IMMUNOSUPPRESSIVE COMPOSITION FOR USE IN TREATING IMMUNOLOGICAL DISORDERS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority of Singapore provisional application No. 10201606949Q, filed 19 August 2016, the contents of it being hereby incorporated by reference in its entirety for all purposes.

FIELD OF THE INVENTION

[0002] The present invention relates generally to the field of molecular biology. In particular, the present invention relates to compositions for the treatment of immunological disorders.

BACKGROUND OF THE INVENTION

[0003] Mesenchymal stromal cell (MSC) therapy has been shown to be effective in, for example, modulating immunological disorders, alloimmune disease (graft versus host disease (GVHD) after allogeneic hematopoietic cell transplantations) and autoimmune diseases systemic lupus erythematosus (SLE), lupus nephritis, type-I diabetes mellitus, systemic sclerosis, inflammatory bowel disease (IBD), Crohn's disease, etc.). However, MSC therapy trials still face challenges regarding unforeseen long-term complications, potential tumorigenicity and uncontrolled differentiation to unwanted cells or tissue types. Also, the use of human mesenchymal stromal cells raises the question of the equivalence of cells isolated from different sources and using different expansion methods.

[0004] Therefore, there is a need for a replacement for mesenchymal stromal cell (MSC) therapy for the treatment of immunological diseases.

SUMMARY

[0005] In one aspect, the present disclosure refers to the use of a pharmaceutical composition comprising CXCL5 (ENA-78) in the manufacture of a medicament for the treatment of an immunological disorder, wherein the immunological disorder is an alloimmune or an autoimmune disease.

[0005a] In another aspect, the present disclosure refers to the use of a pharmaceutical composition comprising at least one antibody and/or at least one mesenchymal stromal cell-derived protein in the manufacture of a medicament for treating an immunological disorder, wherein the antibody targets one or more of the cytokines selected from the group consisting of macrophage colony-stimulating factor (M-CSF), Interleukin-1beta (IL-1β),

CCL-1 (I-309) and CCL24 (Eotaxin-2); wherein the mesenchymal stromal cell-derived protein is selected from the group consisting of PGE2 (prostaglandin E2), OPG, CCL7 (MCP-3), CCL8 (MCP-2), CCL20 (MIP-3α), CXCL5 (ENA-78), IL-10 and CXCL6 (GCP-2), wherein the immunological disorder is an alloimmune or an autoimmune disease, and wherein the pharmaceutical composition is as shown in the table below:

Composition	
C2a	CXCL5; anti-CCL1; anti-IL1b; anti-M-CSF; anti-CCL24
C4a	CCL8; CCL7; OPG; IL-10; CXCL5; anti-CCL1; anti-IL1b; anti-M-CSF
C6a	CCL20; CXCL6; OPG; IL-10; CXCL5; anti-CCL1; anti-CCL24
C8a	CCL20; CXCL6; CCL8; CCL7; CXCL5; anti-CCL1
C10a	PGE2; CXCL6; CCL7; IL-10; CXCL5; anti-IL1b; anti-CCL24
C12a	PGE2; CXCL6; CCL8; OPG; CXCL5; anti-IL1b
C14a	PGE2; CCL20; CCL7; OPG; CXCL5; anti-M-CSF; anti-CCL24
C16a	PGE2; CCL20; CCL8; IL-10; CXCL5; anti-M-CSF
C17a	CXCL5; CXCL6; anti-CCL1; CCL20
C19a	IL-10; OPG; CXCL5; CXCL6
C21a	anti-CCL24; OPG; CXCL5; anti-CCL1
C23a	anti-CCL24; IL-10; CXCL5; CCL20
C27a	CXCL5

C30a	anti-CCL1; CXCL5
C33a	OPG; CXCL5
C35a	anti-CCL1; anti-CCL24; CXCL5
C36a	anti-CCL1; OPG; CXCL5
C37a	anti-CCL24; OPG; CXCL5

[0005b] In another aspect, the present disclosure refers to a pharmaceutical composition comprising at least one antibody and at least one mesenchymal stromal cell-derived protein, wherein the antibody targets one or more of the cytokines selected from the group consisting of macrophage colony-stimulating factor (M-CSF), Interleukin-1beta (IL-1β), CCL-1 (I-309) and CCL24 (Eotaxin-2); wherein the mesenchymal stromal cell-derived protein is selected from the group consisting of PGE2 (prostaglandin E2), OPG, CCL7 (MCP-3), CCL8 (MCP-2), CCL20 (MIP-3α), CXCL5 (ENA-78), IL-10 and CXCL6 (GCP-2), and wherein the pharmaceutical composition is as shown in the table below:

