

A step closer to liquid biopsy replacing tissue biopsy

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INTRODUCTION

- Circulating tumor cells (CTCs) are viable tumor-derived cells in circulation, the molecular and functional evaluation of which may be comparable to that of the tumor tissue from which they originate.
- Circulating tumor analytes in blood has received attention for the non-radiological, non-invasive detection of solid organ cancers including lung cancer.
- The entire management of lung cancer hinges on obtaining a confirmatory diagnosis and further cancer subtyping on histopathology, making it difficult to treat individuals who are unable to undergo a biopsy.
- There is currently an unmet need for a non-invasive assay that can aid in the diagnosis and subtyping of lung cancer in difficult-to-biopsy cases.

OBJECTIVES

- We present a unique immunocytochemistry (ICC) based organ-specific and cancer-subtype specific antibody profiling assay of CTCs in individuals with suspected lung cancers (TruBlood™ Lung) for non-invasive diagnosis and histological subtyping and its utility in patients unable to undergo physical biopsies

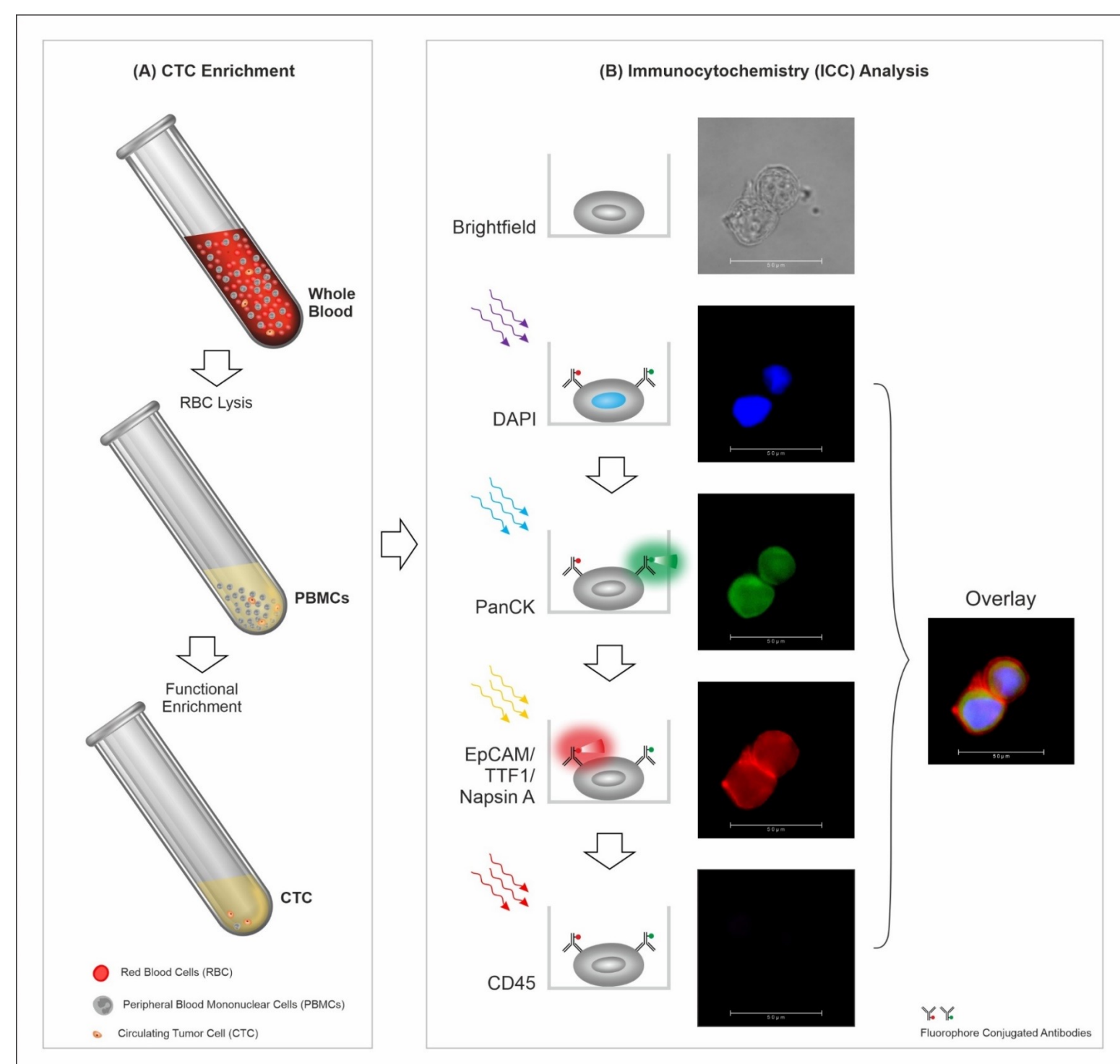
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METHODS

