facilitate treatment of diseases or conditions responsive at least partial blocking or inhibition of CD96, such as cancers and/or viral infections.

In one aspect, the present invention refers to use of a CD96-inhibitory agent in the manufacture of a medicament for reducing or relieving immune inhibition in a mammal by at least partly inhibiting or reducing CD96 activity in one or more cells of the mammal to thereby relieve immune inhibition and/or enhance or restore immune surveillance to prevent or treat cancer, cancer metastasis and/or a viral infection in the mammal, wherein at least partly inhibiting or reducing CD96 activity in the mammal does not include, or at least depend upon killing of CD96-expressing cells in the mammal. In one example, there is disclosed use of a CD96-inhibitory agent in the manufacture of a medicament for reducing or relieving immune inhibition in a mammal by at least partly inhibiting or reducing CD96 activity in one or more cells of the mammal to thereby relieve immune inhibition and/or enhance or restore immune surveillance in the mammal, wherein at least partly inhibiting or reducing CD96 activity in the mammal does not include, or at least depend upon killing of CD96-expressing cells in the mammal. In one example, there is disclosed a method of reducing or relieving immune inhibition in a mammal, said method including the step of at least partly inhibiting or reducing CD96 activity in one or more cells of the mammal to thereby relieve immune inhibition and/or enhance or restore immune surveillance in the mammal.

Suitably, the step of inhibiting or reducing CD96 activity in the mammal does not include, or at least depend upon, killing of CD96-expressing cells in the mammal. In some examples, the step of inhibiting or reducing CD96 activity in the mammal includes inhibiting or reducing CD96 binding to CD155 and/or intracellular signaling in one or more cells of the mammal that express CD96. In some examples, the step of inhibiting or reducing CD96 activity in the mammal includes removing and/or down-regulating cell surface expression of CD96.

In one example, the step of inhibiting or reducing CD96 activity in the mammal includes increasing or enhancing expression, production and/or secretion of one or more cytokines or chemokines. Preferably, the cytokine is interferon γ (IFN-γ). Typically, the one or more cells of the mammal are T cells, inclusive of $CD4^+$ and $CD8^+$ T cells, γδT cells, NKT cells, and natural killer (NK) cells.

In another example, the method relieves immune inhibition and/or enhances or restores immune surveillance in the mammal to thereby treat or prevent cancer or cancer metastasis in the mammal.

In other examples, the method relieves immune inhibition and/or enhances or restores immune surveillance in the mammal to thereby treat or prevent a viral infection in the mammal.

In one aspect, the present invention refers to a method of screening, designing, engineering or otherwise producing a CD96-inhibitory agent, said method including the steps of determining that a candidate molecule at least partly inhibits or reduces CD96 activity to thereby relieve immune inhibition and/or enhance or restore immune surveillance in a mammal, wherein the CD96-inhibitory agent binds or interacts with one or a plurality of external immunoglobulin-like domains of CD96 and determining that at least partly inhibiting or reducing CD96 activity in the mammal does not include, or at least depend upon killing of CD96-expressing cells in the mammal. In one example, there is disclosed a method of screening, designing, engineering or otherwise producing a CD96-inhibitory agent, said method including the step of determining whether a candidate molecule is capable of at least partly inhibiting or reducing CD96 activity to thereby relieve immune inhibition and/or enhance or restore immune surveillance in a mammal, wherein the CD96-inhibitory agent binds or interacts with one or a plurality of external immunoglobulin-like domains of CD96 and wherein at least partly inhibiting or reducing CD96 activity in the mammal does not include, or at least depend upon killing of CD96-expressing cells in the mammal. In another example, there is described a method of screening, designing, engineering or otherwise producing a CD96-inhibitory agent, said method including the step of determining whether a candidate molecule is capable of at least partly inhibiting or reducing CD96 activity to thereby relieve immune inhibition and/or enhance or restore immune surveillance in a mammal.