Composition	
C2a	CXCL5; anti-CCL1; anti-IL1b; anti-M-CSF; anti-CCL24
C4a	CCL8; CCL7; OPG; IL-10; CXCL5; anti-CCL1; anti-IL1b; anti-M-CSF
C6a	CCL20; CXCL6; OPG; IL-10; CXCL5; anti-CCL1; anti-CCL24
C8a	CCL20; CXCL6; CCL8; CCL7; CXCL5; anti-CCL1
C10a	PGE2; CXCL6; CCL7; IL-10; CXCL5; anti-IL1b; anti-CCL24

C12a	PGE2; CXCL6; CCL8; OPG; CXCL5; anti-IL1b
C14a	PGE2; CCL20; CCL7; OPG; CXCL5; anti-M-CSF; anti-CCL24
C16a	PGE2; CCL20; CCL8; IL-10; CXCL5; anti-M-CSF
C17a	CXCL5; CXCL6; anti-CCL1; CCL20
C21a	anti-CCL24; OPG; CXCL5; anti-CCL1
C23a	anti-CCL24; IL-10; CXCL5; CCL20
C30a	anti-CCL1; CXCL5
C35a	anti-CCL1; anti-CCL24; CXCL5
C36a	anti-CCL1; OPG; CXCL5
C37a	anti-CCL24; OPG; CXCL5

[0005c] In yet another aspect, the present disclosure refers to use of a pharmaceutical composition as disclosed herein in the manufacture of a medicament for modulating the immune system.

[0005d] In still another aspect, the present disclosure refers to a kit comprising at least one antibody and at least one mesenchymal stromal cell-derived protein as disclosed herein.

[0005e] In one example, the present disclosure refers to a pharmaceutical composition comprising at least one antibody and at least one mesenchymal stromal cell-derived protein, wherein the antibody targets one or more of the cytokines selected from the group consisting of macrophage colony-stimulating factor (M-CSF), Interleukin-1beta (IL-1β), CCL-1 (I-309) and CCL24 (Eotaxin-2); wherein the mesenchymal stromal cell-derived protein is selected from the group consisting of PGE2 (prostaglandin E2), OPG, CCL7 (MCP-2), CCL8 (MCP-3), CCL20 (MIP-3α), CXCL5 (ENA-78), IL-10 and CXCL6 (GCP-2).

Claims

1. Use of a pharmaceutical composition comprising CXCL5 (ENA-78) in the manufacture of a medicament for the treatment of an immunological disorder, wherein the immunological disorder is an alloimmune or an autoimmune disease.

2. Use of a pharmaceutical composition comprising at least one antibody and/or at least one mesenchymal stromal cell-derived protein in the manufacture of a medicament for treating an immunological disorder,
wherein the antibody targets one or more of the cytokines selected from the group consisting of macrophage colony-stimulating factor (M-CSF), Interleukin-1beta (IL-1β), CCL-1 (I-309) and CCL24 (Eotaxin-2);
wherein the mesenchymal stromal cell-derived protein is selected from the group consisting of PGE2 (prostaglandin E2), OPG, CCL7 (MCP-3), CCL8 (MCP-2), CCL20 (MIP-3α), CXCL5 (ENA-78), IL-10 and CXCL6 (GCP-2), wherein the immunological disorder is an alloimmune or an autoimmune disease, and wherein the pharmaceutical composition is as shown in the table below:

Composition	
C2a	CXCL5; anti-CCL1; anti-IL1b; anti-M-CSF; anti-CCL24
C4a	CCL8; CCL7; OPG; IL-10; CXCL5; anti-CCL1; anti-IL1b; anti-M-CSF
C6a	CCL20; CXCL6; OPG; IL-10; CXCL5; anti-CCL1; anti-CCL24
C8a	CCL20; CXCL6; CCL8; CCL7; CXCL5; anti-CCL1
C10a	PGE2; CXCL6; CCL7; IL-10; CXCL5; anti-IL1b; anti-CCL24
C12a	PGE2; CXCL6; CCL8; OPG; CXCL5; anti-IL1b
C14a	PGE2; CCL20; CCL7; OPG; CXCL5; anti-M-CSF; anti-CCL24
C16a	PGE2; CCL20; CCL8; IL-10; CXCL5; anti-M-CSF
C17a	CXCL5; CXCL6; anti-CCL1; CCL20
C19a	IL-10; OPG; CXCL5; CXCL6
C21a	anti-CCL24; OPG; CXCL5; anti-CCL1
C23a	anti-CCL24; IL-10; CXCL5; CCL20

