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

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ABSTRACT

Background

Screening and early detection of Breast Cancer is associated with reduced mortality and morbidity. Presently, the most common mode for Breast Cancer Screening in Asymptomatic or Suspected Individuals is Mammography, which is associated with low sensitivity and radiation exposure. Since thromboembolism is common in cancer patients, we hypothesized that detection of thrombotic clusters (Circulating Ensembles of Tumor Associated Cells, C-ETACs) in peripheral blood can non-invasively and unambiguously identify patients with Breast Cancer as well as individuals at risk of Breast Cancer.

Methods

15 ml of peripheral blood was collected from 13,930 females including 3,361 previously diagnosed cases of breast cancer (all stages) and 10,569 females who had no suspicious findings (BIRADS = 1) on a recent Mammography scan. 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 and GCDPF15).

Results

C-ETACs were detected in 3001/3361 cases of Breast Cancers (Sensitivity = 89.3%). There appeared to be no significant differences in C-ETACs prevalence in sub-populations based on metastatic or prior treatment status. Among the 10,569 healthy individuals with unremarkable mammography, C-ETACs were detected in 494 individuals (Specificity = 95.3%). Healthy individuals whose samples were positive for C-ETACs were advised clinical follow-up and surveillance.

Conclusions

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