- In a prospective blinded study, blood samples from suspected lung cancer patients (n=99) were profiled for detection of CTCs.
- Along with CK/EPCAM/CD45, organ-specific and cancer subtype-specific antibody profiling with immunocytochemistry (ICC) markers including TTF1, CK7, Napsin A, p40, Synaptophysin, and Chromogranin was performed to detect lung adenocarcinoma, squamous cell carcinoma, and neuroendocrine tumors.
- After unblinding, the performance of the CTC-based assay was compared with the histopathological diagnosis of the corresponding tissue samples

ENRICHMENT AND IMMUNOPROFILING OF LUNG CANCER SPECIFIC CTCs

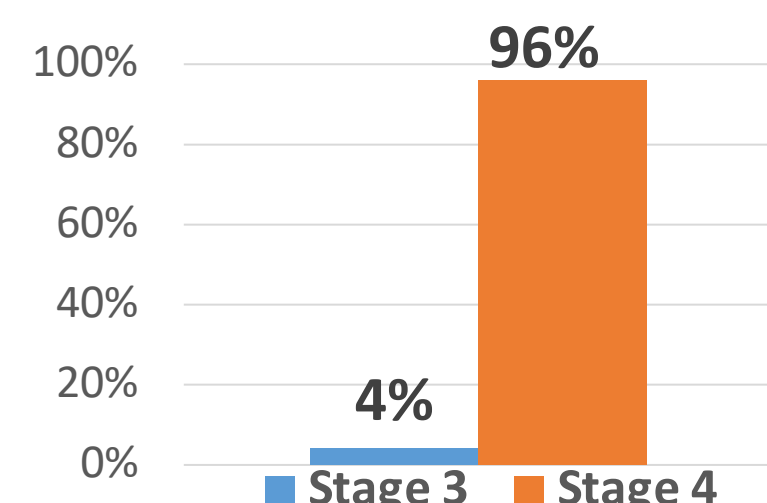


STUDY POPULATION

Median Age and Gender

N=93	Median Age in years (Range)
Overall	58 (22-82)
Males (58%)	59 (22-82)
Females (42%)	56 (28-82)

Distribution by Stage (N=93)

