Microfluidic detection of circulating tumor cells from pediatric sarcoma patients

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Background & objectives

Sarcomas are a heterogeneous group of mesenchymal tumors that make up ~10% of childhood cancers. Despite medical advancements, recurrent or metastatic disease remains lethal with a 5-year survival rate as low as 50% for some subtypes. Circulating tumor cells (CTCs) are blood-borne liquid biopsy biomarkers that have gained much attention as a prognostic tool for cancers of epithelial origin. Unfortunately, similar research efforts towards sarcoma CTCs are severely lacking. Our goal is to investigate the effects of cell surface marker selection on sarcoma CTC detection.

Methods

We analyzed 36 blood samples from 23 pediatric sarcoma patients. CTCs were enumerated using the lateral filter array microfluidic (LFAM) device that combined immunoaffinity-based and filtration-based mechanisms. For cell capture, antibodies against sarcoma-specific markers, gangliosides 2 and cell-surface vimentin (CSV), were used. For CTC detection, antibodies against tumor-specific markers – cytokeratins (*CK*), pan-cytokeratins (*panCK*), and *CSV* – were used for immunochemistry staining.

Results

Twenty-five samples from patients with various sarcoma subtypes and disease status were randomly subjected to one of three staining methods for CTC detection: *CK*, *panCK*, or *panCK+CSV*. CTCs were detected in 64% of the samples, with a significant difference in CTC enumeration detected between *CK* and *panCK+CSV*. Samples subjected to *CK* staining were further stratified by disease status. CTCs were detected in 29% of the blood samples from patients with localized sarcoma and in 100% of the blood samples from patients with metastatic sarcoma, with samples from metastatic cancer patients having a significantly higher median CTC value than those from patients with localized disease. The remaining samples in the study were stratified based on the sarcoma subtype. For samples from patients with synovial sarcoma or desmoplastic small round cell tumors, *panCK* detected a significantly higher number of CTCs than the more selective *CK*. For samples from osteosarcoma patients, a similar trend was observed with *panCK+CSV* detecting higher numbers of CTCs than *panCK*.

Conclusion

This study highlights the importance of sarcoma-subtype-based stratification and cell surface marker selection in sarcoma CTC detection. Increased sample sizes are needed to further confirm the results of this study and validate the clinical utility of sarcoma CTCs detection.