Use Of Myeloid-Derived Suppressor Cells As A Targeted And Promising Delivery System For Tumor Immunotherapy

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Abstract

The highly important roles of immune system in cancer development has made immune cells and their related factors as attractive research tools in cancer immunotherapy. One of these cell types includes myeloid-derived suppressor cells (MDSCs), a heterogeneous population of myeloid progenitor cells, i.e., immature granulocytes, macrophages, and dendritic cells (DCs). Two major types of MDSCs are: CD11b+Gr1high (CD11b+Ly6G+Ly6Clow) with a granulocytic phenotype (gMDSC), and CD11b+Gr1low (CD11b+Ly6G-Ly6Chigh) with a monocytic phenotype (mMDSC). In cancer patients, these immature cells, in response to some tumor related cytokines or factors such as GM-CSF or S100, migrate from the bone marrow to primary or metastatic tumors. These tumors block their differentiation to mature cells and instigate them to produce some immunosuppressive cytokines such as IL-6, IL-10, and TGF-β, and some factors such as arginase 1, reactive oxygen species (ROS) and inducible nitric oxide synthetase, that modulate cancer cell killing responses of T cells and natural killer cells in the tumor microenvironment (TME). In tumor-bearing mice, ROS impair DC maturation while sustaining the accumulation of myeloid-derived cells with an immature phenotype, i.e. MDSCs. Due to specifically homing of MDSCs in tumors, in recent studies, MDSCs have been used for specific delivery of curative agents to TME in two approaches: first, as vehicles for delivery of immune cells activator agents, such as bacteria, to tumors; afterwards, this infected tumor cells will become a target for the activated immune cells. In second approach, MDSCs have been used as delivery systems for tumor cytotoxic agents to TME; in case of engineered tumor killing bacteria, injection of bacteria-infected MDSCs into the tail vein of tumor-bearing mice, resulted in selectively delivery of bacteria to metastatic sites, where it could spread from One cell to another without being eliminated by the immune system; however, it was very poorly delivered to normal tissues such as spleen. These observations indicate high capacity of MDSCs to be targeted to various histological types of cancers and highlight the great potential of immune cells that naturally home to the TME for selective delivery of anticancer agents.

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