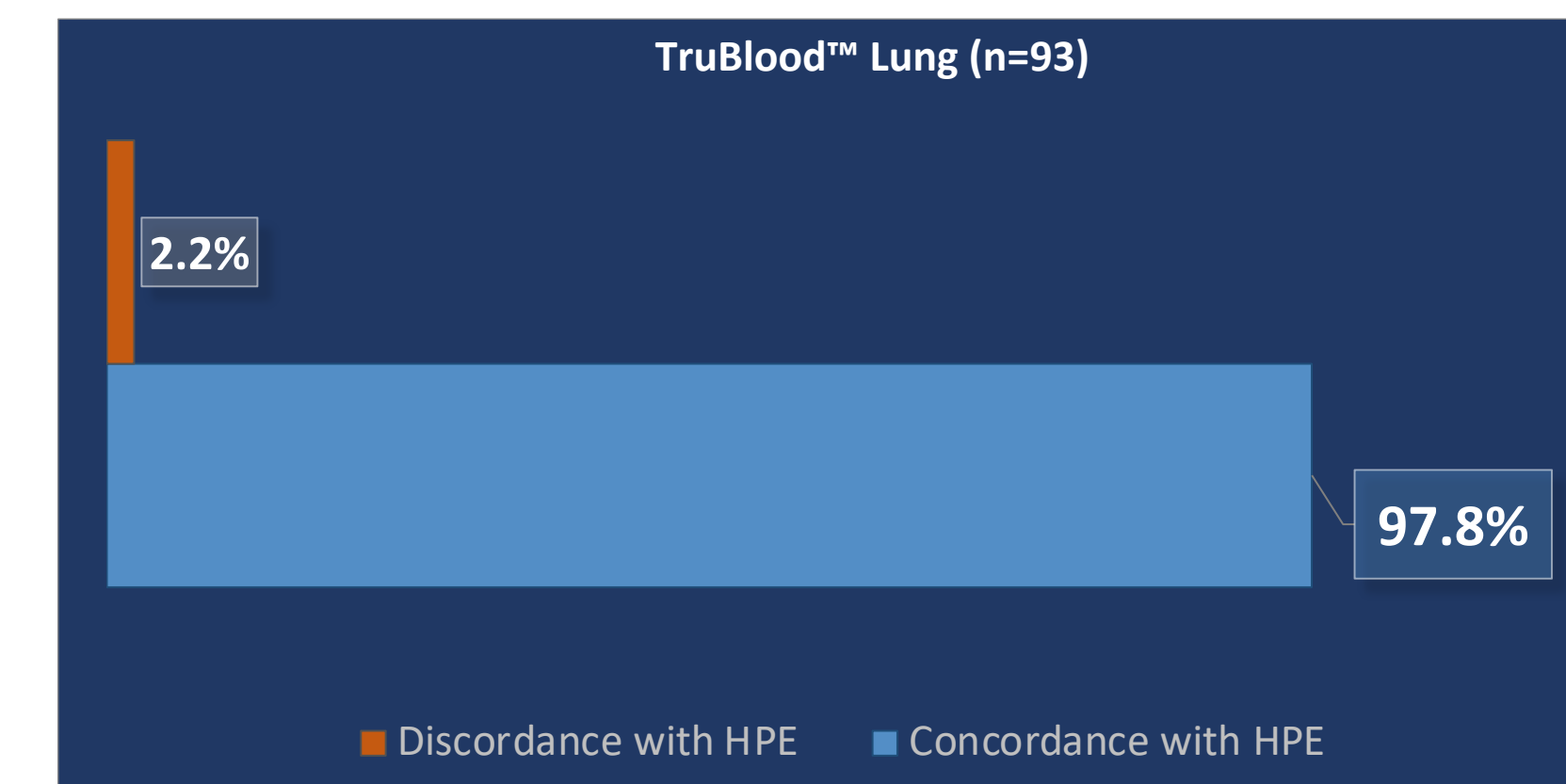


- Functional enrichment of CTCs is achieved using a proprietary CTC enrichment medium (CEM) that eliminates all non-malignant cells and permits tumor-derived malignant cells to survive.
- Multiplexed ICC then evaluates and identifies lung cancer-specific CTCs based on the positivity of the indicated markers.

