

Unveiling the extracellular vesicles potential for the early detection of resistance to immunotherapy in melanoma patients.

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Abstract

Background. Although immunotherapy has revolutionized the management of melanoma patients, there is an urgent need to find useful biomarkers to follow disease evolution and response to therapy. In this view, extracellular vesicles (EVs) have been emerging as a promising biomarker giving their established role in tumor progression, with specific regard to the critical role in tumor escaping from immune surveillance.

Objective. Melanoma patients were longitudinally monitored, and tumor EV-related PD-L1 levels in plasma investigated for a correlation with response to treatment.

Methods. Twenty stage III unresectable/IV melanoma patients, treated with anti-PD-1, were enrolled and followed for up to 24 months. A longitudinal screening at different timepoints was applied to explore the usefulness of PD-L1-positive melanoma-derived EVs in monitoring patient response. Melanoma EVs were counted and characterized directly from a few microliters of patient plasma, taking advantage of the ExoView platform, an innovative technology that immunocaptures tetraspanins positive EVs and then evaluates the presence of EV surface-specific antigens through a customized cocktail of antibodies (CD146, Mart1, PD-L1).

Results. EVs revealed a size of 55 to 116 nm in diameter for both melanoma patients and a cohort of healthy donors (HD). Nevertheless, a higher number of total EVs was found at the baseline in non-responding (NR) patients when compared to those found in HD and responding (R) patients. The pre-treatment levels of total PD-L1- or melanoma antigen positive EVs were found to be higher in NR than in R patients. Moreover, the pre-treatment levels of tumor-derived PD-L1+ EVs (CD146+, Mart1+) were higher in NR than in R patients.

Conclusions. This pilot study provides proof-of-principle of the possibility to directly analyze EVs in the whole plasma with no need of previous purification, thus avoiding issues related to EV isolation and contamination. Moreover, a specific subpopulation of circulating melanoma EVs was identified, PD-L1 positive, as a possible biomarker for discriminating non-responders from responders.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.