M2 phenotype

The M2 phenotype refers to a functional state of macrophages or microglia, characterized by an anti-inflammatory, pro-repair, and immunosuppressive role. M2 macrophages are often involved in tissue repair, wound healing, and tumor progression. This contrasts with the M1 phenotype, which is pro-inflammatory and geared toward pathogen destruction and anti-tumor immunity.

Polarization and Activation M2 macrophages are polarized by stimuli such as:

IL-4 and IL-13 (major drivers of M2 activation). IL-10, TGF-β (anti-inflammatory cytokines). Glucocorticoids. Immune complexes. M2 macrophages can be further classified into subtypes based on the activating stimulus:

M2a: Induced by IL-4/IL-13, involved in tissue repair and fibrosis. M2b: Induced by immune complexes, playing a role in immunoregulation. M2c: Induced by IL-10, TGF-β, or glucocorticoids, contributing to immunosuppression and tissue remodeling. M2d: Found in tumors, associated with angiogenesis and immune suppression. Key Functions Tissue Repair and Remodeling:

Secrete growth factors such as VEGF, TGF-β, and EGF to promote angiogenesis and wound healing. Produce matrix remodeling enzymes like matrix metalloproteinases (MMPs). Immunosuppression:

Release IL-10 and TGF-β to suppress inflammatory responses. Recruit regulatory T cells (Tregs) via chemokines such as CCL17 and CCL22. Tumor Progression:

Promote tumor growth by supporting angiogenesis, immune evasion, and metastasis. Create a favorable microenvironment for cancer cells through the secretion of anti-inflammatory and pro-angiogenic molecules. Pathogen Response:

Participate in responses to parasitic infections (e.g., helminths) through mechanisms such as arginase-mediated metabolism. Key Markers of the M2 Phenotype M2 macrophages are characterized by distinct surface markers, cytokines, and metabolic enzymes:

Surface Markers:

CD206 (mannose receptor). CD163 (hemoglobin scavenger receptor). CD204 (scavenger receptor A). Cytokines:

High levels of IL-10 and TGF-β. Low levels of pro-inflammatory cytokines (e.g., TNF-α, IL-6). Enzymes:

Arginase-1 (ARG1): Converts L-arginine into ornithine, promoting repair over nitric oxide production. Chitinase-like proteins: Involved in tissue remodeling. Role in Diseases Cancer:

M2 macrophages, also known as tumor-associated macrophages (TAMs), promote tumor growth, immune evasion, and metastasis. Targeting M2 macrophages is a therapeutic strategy in oncology. Fibrosis:

M2 macrophages contribute to the development of fibrotic diseases by secreting TGF-β, which stimulates fibroblast activation. Chronic Infections:

Parasites such as helminths elicit an M2 response to limit tissue damage but can also promote chronic infection. Neurodegenerative Diseases:

M2 microglia may aid in clearing debris and limiting inflammation but can also support a pro-degeneration environment in chronic conditions. Therapeutic Implications Repolarization Therapies:

Convert M2 macrophages into the pro-inflammatory M1 phenotype for cancer therapy. Target pathways like STAT6, PPARγ, or IL-4/IL-13 signaling. Blocking Recruitment:

Inhibit chemokines like CCL2 to reduce M2 macrophage accumulation in tumors. Enhancing M2 Function:

In diseases requiring repair and anti-inflammatory activity, stimulate M2 macrophages using IL-4 or IL-10.