CLAIMS

1. Use of a glucocorticoid in the manufacture of a medicament for producing a population of natural killer T-cell like cells (NKT-like cells), wherein the glucocorticoid is to be administered to a human subject at a dose equivalent to about at least 6 mg/kg human equivalent dose (HED) of dexamethasone base;

wherein the population of NKT cells are characterized in that at least 60, 70, 80, 90, 95, 96, 97, 98, or 99 % of the cells express CD56, TCR gamma/delta, and iTCR; or at least 60, 70, 80, 90, 95, 96, 97, 98, or 99 % of the cells express TCR gamma/delta and iTCR.

2. The use according to claim 1, wherein the population of NKT-like cells are characterized in that at least 60, 70, 80, 90, 95, 96, 97, 98, or 99 % of the cells:

i) express CD56, TCR gamma/delta, iTCR, CD16, NKp44, CD3, CD8, CD14, CD19, CD45, TCR alpha/beta, CD34, and / or ICAM3;

ii) express CD56, TCR gamma/delta, iTCR, CD16, NKp44, CD3, CD8, CD14, CD19, CD45, and / or TCR alpha/beta; and / or

iii) do not express: CD4.

3. The use according to claim 2, wherein the NKT-like cells express CD56, TCR gamma/delta, and iTCR, and:

i) CD16 and NKp44;

(ii) TCR alpha/beta;

(iii) CD16, NKp44, and TCR alpha/beta;

(iv) CD16, NKp44, CD8, CD14, and CD19;

(v) CD16, NKp44, CD3, CD8, CD14, CD19, and CD45; or

(vi) CD16, NKp44, CD3, CD8, CD14, CD19, CD45, and TCR alpha/beta.

4. The use according to claim 2 or 3, wherein the NKT-like cells are:

i) CD3+/dim;

ii) CD8+/dim;

iii) CD3+/dim and CD8+/dim;
optionally, wherein the expression levels are determined relative to the average expression level in a population of reference cells derived from a common source, which have not been contacted with the glucocorticoid-receptor (GR) modulating agent or ICAM3 modulating agent.

5. The use according to any one of claims 1-4, wherein the glucocorticoid is selected from the group consisting of: dexamethasone, hydrocortisone, methylprednisolone, prednisone, prednisolone, prednylidene, cortisone, budesonide, betamethasone, flumethasone and beclomethasone.

6. The use according to claim 5, wherein the glucocorticoid is dexamethasone sodium phosphate.

7. The use according to any one of claims 1-6, wherein the glucocorticoid is to be administered at a dose equivalent to about:

i) at least 6-12 mg/kg human equivalent dose (HED) of dexamethasone base;
ii) at least 6 mg/kg human equivalent dose (HED) of dexamethasone base;
iii) at least 12 mg/kg human equivalent dose (HED) of dexamethasone base;
iv) at least 15 mg/kg human equivalent dose (HED) of dexamethasone base;
v) at least 21 mg/kg human equivalent dose (HED) of dexamethasone base;
vi) at least 24 mg/kg human equivalent dose (HED) of dexamethasone base;
vii) 15 mg/kg human equivalent dose (HED) of dexamethasone base;
viii) 24 mg/kg human equivalent dose (HED) of dexamethasone base; or
ix) 45 mg/kg human equivalent dose (HED) of dexamethasone base.

8. The use according to any one of claims 1-7, wherein:

a) the glucocorticoid is to be administered as a single acute dose, or as a total dose given over about a 72 hour period;

b) one or more further doses of a glucocorticoid is to be administered to the subject; and/or

c) an NKT cell activator, T cell activator, and/or NK cell activator is to be administered to the subject; optionally wherein the NKT cell activator, T cell activator, and/or NK cell activator is to be administered within or around 1 hour after the glucocorticoid has been administered.

9. The use according to any one of claims 1-8, wherein the subject has, is suspected of having, or has been diagnosed with a disease selected from the group consisting of: cancer, autoimmune disease, or infectious disease; and/or the NKT-like cells treat a disease selected from the group consisting of: cancer, autoimmune disease, or infectious disease in the subject.

10. The use according to claim 9, wherein:

a) the cancer is a solid tumour cancer;

b) the cancer is lymphoma, preferably a B cell lymphoma, a T cell lymphoma, or non Hodgkin lymphoma, or a leukaemia, preferably T-ALL or B-ALL;

c) the NKT-like cells treat the cancer *via* tumour infiltration;

d) the NKT-like cells promote infiltration of other immune cells into the tumour;

e) the NKT-like cells directly kill cancer cells *via* CD1d-directed apoptosis; and/or

f) the NKT-like cells treat the cancer by causing tumor necrosis.

