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Roles and activities of myeloid-derived suppressor cells (MDSC)

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Abstract

The term "myeloid-derived suppressor cells" (MDSC) refers to a diverse community of primarily immature myeloid cells that are pathologically activated and have strong immunosuppressive properties. They are in charge of the immune response in a variety of pathological conditions and are intimately connected to subpar clinical results in the progression of cancer. Depending on the expression of cell surface markers, they are divided into three groups: polymorphonuclear (PMN-MDSC), monocyte (M-MDSC), and early MDSCs. PMN-MDSCs in this group share morphological and phenotype features with neutrophils, while M-MDSCs are characterized by their similarity to monocytes and high plasticity. MDSCs enter the circulation before they complete their maturation, as a result of stimulation of the bone marrow by different growth factors, chemokines, and cytokines, which are caused by inflammation, in anti-tumor immune responses. In this study, we will review the functions and activities of MDSCs.

Introduction

Due to inflammation, many elements of the natural immune system around the tumor exist. These elements are; mast cells, dendritic cells, neutrophils, macrophages, natural killer cells (NK), and MDSCs [1]. They are directly linked to poor clinical outcomes in the development of cancer and are in control of the immune response in a number of pathological conditions [2].

MDSCs are high in humans and mice with different pathological conditions. MDSCs have functions such as potent immunosuppression. They also act as an important negative regulator of immune response in cancer and chronic inflammation [3]. The source of this evil role in cancer disease is the promotion of tumor angiogenesis, drug resistance, immune suppression, and tumor metastases. Tumor metastasis contain the physical migration of cancer cells from the primary tumor to distant organs and the subsequent process of cancer colonization in the organ. Although the ability of MDSCs to create a microenvironment in distant organs before metastasis is often unknown, it has been proven to have an important effect on metastasis formation. They are directly linked to poor clinical outcomes in the development of cancer and are in control of the immune response in a number of pathological disorders [4].

Granulocyte/polymorphonuclear MDSCs (PMN-MDSCs) and monocytic MDSCs (M-MDSCs), which are categorized based on their granulocyte or monocytic myeloid cell lineage, respectively, are the two major groups of MDSCs in humans and mice. Additionally, there are early MDSCs, a small subset of myeloid precursors with characteristics unique to MDSCs in people. This group shows a potent immunosuppressive property. It is more often composed of precursors and myeloid progenitors [5].

The initiation of the development of MDSCs occurs when HSCs in the bone marrow differentiate into CMPs and CMPs into GMPs. This process is controlled by the growth factors G-CSF, SCF, GMCSD, and MCF. GMPs differentiate into myeloblasts (myeloblasts, MB) and macrophage/dendritic cell progenitors (macrophage/dendritic cell progenitors, MDP). With the presence of VEGF, IL-1 β and IL-6, MBs are involved in GMDSC; MDPs differentiate into M-MDSC [6].

Their ability to inhibit immune reactions in reactions with B cells, natural killer (NK) cells,and T cells is the most basic feature that defines MDSCs. PMN-MDSC and M-MDSC, are the basic biochemical features in the suppression of immune responses; They share induction of ER stress, S100A8/A9 expression, an activator of transcription 3 (STAT3) expression, upregulation of arginase 1 expression and signal transducer. Additionally, they possess special qualities that have an impact on their capacity to control various features of immune reactions. For instance, while PMN-MDSCs use prostaglandin E2 (PGE2), reactive oxygen species (ROS), peroxynitrite and arginase 1; M-MDSC uses the expression of immune regulatory molecules such as PDL1 and immunosuppressive cytokines such as TGFβ, nitric oxide and IL-10 [5].

Reactive oxygen species (ROS) production by MDSCs is dependent on oxidase (NOX_2) and nicotinamide adenine nucleotide phosphate (NADPH) activity, which is regulated by the transcription factor STAT3 and greatly enhanced by antigen presentation to T cells. On the contrary, the binding of integrins such as CD29, CD11b, and CD18, tumor-derived factors such as Platellet-derived growth factor (PDGF), TGF-β, IL-10, IL-6, and GM-CSF also increase ROS production [1].

Tumor cell death, IL-13, IL-4, TGF-β, TLR released from activated T cells, and IFN-γ ligands cause MDSCs to be activated for suppression. STAT1 and STAT6 pathways, which act as signal transducers and transcription activators, play a leading role here. Tumor-derived TGF-β acts as a regulator of neutrophil polarization and MDSC accumulation [1].

Results

MDSCs are involved in various processes in the regulation of immunity in autoimmune diseases, infection, and similar diseases, especially in cancer and chronic inflammation [7]. By preventing T and natural killer cell growth and operation, MDSCs also suppress antitumor immunity. Thus, they support the development of tumors by making a significant contribution to immune suppression [8].

Conclusion

MDSCs have reached an important point in tumor immunology today. A better understanding of their biological roles may be possible with the development of methods that selectively target these cells. Additionally, identifying particular markers of these cells is necessary for a better comprehension of the molecular processes underlying the development of these cells [9]. The beneficial effects of altering the biology and function of MDSCs have been observed through preclinical and clinical studies to date. As a result of all these, it is thought that immunotherapeutic strategies such as targeting MDSCs, immune checkpoint inhibition, or strengthening the immune system by means such as vaccination may be promising in the future [10].

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