

PUBLICATIONS



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Circulating Ensembles of Tumor Associated Cells are a Hallmark of Lung Cancer and Rare in Healthy Individuals

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ABSTRACT

Background

Screening for Lung Cancer in suspected cases is based on Low-Dose Computed Tomography (LDCT) scans which are neither highly sensitive nor confirmatory, i.e., an invasive biopsy is still necessitated for confirmation of malignancy. We hypothesized that it would be possible to non-invasively and unambiguously ascertain the presence of malignancy in suspected lung cancer cases based on detection of thrombotic clusters (Circulating Ensembles of Tumor Associated Cells, C-ETACs) in peripheral blood.

Methods

15 ml of peripheral blood was collected from 19,741 individuals including 1,198 previously diagnosed cases of Lung Cancer (all stages) and 18,543 healthy individuals with LungRADS category 1 finding on a recent LDCT scan which indicated no evidence of malignancy. Peripheral blood mononuclear cells (PBMCs) were isolated from the blood samples and treated with an epigenetically activated medium which induces cytotoxicity in normal cells (active apoptotic machinery) but confers survival privilege on apoptosis-resistant cells of tumorigenic origin and clusters of such cells (C-ETACs). C-ETACs were identified by immunofluorescent staining (EpCAM, Pan-CK, CD45, Napsin A and TTF-1).

Results

C-ETACs were detected in 1020 / 1198 cases of Lung Cancers (sensitivity = 85.1%). There appeared to be no significant differences in C-ETACs prevalence in sub-populations based on metastatic or prior treatment status. Among the 18,543 healthy individuals with unremarkable LDCT, C-ETACs were detected in 840 individuals (Specificity = 95.5%). These patients were recommended to stay in surveillance and close clinical follow-up.

Conclusions

The present study demonstrates that C-ETACs are a systemic hallmark of cancer since they are frequently encountered in Lung Cancers regardless of stage and treatment status, and at the same time, are rare in healthy individuals with a negative LDCT scan. Detection of C-ETACs is a powerful non-invasive diagnostic tool, since their detection in suspected Lung Cancer cases is an unambiguous evidence of malignancy.