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Editorial Open Access

M1 and M2 Myeloid Cells in Inflammation

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Editorial

Inflammation is triggered in the innate immune response by tissue myeloid cells, macrophages in peripheral tissue and microglia in the nervous system, in response to microbial or endogenous danger signals [1]. The plasticity of these cells developing into pro-inflammatory M1 and anti-inflammatory M2 phenotypes is remarkable. Polarization of macrophages depends on local environmental factors, especially cytokines and growth factors. Interferon-γ (IFN-γ) and bacterial lipopolysaccharide (LPS) together polarize macrophage into the M1 phenotype which produces reactive oxygen species (ROS), nitric oxide (NO), and inflammatory cytokines such as tumor necrosis factor-α (TNF-α). However, NO appears to play a negative role in M1 macrophage differentiation [2]. M2 polarized phenotypes can be polarized by interleukins 4, 10 or 13 (IL-4 or IL-10 or IL-13) and produce anti-inflammatory molecules such as the autocrine IL-10, and are responsible for tissue remodeling and angiogenesis. M2 cells are also involved in IgE-mediated allergy.

The beneficial biological effects of the M1 phenotype are activation of macrophages to heightened microbicidal activity and the killing of tumor cells. In contrast, adverse effects can be attributed to tissue destruction by ROS, NO and TNF-α in autoimmune inflammation.

The anti-inflammatory effects of the M2 phenotypes are obvious in stimulating tissue repair and inhibiting .the effects of the M1 cells. The adverse effect of these M2 cells is clearly shown in tumor immunology in that the myeloid cells associated with the malignant tissue sites are of the M2 phenotype which enhances angiogenesis. IL-10 activates CD4+ Foxp3+ T regulatory cells (Tregs) [3]. Consequently, Treg cells produce more IL-10 and transforming growth factor β (TGF-β) which block the development of effector T cells, namely CD8+ cytotoxic T cells and CD4+ Th17 cells [4]. Paradoxically, IFN-γ induces expression of Foxp3 by CD4+ Cd25- T cells which then become CD4+Treg cells [5]. In relation to tumor immunity, the M2 phenotypes are referred to as myeloid-derived suppressor cells (MDSC).Yang colleagues [6] demonstrated two subsets of these MDSC (monocytic-M and granulocytic-G) are polarized from the classically activated M1 phenotype. The M2 phenotypes can be repolarized to the M1 phenotype and may represent a potential therapeutic strategy.

The mTOR pathway is involved in macrophage polarization [7]. Nutrient sensing and metabolism are implicated in control of macrophages functions. Byles, et al.cite that differences in metabolism of M1 and M2 macrophages are evident. M1 cells basically use glycolytic metabolism and M2 macrophages rely on the use of fatty acid oxidation.

Phenotypes and functions of not only macrophages but also of dendritic cells and microglia are regulated by suppressor of cytokine signaling (SOCS) proteins [8]. Recent studies have highlighted the importance of M1 macrophages and certain of SOCS proteins in tumor immunology. Benveniste's group used a syngeneic murine model of glioma in which only the myeloid cells were deficient in SOCS3. In this model, decreased infiltration of gliomas by M2 polarized macrophages occurred. This loss of SOCS3 in myeloid cells was associated with an increased infiltration of the tumors by M1 macrophages and CD8+cytotoxic T cells with a concomitant decrease in infiltrating Treg cells [9]. This same group had previously shown that SOCS3 deficiency enhanced M1 polarization and inflammation and conversely, that SOCS3 and M2 polarized macrophages ameliorated neuroinflammation [10]. Up-regulation of SOCS3 expression is suggested as a potential strategy for inhibition of Treg cells to prevent Foxp3 and CTLA-4 expression and resulting immune suppressive functions [11].

Polarized myeloid cell phenotypes and associated SOCS1-SOCS3 proteins play key roles in inflammation as well as in immune regulation.

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