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MDSCs as major inducers of immunosuppression in melanoma

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Abstract

Myeloid-derived suppressor cells (MDSCs) represent a heterogeneous population of myeloid cells enriched and activated in tumor microenvironment under chronic inflammatory conditions. They substantially contribute to immunosuppression in many cancer types including melanoma and represent thereby a valuable therapeutic target. It has been recently demonstrated that such MDSC accumulation in the tumor-bearing host could be mediated not only by a long-term production of soluble inflammatory factors, leading to an impairment of normal differentiation of myeloid cells but also via the acquisition of immunosuppressive properties by mature myeloid cells. This conversion of normal myeloid cells into MDSC could be influenced by extracellular vesicles (EV) secreted by tumor cells that contain a broad range of proteins, mRNA, microRNA and lipids and are considered as mediators of intercellular communication. Furthermore, the EV cargo, including HSP90□, S100A8/A9 and HMGB1 could contribute to this process of MDSC generation. The mechanisms of conversion of mature myeloid cells into MDSC and possible approaches for MDSC targeting in preclinical mouse tumor models and in melanoma patients will be discussed.