

MDSC as a new target for cancer immunotherapy

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Tumor microenvironment is characterized by a strong immunosuppression, where myeloid-derived suppressor cells (MDSC) induced by chronic inflammation play a major role. Using ret transgenic mouse melanoma model, which mimics clinical situation in human melanoma, we demonstrated MDSC accumulation in melanoma lesions that correlated with reduced anti-tumor T cell reactivity and accelerated tumor progression. The accumulation and activation of MDSC could be mediated not only by soluble inflammatory factors but also by tumor-derived extracellular vesicles, converting immature myeloid cells into immunosuppressive MDSC. Targeting of MDSC migration and functions significantly prolonged survival of tumor-bearing mice associated with the restoration of T cell anti-tumor reactivity. In advanced melanoma patients resistant to immunotherapy with immune checkpoint inhibitors, MDSC targeting induced a beneficial therapeutic effect. We suggest that chronic inflammatory mediators and MDSC are of critical importance for melanoma pathogenesis and their neutralization should be included in combined melanoma immunotherapies to increase their efficiency.