CLAIMS

1. Use of a CD96-inhibitory agent in the manufacture of a medicament for reducing or relieving immune inhibition in a mammal by at least partly inhibiting or reducing CD96 activity in one or more cells of the mammal to thereby relieve immune inhibition and/or enhance or restore immune surveillance to prevent or treat cancer, cancer metastasis and/or a viral infection in the mammal, wherein at least partly inhibiting or reducing CD96 activity in the mammal does not include, or at least depend upon killing of CD96-expressing cells in the mammal.

2. The use of Claim 1, wherein the CD96-inhibitory agent binds or interacts with one or a plurality of external immunoglobulin-like domains of CD96.

3. The use of Claim 2, wherein the CD96-inhibitory agent binds or interacts with: one or a plurality of external immunoglobulin-like domains of CD96 selected from the group consisting of; domain 1; domain 2; domain 3; domain 1 and domain 2; domain 1 and domain 3: domain 2 and domain 3; and domain 1, domain 2 and domain 3.

4. The use of Claim 2 or Claim 3, wherein the CD96-inhibitory agent binds or interacts with one or a plurality of external immunoglobulin-like domains of human CD96 isoform 2 (SEQ ID NO:2).

5. The use of any one or Claims 1-4, wherein the CD96-inhibitory agent at least partly blocks or inhibits CD96 binding to CD 155 and/or intracellular signalling by CD96.

6. The use of Claim 5, wherein the CD96-inhibkory agent is an anti-CD96 antibody or antibody fragment.

7. The use of any preceding claim, wherein the medicament includes one or more other therapeutic agents to be administered.

8. The use of Claim 7, wherein the one or more other therapeutic agents include a chemotherapeutic agent and one or more antibodies or antibody fragments that bind PD1 and/or CTLA4.

9. The use of any preceding claim, wherein the medicament is capable of increasing or enhancing cytokine and/or chemokine expression and/or secretion by one or more cells in the mammal.

10. The use of Claim 9, wherein the cytokine and/or chemokines include MIP-1α, MIP-1β, RANTES, TNF-α and IFN-γ.

11. The use of Claim 10, wherein the cytokine is interferon γ (IFN-γ).

12. The use of Claim 9, Claim 10 or Claim 11, wherein the one or more cells are T cells, inclusive of $CD4^+$ and $CD8^+$ T cells, γδ T cells and NK T cells and natural killer (NK.) cells.

13. The use of any preceding claim, wherein the mammal is a human.

14. A method of screening, designing, engineering or otherwise producing a CD96-inhibitory agent, said method including the steps of determining that a candidate molecule at least partly inhibits or reduces CD96 activity to thereby relieve immune inhibition and/or enhance or restore immune surveillance in a mammal, wherein the CD96-inhibitory agent binds or interacts with one or a plurality of external immunoglobulin-like domains of CD96 and determining that at least partly inhibiting or reducing CD96 activity in the mammal does not include, or at least depend upon killing of CD96-expressing cells in the mammal.

15. The method of Claim 14, wherein the CD96-inhibitory agent binds or interacts with one or a plurality of external immunoglobulin-like domains of CD96 selected from the group consisting of; domain 1; domain 2; domain 3; domain 1 and domain 2; domain 1 and domain 3: domain 2 and domain 3; and domain 1, domain 2 and domain 3.

16. The method of Claim 14 or Claim 15 wherein the CD96-inhibitory agent binds or interacts with one or a plurality of external immunoglobulin-like domains of human CD96 isoform 2 (SEQ ID NO:2).

17. The method of any one of Claims 14-16, wherein the CD96-inhibitory agent is an antibody or antibody fragment.

18. The method of any one of Claims 14-17, wherein the CD96-inhibitory agent is an anti-cancer agent.

19. The method of any one of Claims 14-17, wherein the CD96-inhibitory agent is an anti-viral agent.

20. The method of any one of Claims 14-20, wherein the mammal is a human.