all three assays. Of those five participants, two were subsequently diagnosed with cancer (one with stage III ovarian cancer, and one with stage II endometrial cancer), highlighting the potential for such a test to identify early stage cancers.

The study also found that in the participants with lung cancer, more than 54% of somatic mutations detected in the blood samples were derived from white blood cells and not from tumors. These mutations are likely due to natural aging processes (so-called clonal hematopoiesis of indeterminate potential, or CHIP) and will be important to consider when developing blood tests for early detection of cancer, noted Dr. Oxnard.

"We're one step closer to being able to detect early lung cancer from a simple blood test. While there's still a way to go before cell-free DNA from blood can be used for cancer detection on a broad scale, this research serves as a building block for the development of future tests," said ASCO Expert David Graham, MD, FASCO.

The researchers are verifying these results in an independent group of approximately 1,000 participants from CCGA as part of the same sub-study.

"These are promising early results, and next steps are to further optimize the assays and validate results in a larger group of people," said Dr. Oxnard. With increased sample sizes, machine learning approaches are expected to improve assay performance, he noted.

This study was funded by GRAIL, Inc.

ASCO2018特集