

Analysis of circulating cancer-associated fibroblasts and circulating tumor cells in advanced melanoma patients using continuous centrifugal microfluidics technology

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Abstract

Background: Malignant melanoma is one of the cancers with the highest mortality rate despite increasing overall survival due to new therapies. Risk stratification remains challenging, with lactate dehydrogenase (LDH) and S100 being the only clinically established blood-based biomarkers. Circulating tumor cells (CTCs) and circulating cancer-associated fibroblasts (cCAFs) can be found in the blood of cancer patients and may be suitable as prognostic markers in malignant melanoma either alone or in combination with established markers.

Objective: This study aims to evaluate the detection of rare cells as potential prognostic biomarkers in advanced melanoma patients using an automated negative depletion-based continuous centrifugal microfluidics system.

Methods: Blood samples of 22 advanced melanoma patients (AJCC stage III/ IV) enrolled at the University Medical Center Hamburg-Eppendorf were obtained. Six milliliters per blood sample were processed using the CTCceptor, an automated, continuous centrifugal microfluidics system combining density gradient-based enrichment and CD45-based depletion. After enrichment, the cells were stained with DAPI, MART-1, MCAM, α -SMA, and CD45, evaluated, and correlated with clinico-pathological parameters. CTCs were defined as DAPI+, MART-1/MCAM+, CD45- cells and cCAFs as DAPI+, α -SMA+, CD45- cells.

Results: CTCs were detected in 12 out of 22 patients (54.5%), while cCAFs were found in 9 out of 22 patients (40.9%). Out of the positive patients, six patients had both detectable CTCs and cCAFs. Although CTCs were detected in more patients, their average cell count was lower (mean: 5, range: 1-20 cells) compared to cCAFs (mean: 16, range: 1-60 cells). The median progression-free survival (PFS) of cCAF+ patients was 3.7 months, whereas cCAF- patients did not reach the median PFS ($p=0.21$) within the follow-up period. In combination with high LDH or high S100 levels, cCAF positivity was associated with impaired PFS (high LDH: 10.5 months; high S100: 3.3 months; cCAF+/high S100 or cCAF+/high LDH: 2.9 months) and improved risk stratification.

Conclusion: This pilot study provides initial proof-of-principle data indicating that cCAFs could be promising future biomarkers in patients with advanced melanoma.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.