Multiplex phenotyping of circulating cancer associated macrophage-like cells in patients with solid tumors

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ABSTRACT

Cancer associated macrophage-like cells (CAMLs) are a recently identified cancer specific giant cell circulating in the blood of patients with solid tumors. However, since their discovery few studies have been done to elucidate their lineage or phenotypic identity. The difficulty in classifying CAMLS is exemplified by recent publications describing their expression of multiple heterogeneous markers that defy conventional identification. Recently, we described a restaining method (QUAS-R) to screen individual rare cells using an array of up to 15 biomarkers. We used this method to screen CAMLS isolated from 152 cancer patient samples in 4 types of solid tumors to classify CAMLs by phenotypic immunostaining. These data suggest that CAMLS are a morphologically diverse and phenotypically heterogeneous population of cancer specific giant cells with overlapping myeloid, epithelial, and endothelial phenotypes.

INTRODUCTION

CAMLs are specialized myeloid polyloid cells transiting the circulation of patients with various types of solid malignancies and appearing in all stages of cancer1,2. However, while CAMLS are easy to identify by their large size and polyloid nucleus, their expression of multiple heterogeneous markers have defied conventional characterization and have made study difficult using most isolation technologies.

Size exclusion is a technique for isolating large cells from peripheral patient blood irrespective of their 100% surface marker expression. CellSieve™ microfilters are size exclusion membranes which efficiently isolate CAMLS and circulating tumor cells (CTCs) from whole blood, making it possible to study both cell types in conjunction with and in relation to malignant disease1,4.

RESULTS

CAMLs were found in 96% of cancer patients (n=131/152), but in none of the healthy control samples

1 CAMLS were commonly found in stage 1 (71%), stage 2 (94%) and stage 3 (88%) to stage 4 (88%) (Fig. 2).

2 Breast cancer had the most CAMLS per sample (14.1 cells/7.5mL), followed by prostate (6.8), renal cell carcinoma (3.8) and prostate (3.3) (Fig. 2).

3 CD3 was most the prevalent, marker found on 96% of CAMLS, followed by cytokeratin (89%), CD45 (87%), CD41 (78%), CD61 (75%), CD45 (74%), etc. (Figure 2).

CONCLUSIONS

CAMLs express overlapping phenotypes from a variety of lineages i.e. macrophage (CD14/CD68/CD11c), epithelial (cytokeratin/EpCAM), endothelial (CD146/TIE-2) and megakaryocyte (CD41/CD61).

Multi-phenotypic subtyping can identify and subtype CAMLS from cancer patients with multiple solid tumor types.

CAMLs cannot be grouped into any known cell subtype but seem to represent a variably heterogeneous population of myeloid lineage with stem cell like phenotypes.

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References


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