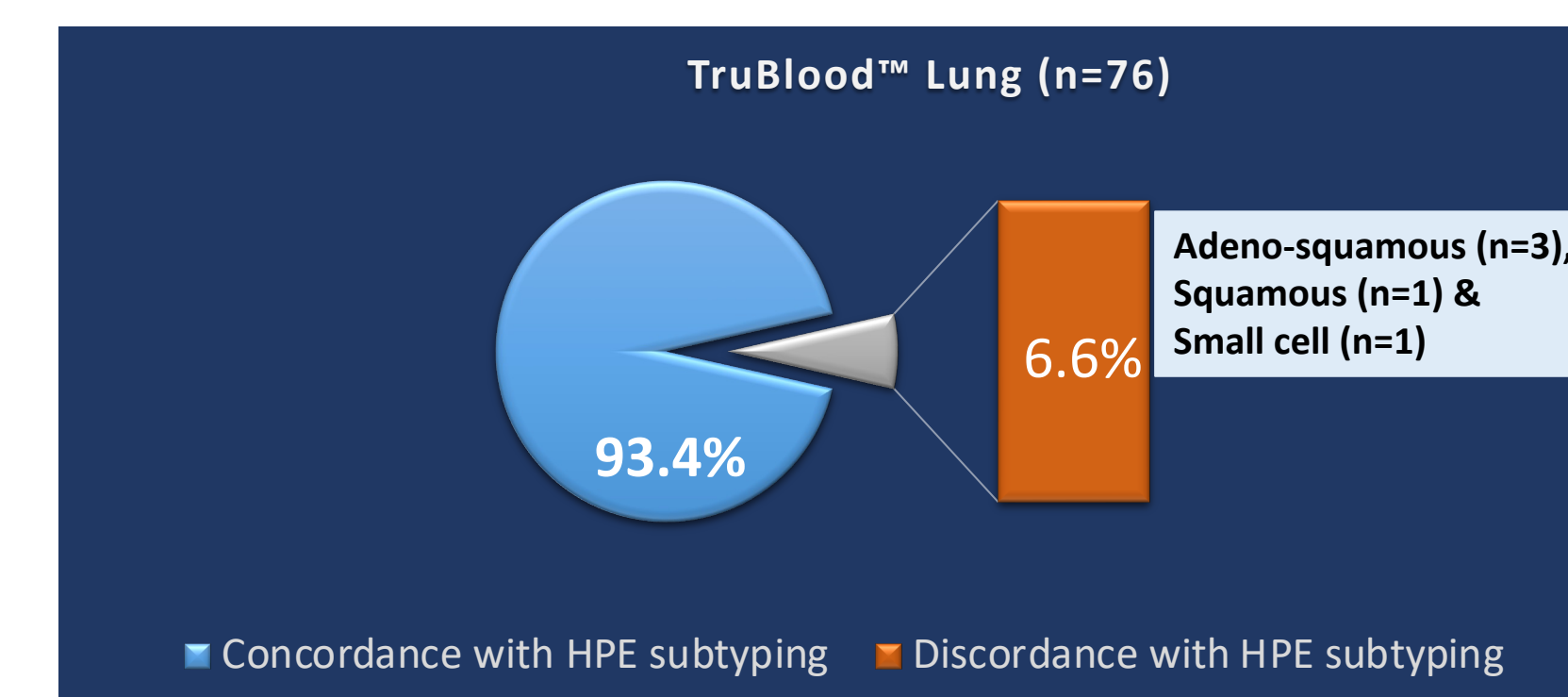
RESULTS

- Concordance analysis could be performed on 93 cases (total evaluable cohort).
- Tissue HPE was inconclusive in 4 patients, and CTC assay could not be performed in 4 patients.
- The concordance rate between cancer diagnosis by CTC assay and HPE was 97.8% (91/93).
- Among cases identified as positive for lung cancer based on CTC assay (n=91), cancer subtyping by histopathological examination (HPE) could be performed in 83.5% (76/91) cases.
- The CTC assay was able to detect cancer, but unable to assign a histological subtype (subtype indeterminate) in 16.4% (15/91) cases.
- Among cases that were able to be subtyped by the CTC assay, the concordance rate with HPE diagnosis was 93.4% (71/76), with concordant subtyping in 76.3% (71/93) of the total evaluable cohort.
- Discordance with histological subtyping was seen in 6.6% (5/76) cases with CTC-based assay failing to identify adeno-squamous (n=3), small cell (n=1), and squamous cell (n=1) carcinoma subtypes.
- Interestingly, in five cases of poorly differentiated carcinoma where conclusive histopathological subtyping was not possible by tissue HPE, the CTC-based assay was able to assign a subtype.

CONCORDANCE OF LUNG CANCER DIAGNOSIS BY TRUBLOOD™ LUNG WITH HISTOPATHOLOGY



CONCORDANCE OF LUNG CANCER SUBTYPING BY TRUBLOOD™ LUNG WITH HISTOPATHOLOGY



CONCLUSIONS

- Our results demonstrate the potential of CTC-based TruBlood™ Lung liquid biopsy to replace tissue biopsy in a diagnostic setting. With further improvement in existing sensitivity to provide concordant HPE subtyping in 76.3% (71/93) and sensitivity of 93.4% (71/76) in histopathological subtyping, this TruBlood™ Lung liquid biopsy can be utilized for diagnostic profiling of lung cancer, especially in patients who are unable to undergo tissue sampling. When coupled with molecular profiling assay, this liquid biopsy assay can potentially provide end-to-end diagnostic and theranostic molecular profiling of lung cancer with a blood sample.