by CCL5 binding to the CCR5 receptor. The competitive inhibitors to the CCR5 receptor of the present disclosure may or may not have CCL5 agonist activity upon binding to the CCR5 receptor. Preferred competitive inhibitors to the CCR5 receptor of the present disclosure do not have CCL5 agonist activity upon binding to the CCR5 receptor.

In one aspect, the present invention refers to use of PRO 140 or conjugate of PRO 140 in the manufacture of a medicament for treating inflammation associated with a severe acute respiratory syndrome (SARS) infection in a subject in need of CCR5 receptor signaling immunomodulatory intervention, wherein the PRO 140 or conjugate of PRO 140 does not itself have CCL5 agonist activity, wherein the PRO 140 or conjugate of PRO 140 medicament is to be administered to the subject to reduce CCL5 ligand and CCR5 receptor signaling in the subject, and wherein the subject is to be tested to measure immunomodulation triggered by the administration of the PRO 140 or conjugate of PRO 140 medicament.

In another aspect, the present invention refers to use of PRO 140 or conjugate of PRO 140 in the manufacture of a medicament for treating inflammation associated with a severe acute respiratory syndrome (SARS) infection in a subject, wherein the PRO 140 or conjugate of PRO 140 medicament is to be administered to the subject to reduce CCL5 ligand bound to CCR5 receptor activity, wherein the subject is to be tested to measure immunomodulation triggered by the administration of the PRO 140 or conjugate of PRO 140, and wherein the subject is to be monitored to assess the therapeutic effectiveness of the PRO 140 or conjugate of PRO 140.

In a preferred example, the competitive inhibitors to the CCR5 receptor of the present disclosure when bound to the CCR5 receptor do not have detectable CCL5 agonist activity (in terms of decreased cAMP measurements or induced cell migration) and at the same time stymie the effects of CCL5 ligands bound to CCR5 receptors. That is, in an example of the present disclosure, the competitive inhibitors to the CCR5 receptor do not have independent CCL5 agonist activity.

The competitive inhibitors to the CCR5 receptor of the present disclosure may cause therapeutic effect in a dose dependent manner. Accordingly, it is contemplated that the amount of active agent administered to a subject may be adjusted to meet their immunomodulatory needs, whether these are of minor, moderate, or severe nature.

CLAIMS

1. Use of PRO 140 or conjugate of PRO 140 in the manufacture of a medicament for treating inflammation associated with a severe acute respiratory syndrome (SARS) infection in a subject in need of CCR5 receptor signaling immunomodulatory intervention, wherein the PRO 140 or conjugate of PRO 140 does not itself have CCL5 agonist activity, wherein the PRO 140 or conjugate of PRO 140 medicament is to be administered to the subject to reduce CCL5 ligand and CCR5 receptor signaling in the subject, and wherein the subject is to be tested to measure immunomodulation triggered by the administration of the PRO 140 or conjugate of PRO 140 medicament.

2. The use of claim 1, wherein the PRO 140 or conjugate of PRO 140 results in inhibition of CCL5 induced decrease in cAMP levels in the presence of CCL5 ligand in the subject.

3. The use of claim 1, wherein the PRO 140 or conjugate of PRO 140 reduces CCL5 induced cell migration in the presence of CCL5 ligand in the subject.

4. The use of claim 1, wherein the PRO 140 or conjugate of PRO 140 measurably reduces an immunomodulatory downstream effect of the CCL5 ligand bound to CCR5 receptor activity comprising decreased CCL5 induced cAMP levels in CD4+ CCR5 T-cells in the presence of CCL5 ligand in the subject and/or increased CCL5 induced T cell migration in the presence of CCL5 ligand in the subject.

5. The use of claim 1, further comprising that the subject is to be monitored to assess the therapeutic effectiveness of the PRO 140 or conjugate of PRO 140.

6. The use of claim 1, further comprising that a dose amount of the PRO 140 or conjugate of PRO 140 is to be adjusted to achieve down-regulation of CCL5 induced T-cell migration to an inflammatory site in the presence of CCL5 ligand in the subject.

7. The use of claim 1, further comprising that a dose amount of the PRO 140 or conjugate of PRO 140 is to be adjusted to achieve inhibition of CCL5 induced decrease in cAMP levels in CD4+ CCR5 T-cells in the presence of CCL5 ligand in the subject.

8. The use of claim 1, further comprising that an immunomodulatory intervention with maraviroc is to be replaced with PRO 140 or conjugate of PRO 140.

9. The use of claim 1, further comprising that an immunomodulatory intervention with maraviroc is to be supplemented with PRO 140 or conjugate of PRO 140.

10. Use of PRO 140 or conjugate of PRO 140 in the manufacture of a medicament for treating inflammation associated with a severe acute respiratory syndrome (SARS) infection in a subject, wherein the PRO 140 or conjugate of PRO 140 medicament is to be administered to the subject to reduce CCL5 ligand bound to CCR5 receptor activity, wherein the subject is to be tested to measure immunomodulation triggered by the administration of the PRO 140 or conjugate of PRO 140, and wherein the subject is to be monitored to assess the therapeutic effectiveness of the PRO 140 or conjugate of PRO 140.

11. The use of claim 10, wherein the PRO 140 or conjugate of PRO 140 results in inhibition of CCL5 induced decrease in cAMP levels in the presence of CCL5 ligand in the subject.

12. The use of claim 10, wherein the PRO 140 or conjugate of PRO 140 reduces CCL5 induced cell migration in the presence of CCL5 ligand in the subject.

13. The use of claim 10, further comprising that the subject is to be monitored to assess the therapeutic effectiveness of the PRO 140 or conjugate of PRO 140.

14. The use of claim 10, further comprising that a dose amount of the PRO 140 or conjugate of PRO 140 is to be adjusted to achieve down-regulation of CCL5 induced T cell migration to an inflammatory site in the presence of CCL5 ligand in the subject.

15. The use of claim 10, further comprising that a dose amount of the PRO 140 or conjugate of PRO 140 is to be adjusted to achieve inhibition of CCL5 induced decrease in cAMP levels in CD4+ CCR5 T-cells in the presence of CCL5 ligand in the subject.

16. The use of claim 10, further comprising that an immunomodulatory intervention with maraviroc is to be replaced with PRO 140 or conjugate of PRO 140.

17. The use of claim 10, further comprising that an immunomodulatory intervention with maraviroc is to be supplemented with PRO 140 or conjugate of PRO 140.

18. The use of claim 10, further comprising that a second competitive inhibitor to a CCR5 cell receptor is to be administered.

19. The use according to any of the preceding claims, wherein a dose amount comprises PRO 140 at a concentration of 175 mg/mL.

20. The use according to any of the preceding claims, wherein a dose is provided as a subcutaneous dose.