also by secreting immunosuppressive and anti-inflammatory cytokines, thus potentiating the therapeutic efficacy of standard unmodified MSCs.

Summary

In one aspect, the present disclosure provides a DNA expression cassette comprising: a. A promoter; b. A sequence encoding the chemokine receptor type 4 CXCR4; and c. A sequence encoding interleukin IL-10.

In one aspect, the present disclosure provides a recombinant gene delivery integrative vector comprising the expression cassette as disclosed herein.

In one aspect, the present disclosure provides a cell comprising the expression cassette as disclosed herein, or the recombinant gene delivery integrative vector as disclosed herein.

In one aspect, the present disclosure provides a pharmaceutical composition comprising the recombinant gene delivery integrative vector as disclosed herein, or the cell as disclosed herein and, optionally, a pharmaceutically acceptable excipient or carrier.

In one aspect, the present disclosure provides gene delivery integrative vector as disclosed herein, or the cell as disclosed herein for use as medicament.

In one aspect, the present disclosure provides use of the gene delivery integrative vector as disclosed herein, or the cell as disclosed herein, in the manufacture of a medicament for the treatment of inflammatory diseases.

In one aspect, the present disclosure provides use of the gene delivery integrative vector as disclosed herein or the cell as disclosed herein, in the manufacture of a medicament for the treatment of Graft-versus-host disease (GvHD), sepsis, rheumatoid arthritis, or inflammatory bowel disease.

Description of the invention

Brief description of the invention

As explained above, the present invention is focused on improving the therapeutic efficacy of MSCs, particularly by enhancing the migration of MSCs towards inflamed sites and by enhancing the release of immunosuppressive and anti-inflammatory cytokines as compared to standard unmodified MSCs.

In order to do so, the inventors of the present invention have used MSCs which have been transduced with an integrative expression vector co-expressing the chemokine receptor type 4 CXCR4 and the interleukin IL-10.

Particularly, a lentiviral vector encoding for CXCR4 and IL-10 was constructed in the context of the present invention. This expression vector was used for transducing MSCs thus co-expressing in a stable manner both CXCR4 and IL-10.

Example 2.1 shows that MSCs transfected with a CXCR4-IL10 mRNA exert anti-inflammatory properties in a mouse model of local inflammation. Nevertheless, these cells do not show enhanced anti-graft versus host disease (GvHD) properties compared to WT MSCs (**Example 2.2**). In contrast to MSCs transfected with the CXCR4-IL10 mRNA, MSCs that had been transduced with a lentiviral vector carrying the CXCR4-IL10 sequence (**Example 2.3**), not only exerted enhanced *in vitro* immunomodulatory properties (**Examples 2.4** and **2.5**) and local *in vivo* anti-inflammatory effects compared to WT MSCs (**Example 2.3 -2.6**), but strikingly also developed a significant anti GvHD effect, as shown in **Example 2.7** of the present invention.

In fact, the *in vitro* experiments included in the present invention show that the stable co-expression of these molecules efficiently enhanced the migration of MSCs towards SDF-1 and improved the immunosuppressive properties of these cells. Moreover, the preferential homing of MSCs ectopically expressing CXCR4 and IL10 to inflamed pads was demonstrated in a mouse model in which a local pad inflammation was induced. Taken together, these results demonstrate that the stable co-expression of specific homing and anti-inflammatory molecules, such as CXCR4 and IL10, in human MSCs confers an enhanced anti-inflammatory potential in these cells compared to WT MSCs.