Cancer Associated Macrophage-Like cells in the blood of cancer patients

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ABSTRACT

Using a “liquid biopsy” for recovering Circulating Tumor Cells (CTCs) has revealed an accompanying circulating macrophage subset that may be a highly sensitive blood based biomarker for solid tumors. This newly discovered cell was defined as circulating cancer associated macrophage-like cell (CAML) and has been identified as a specialized cancer specific blood monocyte (CD14+). We studied the peripheral blood of 100 cancer patients with breast, prostate, pancreatic or lung cancer; stages including I-IV; to study the prevalence of this cell in relation to CTCs. As CTCs and CAMLs appear numerically independent (R2=0.13, p=0.21), we looked to see how both CAMLs and CTCs might be used as blood based biomarkers for tracking malignant disease. Here, we supply evidence that this specialized circulating blood cell can be used in conjunction with CTCs to sequentially track cancer treatment and provide clinical utility in patients with solid tumors using non-invasive sampling techniques.

RESULTS

- CAMLs were found in 96% of patients with Stage III/IV cancer, 88% with Stage I/II and 91% of patients overall, regardless of cancer type.
- CTCs were found in 48% of the total sample set.
- CAMLs were found in 89% (lung), 79% (prostate), 97% (pancreatic), and 97% (breast).
- CAML and CTC number both seemed to correlate with treatment and stage of cancer.

INTRODUCTION

CTCs have been shown to be an indicator of malignant disease, used to monitor therapy response and predict outcomes in late stage patients. However, CTCs are not common in all disease stages and are found in low frequencies in a number of cancers, including lung and prostate.

CAMLs are immunological cells which have been shown to be highly differentiated monocytic cells, classified as circulating cancer associated macrophage-like cells that may be a highly sensitive blood based biomarker for solid tumors. This newly discovered cell was defined as a specialized cancer specific blood monocyte (CD14+). We studied the peripheral blood of 100 cancer patients with breast, prostate, pancreatic or lung cancer; stages including I-IV; to study the prevalence of this cell in relation to CTCs. As CTCs and CAMLs appear numerically independent (R2=0.13, p=0.21), we looked to see how both CAMLs and CTCs might be used as blood based biomarkers for tracking malignant disease. Here, we supply evidence that this specialized circulating blood cell can be used in conjunction with CTCs to sequentially track cancer treatment and provide clinical utility in patients with solid tumors using non-invasive sampling techniques.

CONCLUSIONS

- Highly differentiated monocytic cells, classified as circulating cancer associated macrophage-like cells transit the blood of most cancer patients.
- CAMLs may be used as a liquid biopsy for early detection and sequential tracking of cancer.
- High prevalence of CAMLs implies that complicated and minimally understood cellular interactions exist in the blood.
- CAMLs should be considered when evaluating blood from cancer patients.
- Detection, characterization and monitoring of multiple cellular components present in the blood is an essential element in proper characterization of solid tumors.

MATERIALS & METHODS

Peripheral blood samples from 100 cancer patients were provided by University of Maryland, Greenebaum Cancer Center, Northwestern University, The Medical College of Wisconsin and Fox Chase Cancer Center. The patient distribution included Stage I (n=21), Stage II (29), Stage III (11), Stage IV (n=39); breast (n=31), pancreatic (n=31), lung (n=9), and prostate (n=29) cancers. We included newly diagnosed/untreated patients (n=42) as well as patients undergoing systemic therapies (n=58). The study included 30 healthy subjects. CellSieve™ microfilters were used to isolate CTCs and CAMLs from 7.5 mL of whole blood. Samples were diluted in a pre-fixation solution and filtered through the microfilters. CTCs and CAMLs collected by this size exclusion technique were fixed, permeabilized, and stained with DAPI, an antibody cocktail against cytokeratins 8, 18 & 19 (FITC), EpCAM (PE), and CD45 (Cy5). CAMLs were defined as large, multinuclear cells with diffuse cytoplasmic cytokeratin. CTCs were defined as filamentous cytokeratin cells that were CD45 negative.

REFERENCES