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Macrophage Polarization and TCM Intervention

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Abstract

Macrophages play a critical role in innate immunity. Macrophage polarization initiated by diverse microenvironment mediators leads to different functions. Recent evidences convincingly demonstrate that various events during macrophage polarization are regulated in epigenetic mechanisms. This review showcased the current knowledge on the polarization of macrophage between M1 and M2, may provide potential therapeutic targets to macrophage-related disorders and candidates from TCM that regulate polarization emerged new strategy to treat chronic inflammatory diseases including immune disorder and cancer.

Keywords: Macrophage; Phenotype; Polarization; TCM

Opinion

Macrophages are solely derived from monocytes and can be generated during embryonic development and adult stages [1].

Macrophages are the critical effect cells of innate immunity and display a broad range of plasticity [2-11]. Under the physiological conditions, quiescent or inactivated macrophages (M0) eat out debris and secret nutritious factors. In the case of external challenges such as infection or injury, macrophages are converted to an M1 phenotype in which they release cytokines, chemokines and reactive oxygen species (ROS), conferring macrophages with host defense to clear pathogens. Macrophages can also alternatively convert to M2 phenotype in which they appear to suppress the pro-inflammatory cascades and promote tissue repair. If these processes are not tightly regulated, chronic inflammation can cause tissue damage and often lead to various pathological conditions [12-14]. Especially, the accumulation of M2-like macrophages is closely associated with metastasis and development of cancers [15].

M1 and M2 phenotypes represent two end points of macrophage polarization statuses [16-19]. In fact, M1, M2 and intermediate polarized sub-populations coexist during disease progression. Upon the exposure to the stimulation from the niche, macrophages can undergo dynamic transition between and M1 and M2 in order to adapt the need of tissue homeostasis [20,21]. Once the balance of sub-population is broken, the dominant sub-population will govern the fates of cells and the disease progression. Environmental factors in the pathological conditions have been recognized as key factors regulating macrophage phenotype switch between M1 and M2. For instance, adipose tissue macrophages from obese C-C motif chemokine receptor 2-knockout (Ccr2-KO) mice display M2-like markers including arginase 1 (Arg-1) and IL10. However, high fat diet increases the population of bone marrow-derived macrophage with M1 characteristics [22]. These findings indicate that this metabolic syndrome creates a microenvironment which domesticates macrophages from M2 to M1 status. In case of cancer, tumor-infiltrating macrophages present a classically activated M1 phenotype and exhibit anti-tumor activities at the earliest stage of neoplasia. Along with tumor development, mediators from the tumor microenvironment progressively drive macrophages to tumor-associated macrophages (TAMs) with an M2-like phenotype [23]. Therefore, targeting the molecular mechanisms controlling macrophage polarization and re-education may represent as attractive therapeutic strategies.

Considering the essential role of macrophages in the progression of diverse diseases, it is not surprising that an increasing attention has been exerted on defining their characteristics during recruitment, activation and polarization to help better clinical diagnosis, prognosis and even therapeutic applications.

Because of the diversity and plasticity of macrophages, the classification of M1 and M2 phenotypes can apparently simplify the complex situations reflecting how milieu signals regulate macrophage phenotypes, functional changes and transcriptional profiles. It has to be noticed that not only the polarized sub-populations but also at single cell level, macrophages can switch one phenotype to the other or coexist at different pathological conditions.

Knowledge on macrophage polarization will undoubtedly provide the benefits to manipulate and control the fate of macrophages under particular pathological conditions. Many natural productions from Traditional Chinese Medicine (TCM) showed their function in regulating polarization, which maybe balance the Yin and Yang of macrophage polarization to decide the fate of cell in diseases progress, thus provide the abundant source for us to develop the drugs for inflammation, immune and cancer [24-26] (Figure 1).

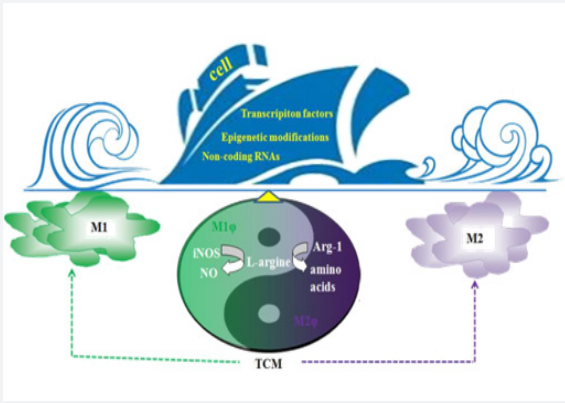

Figure 1

Notes

Author declares no competing financial interest.

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