11. The use according to claim 9, wherein the autoimmune disease is selected from the group consisting of: multiple sclerosis, systemic sclerosis, amyotrophic lateral sclerosis, type 1 diabetes mellitus (T1D), scleroderma, pemphigus, and lupus.

12. The use according to claim 9, wherein the infectious disease is HIV or a disease resulting from infection with a coronavirus, such as COVID-19.

13. The use according to any one of claims 1-12, wherein a population of NKT-like cells is to be isolated from the subject or from a sample derived from the subject,

optionally wherein the isolation is to be performed:

i) at least 48 hours after the glucocorticoid has been administered; or

ii) between 48 hours and 13 days after the glucocorticoid has been administered.

14. The use of claim 13, wherein:

a) the sample is selected from the group consisting of: blood, plasma, a tumor biopsy or surgically removed tumor, bone marrow, liver, and fat or adipose tissue;

b) the isolated NKT-like cells are expanded;

c) the isolated NKT-like cells are expanded with an NKT cell activator, T cell activator, and / or NK cell activator;

optionally wherein the NKT cell activator is selected from alpha GalCer and sulfatide; optionally wherein the T cell activator is selected from zoledronate and mevastatin; and optionally wherein the NK cell activator is selected from the group consisting of: IL-2, IL-12, IL-15, IL-18, IL-21;

d) a nucleic acid encoding a protein is introduced into the isolated NKT-like cells, and the cells are cultured under conditions that facilitate expression of said protein; optionally wherein the protein is selected from the group consisting of one or more of: a T-cell receptor (TCR), a chimeric antigen receptor (CAR), and a split, universal and programmable CAR (SUPRA-CAR);

e) the NKT-like cells are expanded; and/or

f) the NKT-like cells are activated with an NKT cell activator, T cell activator, and/or NK cell activator.

15. Use of an isolated NKT-like cell in the manufacture of a medicament for treating cancer, autoimmune disease, or infectious disease in a subject, wherein the isolated NKT-like cell is produced as defined in any one of claims 1-14.

16. An isolated NKT-like cell or population of NKT-like cells produced as defined in any one of claims 1-14.

17. An isolated NKT-like cell or population of NKT-like cells, characterized in that the cell or at least 60, 70, 80, 90, 95, 96, 97, 98, or 99 % of the cells expresses CD56, TCR gamma/delta, and iTCR; or the cell or at least 60, 70, 80, 90, 95, 96, 97, 98, or 99 % of the cells express TCR gamma/delta and iTCR, and optionally:

i) express CD56, TCR gamma/delta, iTCR, CD16, NKp44, CD3, CD8, CD14, CD19, CD45, TCR alpha/beta, CD34 and / or ICAM3;

ii) expresses CD16, NKp44, CD3, CD8, CD14, CD19, CD45, and / or TCR alpha/beta; and / or

iii) does not express: CD4

18. The isolated NKT-like cell or population of NKT-like cells according to claim 17, wherein:

(i) the NKT-like cell or population of NKT-like cells or its precursor has not been transfected, transduced, or otherwise modified to express TCR gamma/delta; and/or

(ii) the NKT-like cell or population of NKT-like cells or its precursor has not been transfected, transduced, or otherwise modified to express iTCR .

19. The isolated NKT-like cell or population of NKT-like cells according to claim 17-18, wherein the NKT-like cell or its precursor has not been transfected, transduced, or otherwise modified to express CD56, TCR gamma/delta, iTCR, CD16, NKp44, CD3, CD8, CD14, CD19, CD45, TCR alpha/beta, CD34, and/or ICAM3.

20. Use of a glucocorticoid in the manufacture of a medicament for treatment of cancer, autoimmune disease, or infectious disease in a subject, wherein the glucocorticoid is to be administered to the subject at a dose equivalent to about 6 – 45 mg/kg human equivalent dose (HED) of dexamethasone base,

wherein the glucocorticoid induces a population of NKT-like cells characterized in that at least 60, 70, 80, 90, 95, 96, 97, 98, or 99 % of the cells express CD56, TCR gamma/delta, and iTCR; or at least 60, 70, 80, 90, 95, 96, 97, 98, or 99 % of the cells express TCR gamma/delta and iTCR, and optionally:

i) express CD56, TCR gamma/delta, iTCR, CD16, NKp44, CD3, CD8, CD14, CD19, CD45, TCR alpha/beta, CD34 and / or ICAM3;

ii) express CD16, NKp44, CD3, CD8, CD14, CD19, CD45, and / or TCR alpha/beta; and/or do not express: CD4.