C27a	CXCL5
C30a	anti-CCL1; CXCL5
C33a	OPG; CXCL5
C35a	anti-CCL1; anti-CCL24; CXCL5
C36a	anti-CCL1; OPG; CXCL5
C37a	anti-CCL24; OPG; CXCL5

3. The use according to claim 1 or 2, wherein the alloimmune disease is selected from the group consisting of graft versus host disease (GVHD) after allogeneic hematopoietic cell transplantations, alloimmune disease resulting from skin transplant, alloimmune disease resulting from kidney transplant, alloimmune disease resulting from liver transplant, and hemolytic disease of the foetus and newborn.

4. The use according to claim 1 or 2, wherein the autoimmune disease is selected from the group consisting of systemic lupus erythematosus (SLE), lupus nephritis, type-I diabetes mellitus, systemic sclerosis, rheumatoid arthritis, vasculitis, inflammatory bowel disease (IBD) and Crohn's disease.

5. The use according to claim 1 or 2, wherein the pharmaceutical composition results in a decrease in the concentration of one or more of the circulating pro-inflammatory cytokines selected from the group consisting of IFN-γ, IL-6, IL-17A, IL-8, MIP-1β and MCP-1 in the subject.

6. A pharmaceutical composition comprising at least one antibody and at least one mesenchymal stromal cell-derived protein,
wherein the antibody targets one or more of the cytokines selected from the group consisting of macrophage colony-stimulating factor (M-CSF), Interleukin-1beta (IL-1β), CCL-1 (I-309) and CCL24 (Eotaxin-2); wherein the mesenchymal stromal cell-derived protein is selected from the group consisting of PGE2 (prostaglandin E2), OPG, CCL7 (MCP-3), CCL8 (MCP-2), CCL20 (MIP-3α), CXCL5 (ENA-78), IL-10 and CXCL6 (GCP-2), and wherein the pharmaceutical composition is as shown in the table below:

Composition	
C2a	CXCL5; anti-CCL1; anti-IL1b; anti-M-CSF; anti-CCL24
C4a	CCL8; CCL7; OPG; IL-10; CXCL5; anti-CCL1; anti-IL1b; anti-M-CSF
C6a	CCL20; CXCL6; OPG; IL-10; CXCL5; anti-CCL1; anti-CCL24
C8a	CCL20; CXCL6; CCL8; CCL7; CXCL5; anti-CCL1
C10a	PGE2; CXCL6; CCL7; IL-10; CXCL5; anti-IL1b; anti-CCL24
C12a	PGE2; CXCL6; CCL8; OPG; CXCL5; anti-IL1b
C14a	PGE2; CCL20; CCL7; OPG; CXCL5; anti-M-CSF; anti-CCL24
C16a	PGE2; CCL20; CCL8; IL-10; CXCL5; anti-M-CSF
C17a	CXCL5; CXCL6; anti-CCL1; CCL20
C21a	anti-CCL24; OPG; CXCL5; anti-CCL1
C23a	anti-CCL24; IL-10; CXCL5; CCL20
C30a	anti-CCL1; CXCL5
C35a	anti-CCL1; anti-CCL24; CXCL5
C36a	anti-CCL1; OPG; CXCL5
C37a	anti-CCL24; OPG; CXCL5

7. The pharmaceutical composition of claim 6, wherein the antibody is present in a concentration of 0.05µg/ml to 5µg/ml

8. The pharmaceutical composition of claim 7, wherein the antibody is present in a concentration of 1µg/ml or 2µg/ml.

9. The pharmaceutical composition of any one of claims 6 to 8, wherein the mesenchymal stromal cell-derived protein is present in a concentration of 0.5ng/ml to 75ng/ml.

10. The pharmaceutical composition of claim 9, wherein the mesenchymal stromal cell-derived protein is present in a concentration of about 10ng/ml or 50ng/ml.

11. Use of a pharmaceutical composition according to any one of claims 6 to 10 in the manufacture of a medicament for modulating the immune system.

12. A kit comprising at least one antibody and at least one mesenchymal stromal cell-derived protein as defined in any one of claims 6 to 10.