M2 macrophage

Beyond increasing inflammation and stimulating the immune system, macrophages also play an important anti-inflammatory role and can decrease immune reactions through the release of cytokines. Macrophages that encourage inflammation are called M1 macrophages, whereas those that decrease inflammation and encourage tissue repair are called M2 macrophages.

M2-type macrophages, also known as alternatively activated macrophages, are a type of immune cell that plays an important role in tissue repair, remodeling, and immunoregulation. M2-type macrophages are polarized in response to specific stimuli, such as interleukin-4 (IL-4) or interleukin-13 (IL-13), and are characterized by the expression of specific markers, such as CD206 (mannose receptor), arginase-1 (Arg1), and chitinase-like proteins.

M2-type macrophages are involved in a variety of physiological and pathological processes, including wound healing, tissue regeneration, allergic reactions, and parasite infections. M2-type macrophages promote tissue repair and regeneration by secreting growth factors and extracellular matrix proteins, as well as by phagocytosing apoptotic cells and debris.

M2-type macrophages are also involved in immunoregulation, as they can suppress inflammation and promote tissue tolerance. M2-type macrophages can inhibit the activation of pro-inflammatory immune cells, such as T cells and natural killer cells, and can also secrete anti-inflammatory cytokines, such as IL-10 and transforming growth factor-beta (TGF-β).

The dysregulation of M2-type macrophages has been implicated in the pathogenesis of various diseases, including cancer, fibrosis, and chronic infections. Understanding the molecular mechanisms that regulate M2-type macrophage polarization and function is important for developing new therapies for these diseases.

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exosomes derived from M2-polarized macrophages (M2-Exo) in ischemic stroke have not yet been reported. In this study, we established an in vitro oxygen/glucose deprivation and re-oxygen/glucose (OGD/R) model to investigate the potential role of M2-Exo in protecting HT22 neurons against ischemia-reperfusion injury. Interleukin-4 was used to induce the M2 phenotype in macrophages, following which the exosomes were isolated from the supernatant of M2-polarized macrophages and identified by western blotting, transmission electron microscopy, and nanoparticle tracking analysis. After co-incubation with M2-Exo, OGD/R-induced neuronal injury in HT22 cells was improved, accompanied by increased cell viability and decreased lactate dehydrogenase release. In addition, the increase in the percentage of terminal deoxyribonucleotide transferase-mediated dUTP-digoxigenin nick-end labeling-positive cells in OGD/R-treated HT22 cells was attenuated after incubation with M2-Exo. M2-Exo treatment also suppressed reactive oxygen species and malondialdehyde production and improved the reduction of superoxide dismutase activity. Moreover, M2-Exo treatment was found to activate the nuclear factor erythroid related factor 2 (Nrf2)/heme-oxygenase-1 (HO-1) signaling pathway in OGD/R-treated HT22 neurons. Importantly, inhibition of Nrf2 by ML385 partially reversed the protective effects of M2-Exo against OGD/R-induced oxidative damage. Taken together, these data demonstrated that M2-Exo exerted protective effects against OGD/R-induced oxidative damage in HT22 neurons, which was mediated by the activation of Nrf2/HO-1 signaling. Hence, our findings provide a promising therapeutic approach for ischemic stroke [1)].

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Xiao T, Qu H, Zeng Z, Li C, Wan J. Exosomes from M2-polarized macrophages relieve oxygen/glucose deprivation/normalization-induced neuronal injury by activating the Nrf2/HO-1 signaling. Arch Biochem Biophys. 2022 Mar 20:109193. doi: 10.1016/j.abb.2022.109193. Epub ahead of print. PMID: 35321825.