Cancer associated macrophage-like cells in the early detection of solid tumors from numerous malignancies

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ABSTRACT

Blood-based biopsies can be used as a non-invasive method to recover a variety of cancer associated circulating cells, including Circulating Tumor Cells (CTCs) and Circulating Cancer Associated Macrophage-like cells (CAMLs) from the blood of cancer patients. CAMLs are a newly-defined circulating immune cell type, described as a subtype of circulating stromal cells, known specifically to circulate in patients with malignant disease. We studied the peripheral blood of 100 cancer patients to ascertain the prevalence, specificity and sensitivity of CAMLs in relation to their disease status at presentation. We compared a variety of benign and malignant diseases, along with matched healthy control blood samples. We supply evidence that this previously unidentified circulating cell can be used as a screening tool to detect solid tumors in numerous malignancy subtypes in all disease stages.

MATERIALS & METHODS

Peripheral blood samples from cancer patients were provided by University of Maryland, Greenbaum Cancer Center, Northwestern University, The Medical College of Wisconsin, Fox Chase Cancer Center, and Duke University. We ran a prospective blinded study to isolate CAMLs from patients with known invasive carcinomas (n=117), healthy control samples (n=40) and patients with benign-non-malignant conditions (n=21). The patient distribution included Stage I (n=39), Stage II (32), Stage III (16), Stage IV (20); breast (n=31), pancreatic (n=22), lung (n=38), and prostate (n=26) cancers. CellSieve™ microfilters were used to isolate CTCs and CAMLs from 7.5 mL of whole peripheral blood. The 7 μm pore size of the membrane allows isolation of both CTCs and CAMLs based on size. Collected cells were fixed, permeablized, and stained with DAPI and antibodies against cytokeratin 8, 18, 19, and EpCAM, and CD45. CAMLs were defined as enlarged, multinucleated cells with diffuse cytoplasmic cytokeratin staining; they can be either CD45- or CD45+. CTCs were defined as filamentous cytokeratin cells that are CD45-

RESULTS

CASES were found in 87% patients with confirmed malignant disease.

- CAMLs were found in 77% of stage I, 97% of stage II, 94% of Stage III, and 87% of Stage IV patients, regardless of cancer type.
- CAMLs were found in 77% of prostate, 100% of pancreatic, 82% of lung, and 90% of breast patient samples.
- Neither CAMLs nor CTCs were found in healthy individuals (n=40).
- CTCs were found in 21% of the same patient cohort, averaging 0.9 cells per sample.
- CAMLs have vacuoles containing biomarkers from the primary tumor sites.

CONCLUSIONS

- Highly differentiated myeloid cells transit the blood of cancer patients
- CAMLs can be used as a non-invasive blood based biopsy, to detect the anatomical presence of solid malignancies.
- CAMLs sensitivity and specificity suggests a use as a blood biomarker for early stage cancer screening in a broad population.
- This data suggests that larger validation studies should be done to determine the use of CAMLs as a screening tool for cancer.

Funding Sources

This work was supported by a Maryland (TEDCO) MTCTF award, grant R01-CA154624 from the National Cancer Institute, grant KG100240 from the Susan G. Komen Foundation, and the U.S. Army Research Office (ARO) and the Defense Advanced Research Projects Agency (DARPA) (W911NF-14-C-0098). The content of the information does not necessarily reflect the position or the policy of the US Government.

REFERENCES


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