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Research Article

Pharmacological Inhibition of Gal-3 in Mesenchymal Stem Cells Enhances Their Capacity to Promote Alternative Activation of Macrophages in Dextran Sulphate Sodium-Induced Colitis

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Transplantation of mesenchymal stem cells (MSCs) reduces the severity of dextran sulphate sodium- (DSS-) induced colitis. MSCs are able to secrete Galectin-3 (Gal-3), a protein known to affect proliferation, adhesion, and migration of immune cells. We investigate whether newly synthetized inhibitor of Gal-3 (*Davanat*) will affect production of Gal-3 in MSCs and enhance their potential to attenuate DSS-induced colitis. Pharmacological inhibition of Gal-3 in MSCs enhances their capacity to promote alternative activation of peritoneal macrophages *in vitro* and *in vivo*. Injection of MSCs cultured in the presence of Davanat increased concentration of IL-10 in sera of DSS-treated animals and markedly enhanced presence of alternatively activated and IL-10 producing macrophages in the colons of DSS-treated mice. Pharmacological inhibition of Gal-3 in MSCs significantly attenuates concentration of Gal-3 in sera of DSS-treated animals, indicating that MSCs produce Gal-3 in this disease. In conclusion, our findings indicate that Davanat could be used for improvement of MSC-mediated polarization towards immunosuppressive M2 phenotype of macrophages.

1. Introduction

Ulcerative colitis (UC) and Crohn's disease (CD) are the two major forms of inflammatory bowel disease (IBD) and are characterized by an abnormal cell influx to the intestinal tissues and massive release of proinflammatory mediators [1]. One of the most common IBD-related animal models is the *Dextran Sulphate Sodium-* (*DSS-*) induced colitis, originally reported by Okayasu et al. [2]. The clinical features of the DSS-induced colitis are similar to human colitis and include weight loss, loose stool/diarrhea, and occult and gross rectal bleeding. DSS has a toxic effect on epithelial cells, resulting in invasion of intestinal bacteria into subepithelial tissue. Dendritic cells (DCs) and macrophages capture bacteria that have passed through DSS-injured colonic epithelium, and through activation of Toll-like receptors (TLRs), release proinflammatory cytokines (TNF-α, IL-12) and chemokines (macrophage inflammatory protein- (MIP-) 1α, monocyte chemotactic protein- (MCP-) 1, and keratinocyte-derived chemokine (CXCL1/KC), CCL11) which induce migration of inflammatory cells in the colon [3, 4].