Circulating miRNA compositions in liquid biopsies of melanoma patients as biomarker candidates for progression, PD-L1 status and overall survival

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Background & objectives

Melanoma therapy has been revolutionized by immune checkpoint inhibition (ICI), which has led to tremendous improvement in the survival of patients with metastatic melanoma. However, a significant portion of patients does not respond and shows progress under ICI. Thus, there is an urgent need for clinically applicable biomarkers to monitor patients' capabilities to respond to ICI.

The objective of this study was to investigate the expression patterns of circulating miRNAs in plasma of melanoma patients to characterize the stage, progression under ICI, and PD-L1 status of patients, in order to identify clinically applicable biomarkers for monitoring patients' responses to ICI.

Methods

We used a flow cytometric assay to determine up to 63 circulating miRNAs simultaneously in plasma samples from 155 melanoma patients who were treatment-naïve or treated with different regimes of ICI. We investigated the use of expression patterns of circulating miRNAs in liquid biopsies (plasma) to define classifiers for certain melanoma stages and progression. Furthermore, we investigated PD-L1 status by comparing liquid biopsy melanoma miRNA patterns and histological examination.

Results

We discovered that an 8-miRNA classifier in a liquid biopsy can differentiate between melanoma stages < IV and IV. Additionally, we found that a set of six downregulated miRNAs

indicates a non-response to ICI. In a small cohort, we found that a three-miRNA expression pattern can discriminate between negative, low, and high PD-L1 expression in patients. We also found that low miR-199a-5p expression was negatively correlated with overall survival in Kaplan-Meier analysis and remained significantly changed after adjusting for covariates.

Conclusion

Our study suggests that expression levels of circulating miRNAs of melanoma patients are valuable prognostic biomarker candidates in the context of ICI. These findings have important implications for the clinical management of melanoma patients and the development of personalized treatments based on their specific miRNA expression patterns. The identified biomarkers can help to monitor patients' responses to ICI and provide clinicians with important information to make more informed treatment decisions.